

Human Research Protections Manual

(Including Institutional Review Board procedures)

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See Policy and Procedure/Form Creation or Revision to request changes to this document.

Baylor College of Medicine
Human Research Protections Manual

(Including Institutional Review Board procedures)

This manual details the procedures governing human subjects' research and the requirements for the review and approval of research by the Institutional Review Board (IRB) of Baylor College of Medicine and its affiliated institutions.

This manual was developed by the members and staff of the BCM IRB and approved by the BCM Director of Research Compliance-IRB, the Executive Director of Research Compliance, and the Institutional Official. This manual is reviewed by the BCM Director of Research Compliance-IRB with the contributions of IRB chairs, members, leadership and staff.

For VA regulated research, the specific VA requirements in addition to other federal regulations are noted on each procedure statement. The following are the references for the VA research requirements:

- VHA Handbook 1200.05
- VHA Handbook 1058.01
- VHA Handbook 1605.1

For research where Baylor College of Medicine relies on another IRB, the following are the references for Cooperative Research requirements:

- Code of Federal Regulations 45 CFR 46.114
- National Cancer Institute Central IRB Manual

For additional reference materials and resources, IRB members are always welcome to contact the Office of Research.

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Table of Contents

Chapter 1 Ethical and Regulatory Mandate for Protecting Human Subjects
- Overview
- The Nuremberg Code
- The Declaration of Helsinki
- The Belmont Report
- Department of Health and Human Services Regulations
- Food and Drug Administration Regulations
- Federalwide Assurance
- Implementation of the FWA

Chapter 2 Introduction to the IRB
- Table of Contents
- Overview for Introduction to the IRB

Section A How the IRB Functions
- Overview
- Definitions for Protection of Human Subjects
- Purpose and Mission of the IRB
- Institutional Designation of an IRB
- Requirements for Cooperative Research
- Single IRB (sIRB) Review
- Scope of the IRB's Authority
- Process of Setting up the IRB
- Responsibilities of Administrators
- Oversight of the IRB by the Human Subject Signatory Official
- Protection of the IRB from Undue Influence
- Responsibilities of Investigators and Their Research Staff
- PI and Research Personnel Responsibilities Regarding Research Materials
- Principal Investigators
- IRB Special Relationships

Section B IRB Structure and Membership
- Overview
- Appointment of IRB Members, Length of Service, and Duties
- IRB Chairperson
- Evaluation of IRB Members and Chairpersons
- Alternate IRB Members
- Consultants to the IRB

Section C IRB Administrative Support and Records
- Overview
- Organizational Structure
- Responsibilities of the IRB Administrator and Other IRB Staff
- IRB Record Requirements
- IRB File Requirements
- IRB Materials Submission Deadlines

Continued on next page

Table of Contents, Continued

Chapter 3 IRB Reviews
- Table of Contents
- Overview for IRB Reviews

Section A Initial Review
- Overview
- Determination of Human Subjects Research
- Initial Review for Exemptions
- Exempt Review Category of Research
- Exempt Emergency Use of a Test Article
- Expedited Review of Research
- Categories of Expedited Review of Research

Section B Convened Full Board Review
- Overview
- Conduct of a Convened Meeting
- Primary and Team Reviewer System
- Research Materials
- Conflicts of Interest in IRB Review
- Minutes of an IRB Meeting
- Actions Taken at the IRB Meeting
- How an IRB Determination Is Provided

Section C Criteria for Approval of Research
- Overview
- Approval Criteria
- Risks Are Minimized
- Psychological, Social, Economic, and Legal Harms
- Equitable Selection of Subjects
- Informed Consent of Subjects
- Other Considerations for Informed Consent
- Safety Monitoring
- Independent Verification from Other Sources
- Location of Research

Section D Confidentiality of Data
- Overview
- Protecting the Privacy of Subjects and Confidentiality of Data
- Additional Confidentiality Safeguards
- Confidentiality of Data Sets
- Confidentiality with Data or Tissue Banks
- Research Involving Epidemiology
- Genetic and Family Research
- Research Involving Deception or Withholding of Information

Continued on next page

Table of Contents, Continued

Chapter 3 IRB Reviews, Continued
Section E Reviews After Approval
- Overview
- Initial and Continuing Review by the Convened IRB
- Continuing Review Deadline Issues
- Changes in Previously Approved Research
- Suspension or Termination of IRB Approval
- Event Reporting Required of Principal Investigators
- IRB Review of Event Reports for Determination of (UPIRSO) Unanticipated Problems Involving Risks to Subjects or Others
- Reporting and Assessing Compliance Concerns
- Chain of Reporting

Chapter 4 Requirements of Informed Consent
- Table of Contents
- Overview for Requirements of Informed Consent

Section A What Makes up Informed Consent
- Overview
- Introduction to Informed Consent
- Required Elements and Authorization

Section B Waiver, Alteration, or Exception from Informed Consent Requirements
- Overview
- State or Local Public Benefit Programs
- Waiver or Alteration of Consent for Minimal Risk Research
- Research Involving Deception
- IRB Review of Planned Emergency Research – Exception from Informed Consent
- Waiver of Consent Emergency Research – Guidance and Discussion
- Waiver of Documentation of Consent
- Informed Consent in Language Understandable to Potential Subjects
- Documentation
- Completion of the Documentation

Section C Posting of Clinical Trial Consent Form
- Overview
- Common Rule Requirements
- Guidance of Posting Consent Forms

Continued on next page

Table of Contents, Continued

Chapter 5 IRB Review of FDA-Regulated Research: Investigational Drugs, Devices, and Biologics
- Table of Contents
- Overview for IRB Review of FDA-Regulated Research

Section A: Introduction to Investigational Drugs, Devices, and Biologics
- Overview
- Regulations and Terms
- How the College Manages FDA-Regulated Research
- Investigational New Drugs
- Reporting Responsibilities of Investigators/Sponsors

Section B: Research with Investigational Drugs, Devices, and Biologics
- Overview
- Description of an Investigational Device Study
- How a Device Study Is Reviewed
- Off-Label (Unapproved) Use of FDA-Regulated Products in Medical Practice Versus Research
- PI Responsibilities for Handling Investigational Drugs in Research
- PI Responsibilities for Handling Investigational Devices in Research
- Human Gene Transfer (HGT) Research
- Review of Research Involving HGT

Section C: Expanded Access to Investigational Drugs, Biologics, or Devices for Treatment Use
- Overview
- Expanded Access for Drugs and Biologics (Compassionate Use)
- Expanded Access for Individual Patients, Including for Emergency Use
- Expanded Access for Widespread Use (Treatment INDs)
- Expanded Access for Devices
- Expanded Access for Widespread Use (Treatment IDEs)
- Emergency Use of a Test Article Without IRB Review
- Emergency Use of a Test Article Without Informed Consent

Section D: Special Uses of Drugs, Devices, or Biologics
- Overview
- Humanitarian Device Exemptions
- Exception from Informed Consent for Planned Emergency Research

Continued on next page

Table of Contents, Continued

Chapter 6 Special Research Types
- Table of Contents
- Overview for Special Research Types

Section A: Types of Human Subject Research
- Overview
- Research Types
- Quality Assurance/Quality Improvement Activities as Human Subject Research
- Research Activities vs. Innovative Treatments in Medical Practice
- Research Activities vs. Commercial Services
- Epidemiological Research
- Issues in Genetic Research
- Family History Research
- Research Using Potentially Addictive Substances
- How Research Using Large Existing Data Sets Is Reviewed
- U.S. Department of Defense Research

Section B: IRB Review of Research Involving Children
- Overview
- Risk-Benefit Analysis and Permitted Categories
- Assent of the Child
- Documentation of Assent
- Parental Permission
- Wards
- Children in U.S. Department of Education Research

Section C: IRB Review of Research Involving Adults as Vulnerable Subjects
- Overview
- Special Considerations for Vulnerable Subjects
- Research Involving Pregnant Women, Human Fetuses, and Neonates
- Research Involving Prisoners
- Research Involving Potentially Addictive Substances
- Research Involving Other Potentially Vulnerable Adult Subjects
- Research Involving Human Fetal Tissue Transplantation and Deceased Persons

Frequently Used Terms

Chapter 1
Ethical and Regulatory Mandate for Protecting Human Subjects

Overview

Introduction

Date of Last Revision/Review: 04/20/11

This chapter provides the codes, principles, and regulations that provide the basis for all procedures to be followed for all research involving human subjects.

Requirement

Human subject research associated with Baylor College of Medicine and affiliated institutions must be consistent with the basic ethical principles recognized throughout the world as governing research involving human subjects.

It must also comply with all applicable laws and regulations of the United States, the State, or country in which the research is conducted.

Individuals at BCM involved with human subject research are expected to understand and apply their obligation to protect the rights and welfare of research participants.

Ethical principles

The documents discussed in this chapter represent:

- Important milestones in the evolving world-wide acceptance of ethical principles for the conduct of human subject research and in the development of protections for human research subjects in the United States
- Regulations established to protect human subjects used in research in the United States

In this chapter

This chapter covers the following topics:

- The Nuremberg Code
- The Declaration of Helsinki
- The Belmont Report
- Department of Health and Human Services Regulations
- Food and Drug Administration Regulations
- Federalwide Assurance
- Implementation of the FWA

Related standards

AAHRPP I.1.A, I.1.D

The Nuremberg Code

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides the code developed to protect human subjects from atrocities committed in the past.

Background

The modern history of human subject protections begins with the discovery after World War II of numerous atrocities committed by Nazi doctors in war-related research experiments.

The Nuremberg Military Tribunal developed ten principles, known as *The Nuremberg Code*, to judge the Nazi doctors.

Significance

The significance of the Code is that it addressed the necessity to require the voluntary consent of the human subject and that any individual "who initiates, directs, or engages in the experiment" must bear personal responsibility for the quality of consent.

The code

This table lists a summary of the code:

Step	Action
1	The voluntary consent of the human subject is absolutely essential.
2	The experiment should yield fruitful results for the good of society, unprocurable by other means.
3	The experiment should be designed and based on previous animal experimentation and knowledge of the disease such that anticipated results will justify its performance.
4	The experiment should avoid all unnecessary physical and mental suffering and injury.
5	No experiment should be conducted where there is a priori reason to believe that death or disabling injury will occur.
6	The degree of risk should never exceed the humanitarian importance of the problem.
7	The subject should be protected against even remote possibilities of injury, disability, or death.
8	The experiment should be conducted only by scientifically qualified persons.
9	The human subject should be at liberty to end his/her participation in an experiment if the subject has reached the physical or mental state where continuation of the experiment seems to the subject to be impossible.
10	The scientist in charge must be prepared to terminate the experiment if there is probable cause to believe that continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

The Declaration of Helsinki

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides the principles used to maintain ongoing research through reviews.

Call for approval and monitoring

The *World Medical Association Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects* (1964, revised 1975, 1983, 1989, 1996, 2000) calls for prior approval and ongoing monitoring of research by independent ethical review committees.

General principles

The general principles of the *Declaration of Helsinki* follow:

- Research involving human subjects includes research on identifiable human material or identifiable data.
- Considerations related to the well-being of the subject should take precedence over the interests of science and society.
- Even the best medical methods must be challenged continuously through research on effectiveness, efficiency, accessibility, and quality.
- Vulnerable research populations need special protection, particularly economically and medically disadvantaged persons and those who:
  – Cannot consent for themselves
  – May be subject to duress
  – Have no potential of benefiting personally from the research
  – For whom the research is combined with care

Medical research principles

These principles apply to all medical research:

No.	Description
1	The life, health, privacy, confidentiality, physical integrity, mental integrity, and dignity of the human subject must be protected.
2	Caution must be exercised in research which may affect the environment, and the welfare of animals used for research must be respected.
3	Research must conform to scientific principles, be formulated in an experimental protocol that is publicly available, and be submitted for ethical review independent of the investigator or sponsor.
4	Research should be preceded by assessment of predictable risks, burdens, and benefits, and should be conducted only if its importance outweighs the inherent risks and burdens to the subject.
5	Any investigation should cease if risks are found to outweigh potential benefits or if there is conclusive proof of beneficial results.
6	Research is only justified if there is a reasonable likelihood that the populations in which the research is conducted stand to benefit from it.

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The Declaration of Helsinki, Continued

Medical research principles (cont)

These principles apply to all medical research (continued):

No.	Description
7	Research subjects must be volunteers informed about the research aims, methods, funding sources, possible conflicts of interest, institutional affiliations, anticipated benefits, potential risks and discomforts, and the right to abstain or withdraw without reprisal. If written consent cannot be obtained, non-written consent must be formally documented and witnessed.
8	If the subject is in a dependent relationship with the physician or may be under duress, informed consent should be obtained from a qualified research team member who is not engaged in the investigation and is completely independent of this relationship.
9	Informed consent must be obtained from a legally authorized representative if the subject is a minor or is physically or mentally unable to consent. Assent of the subject must also be obtained. These groups should be included only if the research promotes the health of the population they represent and cannot otherwise be carried out.
10	Research should be done on individuals from whom it is not possible to obtain consent only if the condition preventing consent is a necessary characteristic of the research population. Consent to remain in the research should be obtained from the individual or legally authorized surrogate as soon as possible.
11	Authors and publishers have an obligation to publish only research that in accord with the Declaration of Helsinki's ethical principles.

Additional principles

Additional Principles for Research Combined with Medical Care follow:

- The benefits, risks, burdens, and effectiveness of a new method should be tested against the best current methods.
- At the conclusion of the study, every subject should be assured of access to the best methods identified by the study.
- Patients should be fully informed about which aspects of the care are related to the research.
- Where proven methods do not exist or have been ineffective in treating a patient, and with the patient's informed consent, the physician may use unproven measures believed to offer hope of saving life, re-establishing health, or alleviating suffering.

Related standards

AAHRPP I.1.D

The Belmont Report

Requirement

Date of Last Revision/Review: 04/20/11

Baylor College of Medicine and its affiliates are guided in its human subject research by the ethical principles set forth in the *Belmont Report*. All IRB members and IRB support staff should be thoroughly familiar with these most basic ethical principles.

Background

Revelations about the 40-year United States Public Health Service Syphilis Study at Tuskegee and other ethically questionable research resulted in legislation in 1974, calling for the following:

- Regulations to protect human subjects
- A National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research to examine ethical issues related to human subject research

Purpose

The Commission's final and most influential report, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (79 FR 12065, April 17, 1979), defines the ethical principles and guidelines for the protection of human subjects.

Principles

Perhaps the most important contribution of *The Belmont Report* is its elucidation of three basic ethical principles:

Principle	Action for Protection
Respect for Persons	Obtaining informed consent
Beneficence	Weighing risks and benefits
Justice	Selecting subjects fairly

Summary

This table summarizes the application of these principles in research:

Principle	Application in Research
Respect for Persons • Autonomy • Protection	Informed Consent • Information • Comprehension • Voluntariness
Beneficence • Do No Harm • Maximize Benefit/Minimize Harm	Risks versus Potential Benefits • Systematic Assessment • Independent Reviewers
Justice • Individual Justice • Social Justice	Equitable Selection of Subjects • Individual Fairness • Social Fairness

Other guidance

The *Belmont Report* also provides important guidance regarding the boundaries between biomedical research and the practice of medicine.

Related standards

AAHRPP I.1.D

Department of Health and Human Services Regulations

Introduction

Date of Last Revision/Review: 01/28/19

This topic provides the regulations from the Department of Health and Human Services (DHHS) that affect protection of human subjects in research.

Requirement

Baylor College of Medicine and its affiliates meet the requirements set forth in 45 CFR Part 46 for all human subjects research without regard to source of funding or support.

Common Rule

DHHS regulations constitute the Federal Policy (Common Rule) for the protection of human subjects.

Reference: 45 CFR Part 46 Subpart A

Applicability

This Common Rule applies to any human subject research supported by any of the 17 agencies of the federal government that support human subject research.

Additional protections

The DHHS human subject protections regulations also include additional protections for the following:

- Pregnant women (Subpart B)
- Human fetuses and neonates (Subpart B)
- Prisoners (Subpart C)
- Children (Subpart D)

Registration of Institutional Review Boards

Each IRB that is designated by an institution under an assurance of compliance approved for federalwide use by the Office for Human Research Protections (OHRP) under §46.103(a) and that reviews research involving human subjects conducted or supported by the Department of Health and Human Services (HHS) must be registered with HHS. An individual authorized to act on behalf of the institution or organization operating the IRB must submit the registration information 45 CFR 46 Subpart E.

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Department of Health and Human Services Regulations, Continued

Departments and agencies

This table lists the 17 federal departments and agencies to which the Common Rule applies:

Department / Agency	CFR Citation
Department of Agriculture	7 CFR Part 1c
Department of Energy	10 CFR Part 745
National Aeronautics and Space Administration	14 CFR Part 1230
Department of Commerce	15 CFR Part 27
Consumer Product Safety Commission	16 CFR Part 1028
International Development Cooperation Agency, Agency for International Development	22 CFR Part 225
Department of Housing and Urban Development	24 CFR Part 60
Department of Justice	28 CFR Part 46
Department of Defense	32 CFR Part 219
Department of Education	34 CFR Part 97
Department of Veterans Affairs	38 CFR Part 16
Environmental Protection Agency	40 CFR Part 26
Department of Health and Human Services	45 CFR Part 46
National Science Foundation	45 CFR Part 690
Department of Transportation	49 CFR Part 11
Central Intelligence Agency	Executive Order
Social Security Administration	Authorizing Statute

Enforcement

The DHHS Office for Human Research Protections (OHRP) and the relevant Federal Department or Agency enforces these regulations.

Related standards

AAHRPP I.1.D

Food and Drug Administration Regulations

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides the Food and Drug Administration (FDA) regulations that affect protection of human subjects in research.

Requirement

IRB review and approval is required for all clinical investigations and all other research involving products regulated by the FDA for human use, even where an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) is not required.

Reference: See Chapter 5 of this manual for details of FDA requirements.

Products

In general, FDA human subject regulations apply to clinical investigations and other research involving products regulated by FDA, including:

- Food and color additives
- Drugs for human use
- Medical devices for human use
- Biological products for human use
- Electronic products

Regulations

The FDA has codified these regulations that are almost identical to the DHHS regulations:

Topic	CFR Citation
General regulations	
Informed consent	21 CFR Part 50
IRB	21 CFR Part 56
Child protection	• 61 FR 20589 • 21 CFR Part 50, Subpart D
Protection of human subjects	
Investigational New Drug Applications	21 CFR Part 312
Biological Products	21 CFR Part 600
Investigational Device Exemptions	21 CFR Part 812

Federalwide Assurance

Introduction	Date of Last Revision/Review: 01/28/19 This topic provides a discussion and description of the Federalwide Assurance.
Purpose	Through the Federalwide Assurance (FWA) and the Terms of the FWA, the College commits to HHS that it will comply with the requirements in the HHS Protection of Human Subjects regulations at 45 CFR, Part 46. The Federalwide Assurance is the only type of assurance currently accepted and approved by the OHRP
IRB designation	One requirement of the FWA is to designate the Institutional Review Board (IRB) or Institutional Review Boards (IRBs) officially recognized and designated to review the College's research.
Institutional components	The College must identify all of its legal components that operate under different names that will be covered by the FWA. Legal components are generally defined as parts of an institution that may be viewed as separate organizations, but remain part of the legal entity or institution. Baylor College of Medicine does not have any components identified and named on its FWA.
Purpose	The Federalwide Assurance (FWA) authorizes the College to conduct human subject research that is supported by DHHS or any of the other Federal Common Rule agencies.
IRB component	One component of the FWA designates the Institutional Review Board (IRB) or Institutional Review Boards (IRBs) officially recognized and designated to review the College's research.
Regulations requirement	The Federal regulations require that the College conducting human subject research: • Devise mechanisms for the protection of human subjects • File a written Assurance of protection for human subjects • Designate one or more Institutional Review Boards (IRBs) to review its human subject research ***Reference***: Federal regulations at 45 CFR Part 46
Related standards	AAHRPP I.1.D

Implementation of the FWA

Introduction

Date of Last Revision/Review: 01/13/21

This topic discusses how the College has implemented the FWA.

Operational requirements, and use of FWA number

No component of an Institution may operate an IRB without authorization from the designated Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP).

Every Institutional component, of an Institution's FWA must have the following to operate or designate an IRB:

- Concurrence of an institution's Institutional Official who serves as the Human Subject Signatory Official under the Institutional FWA for Protection of Human Subjects, and
- Institutional compliance oversight

All Institutional components are covered under an Institution's FWA and are authorized to cite an Institution's FWA number in communicating with Federal agencies.

***Note*:** Baylor College of Medicine does not have any Institutional Components identified and named on its FWA.

Designated IRBs

The College currently operates and has designated six internal IRBs and several external independent IRBs to accommodate the volume of its human subject research under its Federalwide Assurance (FWA) of Protection for Human Subjects approved by the DHHS Office for Human Research Protections (OHRP).

Under its FWA, the College may designate additional internal or external IRBs as it deems necessary. Designation of an external IRB requires a written agreement (authorization agreement) between BCM and the external IRB.

The agreement should determine at a minimum:

- Whether the relying organization applies its FWA to some or all research, and ensures the IRB review is consistent with requirements in the relying organization's FWA
- Which organization is responsible for obtaining any additional approvals from DHHS when the research involves pregnant women, fetuses, neonates, children, or prisoners

The designated IRBs are registered and listed in the College's OHRP-approved FWA.

What it covers

The FWA covers all human subject research conducted:

- By any employee or agent of Baylor College of Medicine
- In any component of the College (if applicable)

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Implementation of the FWA, Continued

Who it affects	Any investigator is bound by the College's human subject protection policies and requirements when s/he either: • Acts as an employee or agent of the College or any Institutional component (if applicable) • Conducts research within any College facility or with College equipment or resources
Human Subject Signatory Official	The College's Institutional Official serves as the Human Subject Signatory Official for the College's FWA.
Filing responsibility	The designated Human Subject Signatory Official is responsible for filing the Institutional Assurance and registering the IRBs of the College.
Related standards	AAHRPP I.1.A, I.1.D

Chapter 2
Introduction to the IRB

Table of Contents

Overview for Introduction to the IRB
Section A How the IRB Functions
Overview
Definitions for Protection of Human Subjects
Purpose and Mission of the IRB
Institutional Designation of an IRB
Requirements for Cooperative Research
Single IRB (sIRB) Review
Scope of the IRB's Authority
Process of Setting up the IRB
Responsibilities of Administrators
Oversight of the IRB by the Human Subject Signatory Official
Protection of the IRB from Undue Influence
Responsibilities of Investigators and Their Research Staff
PI and Research Personnel Responsibilities Regarding Research Materials
Principal Investigators
IRB Special Relationships
Section B IRB Structure and Membership
Overview
Appointment of IRB Members, Length of Service, and Duties
IRB Chairperson
Evaluation of IRB Members and Chairpersons
Alternate IRB Members
Consultants to the IRB
Section C IRB Administrative Support and Records
Overview
Organizational Structure
Responsibilities of the IRB Administrator and Other IRB Staff
IRB Record Requirements
IRB File Requirements
IRB Materials Submission Deadlines

Overview for Introduction to the IRB

Introduction	Date of Last Revision/Review: 12/17/15 The College's policies and procedures for implementing the requirements for protecting human subjects are provided in this and subsequent chapters of this manual.
Requirement	No component of the College may operate an IRB without authorization from the designated Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP). The College's IRB must comply with the requirements of all relevant regulatory agencies, including the DHHS Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA).
College responsibilities	The College responsibilities follow: • To assure Federal Research Oversight agencies in writing that the College complies with all federal laws and regulations governing the protection of human research subjects • To develop policies and procedures for conducting human subject research in a responsible and ethical fashion as part of its written Assurance to the government
Shared responsibility	The ethical conduct of research is a shared responsibility. It requires cooperation, collaboration, and trust among: • All Institutional components and administrators • Investigators and their research staff • The subjects who enroll in research • The IRB ***Note*:** For information regarding coordination between other Offices, Committees, and Affiliate institutions, please see IRB Special Relationships.
Communications to investigators and the research community	Investigators and other members of the research community are kept informed of changes to BCM's Human Research Protections policies and procedures. Notifications are conducted using College approved methods of notification, such as LISTSERV notices, presentations, and town hall meetings.
In this chapter	This chapter covers these sections: • Section A: How the IRB Functions • Section B: IRB Structure and Membership • Section C: IRB Administrative Support and Records
Related standards	AAHRPP I.1.D

Section A
How the IRB Functions

Overview

Introduction

Date of Last Revision/Review: 12/16/19

This section focuses on a description of the IRB, including the terms used for protection of human subjects and responsibilities of those who support the IRB.

In this section

This section covers the following topics:

- Definitions for Protection of Human Subjects
- Purpose and Mission of the IRB
- Institutional Designation of an IRB
- Requirements for Cooperative Research
- Single IRB (sIRB) Review
- Scope of the IRB's Authority
- Process of Setting up the IRB
- Responsibilities of Administrators
- Oversight of the IRB by the Human Subject Signatory Official
- Protection of the IRB from Undue Influence
- Responsibilities of Investigators and Their Research Staff
- PI and Research Personnel Responsibilities Regarding Research Materials
- Principal Investigators
- IRB Special Relationships

Related standards

AAHRPP I.1.A, I.1.D

Definitions for Protection of Human Subjects

Introduction

Date of Last Revision/Review: 01/28/19

This topic provides the definitions needed to understand the protection of human subjects.

Definitions

These definitions apply to the protection of human subjects:

Term	Definition
Agent	Any Baylor College of Medicine faculty member or employee
Principal investigator	Any Baylor College of Medicine faculty member. ***Explanation**:* Baylor requires that only Baylor faculty may be principal investigators of clinical research protocols.
Co-investigator	May be staff, trainees, employees of the college, or other institutions. Co-investigators may be active participants on the research protocol but may not be principal investigators.
Institutional Review Board (IRB)	A review body established by regulation to protect the welfare of human subjects recruited to participate in research. An institutional review board established in accord with and for the purposes expressed in this policy, 45 CFR 46.102(g). ***Reference***: See Chapter 3, IRB Reviews, for details of IRB authorities and responsibilities.
Research	**Under the Federal Policy and the DHHS Subpart A** 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 45 CFR 46.102(ld). For example, some demonstration and service programs may include research activities. **Under FDA regulations** Synonymous with clinical investigation 21 CFR 56.102(c) **For the VA:** • Research is defined as: – The testing of concepts by the scientific method of formulating an hypothesis or research question – Systematically collecting and recording relevant data – Interpreting the results in terms of the hypothesis or question • The Common Rule (38 CFR 16) defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. The FDA definition of research differs according to the applicable regulations. See 21 CFR 812.3(h), 21 CFR 50.3(c), 21 CFR 56.102(c), and 21 CFR 312.3(b).

Continued on next page

Definitions for Protection of Human Subjects, Continued

Definitions (cont)

These definitions apply to the protection of human subjects (continued):

Term	Definition
Systematic investigation	An activity that involves a prospective research plan which incorporates data collection, either quantitative or qualitative, and data analysis to answer a research question.
Generalizable knowledge	Knowledge from which broader conclusions will be drawn (i.e., knowledge that may be applied to populations outside of the specific study population). A study that is designed and intended to draw conclusions, inform policy, or generate findings that can be applied to a broader population than that of the research study sample. It is intended to add to existing scientific literature from which others may infer relevance to policy, a body of scientific evidence.
Human subject/ human participant	An individual who is the object of study in a research project **Federal Policy (Common Rule)** *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains: • Information or biospecimens through intervention or interaction with the individual and uses, studies, or analyzes the information or biospecimens, or; • Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens 45 CFR 46.102(e)(1) **FDA regulations** *Human subject* means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient 21 CFR 50.3(g) and 56.102(e).
Human subjects research	Activities that meet either the DHHS or FDA definitions of both research and human subjects/participants are considered research involving human subjects and are subject to: • Federal regulations, and • Policies and procedures of the College's human research protection program.
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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record)

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Definitions for Protection of Human Subjects, Continued

Definitions (cont)

These definitions apply to the protection of human subjects (continued):

Term	Definition
Identifiable	The identity of the individual subject that is or may readily be ascertained by the investigator or associated with the information ***Reference***: From DHHS regulations
Minimal risk	The probability and magnitude of harm or discomfort anticipated in the research which are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests ***Reference***: From Federal regulations at 45 CFR 46.102(i), 21 CFR 50.3(k), and 56.102(j)
Minimal risk for prisoners	The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives or in the routine medical, dental, or psychological examination of healthy persons when research involves prisoners ***Reference***: From Federal regulations at 45 CFR 46.303(d)

Related standards AAHRPP I.1.A, I.1.D

Purpose and Mission of the IRB

Introduction	Date of Last Revision/Review: 04/20/11 This topic describes the purpose and mission of the IRB, including a focus on their reviews and compliance requirements.
Purpose	The purpose of the IRB is to protect the rights and welfare of participants involved in human subject research.
Compliance	The IRB monitors human subject research to determine that it is conducted ethically and in compliance with the following for protecting human subjects: • Applicable Federal regulations • Applicable State and foreign nation laws • The College's Assurance • Institutional policies and procedures
Reviews	The IRB fulfills these responsibilities by conducting prospective and continuing review of human subject research, including review of: • The protocol and grant applications or proposals • The informed consent process • Procedures used to enroll subjects • Any adverse events or unanticipated problems reported to the IRB
Prospective review	Prospective review and approval of research or changes to previously approved research ensures that research is not initiated without IRB review and approval.
Communications to investigators	In communications to investigators, the IRB makes investigators aware of the requirement to submit protocol changes to the IRB for review and approval before initiation of such changes except where necessary to eliminate apparent immediate hazards to the subject.
Related standards	AAHRPP I.1.A, I.1.B, I.1.D

Institutional Designation of an IRB

Introduction

Date of Last Revision/Review: 09/05/25

Baylor College of Medicine may enter into agreements to rely on a qualified external IRB for the review of some human research studies.

This procedure describes how BCM may utilize external IRB review processes and fulfill its responsibilities for research when relying upon external IRBs. For questions regarding external IRBs, contact reliance@bcm.edu.

Federal regulations

Once approved by the department or agency head, an institution participating in a cooperative project may:

- Enter into a joint review arrangement
- Rely upon the review of another qualified external IRB, or
- Make similar arrangements for avoiding duplication of effort

Reference: 45 CFR 46.114

BCM's reliance on an external IRB

Below is the standard operating procedure BCM uses for designating an external IRB review:

- The Institutional Official (IO) decides with which external IRBs BCM establishes reliance agreements
- The BCM Human Protections Administrator designates a contact person to review protocols on a case-by-case basis for the applicability of the IRB designation criteria
- The BCM Human Protections Administrator designee notifies the BCM Principal Investigator (PI) in writing if BCM agrees to rely on review by an external IRB
- Each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with Federal policy
- A written agreement will detail the operating procedures for BCM and the external IRB
- BCM requires all industry sponsored and funded research protocols to be submitted to a commercial IRB. See Submission Process for a list of commercial IRBs on which BCM PIs may rely.

Requirements for Cooperative Research

Introduction

Date of Last Revision/Review: 01/13/21

Cooperative research projects are those projects covered that involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects

Requirement

The new common rule regulations at 45 CFR Part 46.114 require that any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The requirement for single IRB review does not apply to organizations outside of the United States.

The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

Exceptions

The following research is not subject to this provision:

- Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or
- Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.

For research not subject to this policy, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

NIH-funded projects

On January 25, 2018, all domestic sites participating in NIH-funded multi-site research studies were required to use a single IRB (sIRB) rather than obtaining local IRB approval from each individual site. This applies to all competing grant applications (new, renewal, revision or resubmission) received on or after January 25, 2018.

This requirement is applicable to sites conducting the same non-exempt human subjects research protocols supported through:

- NIH grants
- Cooperative agreements
- Contracts
- The NIH Intramural Research Program

The requirement does not apply to NIH career development, research training, or fellowship awards.

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Requirements for Cooperative Research, Continued

Regulations and guidance	• DHHS: 45 CFR 46.103(b)(2), 45 CFR 46.103(d), 45CFR 46.109(d), 45 CFR 46.114, • FDA: 21 CFR 56.109(e), 21 CFR 56.114, FDA Information Sheet: Non-Local IRB Review, and Information Sheet: Cooperative Research • Single IRB Use for Multi-Site Research • sIRB FAQs
Related standards	AAHRPP I.9

Single IRB (sIRB) Review

Introduction

Date of Last Revision/Review: 01/13/21

The use of a single IRB of record for multi-site studies where each site will conduct the same protocol will help streamline the IRB review process and remove redundant hurdles to the initiation of such studies.

The intent of this is to allow research to proceed as effectively and expeditiously as possible. Eliminating duplicative IRB review is expected to reduce unnecessary administrative burdens and systemic inefficiencies while maintaining appropriate human subjects protections.

Reference sIRB FAQs

Definition

Authorization agreements, also called reliance agreements, document respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

Determination process

For the review of cooperative research, an institution is either serving as an sIRB or relying on an sIRB for the review of the research study.

There are a couple of factors that may determine which IRB serves as the sIRB for a research study:

- Federally funded studies where the institution is the prime awardee. In most cases, when an institution is the prime awardee for a grant, that institution tends to serve as the sIRB for the research study
- When an institution is the coordinating center for a study, that institution sometimes serves as the sIRB for the research study
- It is important to note that whatever the circumstance may be, in order to be compliant, all institutions participating in a multisite research study must agree to rely on the sIRB selected to conduct IRB review for the study.

Organizational responsibilities

Organizations have the following responsibilities:

- Awardee organizations ensure that authorization agreements are in place and that documentation is maintained
- The reviewing IRB must meet the requirements of the NIH Genomic Data Sharing Policy
- Participating sites are expected to rely on the single IRB, though they may conduct their own review in accordance with NIH policy on exceptions from single IRB review

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Single IRB (sIRB) Review, Continued

BCM sIRB review process

See the tables below for a description of how research is handled when BCM is the prime awardee or subawardee of funding and either:

- BCM is the sIRB of record (central IRB), or
- An external IRB is serving as the sIRB of record

When BCM is the sIRB of Record (Central IRB)
BCM needs the following from the participating sites: • Each site that will participate in the research will enter into a reliance (or authorization) agreement with BCM. BCM will only rely on or accept reciprocal IRB review from the listed IRBs. If there is not a current reliance agreement or reciprocity agreement in place, BCM's preferred reliance agreement process should be used. To confirm if there is a current reliance agreement in place, please review the current list on the reliance website • Each sub-site participating in the research must provide the BCM PI with a Local Context Information Sheet that solicits site-specific information, including: – Site name – Description – Location – FWA number – Name and contact information of the responsible institutional officials at the Site – A primary contact person – Confirmation of conflicts of interest policies – Information about the local research context at that particular site • The BCM PI collects the local context sheets and provides them to the BCM IRB during the review process.
How a protocol is reviewed by BCM IRB as the sIRB of record Upon receipt of the protocol submission in BRAIN containing the Local Context Information Sheets from all participating sites, the BCM IRB will formally review the protocol, the consent form(s), and any other required documentation. Depending on the proposed protocol activities, the protocol will either be reviewed: • By the IRB via an expedited review process, or • At a convened IRB meeting
How approved documents are disseminated The BCM PI is responsible for notifying participating site PIs of the BCM IRB decision and disseminating approved materials, including protocol and consent form(s), to all participating sites.

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Single IRB (sIRB) Review, Continued

When BCM is the sIRB of Record (Central IRB) continued
How the renewal process works The BCM PI will notify each participating site with respect to the information required for continuing review, which includes any updated information regarding the local research context. The BCM PI will incorporate this information into the renewal submission to the BCM IRB. Depending on the proposed protocol activities, the protocol will either be reviewed: • By the BCM IRB via an expedited review process, or • At a convened IRB meeting The BCM PI is responsible for notifying participating site PIs of the BCM IRB decision and disseminating approved materials, including protocol and consent form(s), to all participating sites.
How amendments are reviewed and processed The BCM PI will submit all protocol amendments that apply to all participating sites and all site-specific amendments to the BCM IRB for review. The BCM IRB will not be responsible for the review of changes in participating site research personnel, except for changes in a PI. The BCM PI is responsible for notifying participating site PIs of the BCM IRB decision and disseminating approved materials, including protocol and consent form(s), to all participating sites.
How conflicts of interest are managed Any COIs relating to the protocol will be determined and managed in accordance with BCM's Financial Interests in Research manual.
How HIPAA requirements are handled The BCM IRB will serve as the HIPAA Privacy Board for the purpose of granting full waivers, partial waivers or alterations of authorization as appropriate for each participating site. Participating sites remain responsible for accounting of disclosures pursuant to such waivers or alterations.

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Single IRB (sIRB) Review, Continued

When BCM is the sIRB of Record (Central IRB) continued
How reportable events are handled Investigators must conduct reporting according to BCM's policies on Event Reporting Required of Principal Investigators. The participating site PIs are responsible for notifying the BCM PI of any event meeting the reporting requirements of the BCM IRB. The BCM PI will be responsible for submitting a report to the BCM IRB on behalf of any participating site PI who reports such events. The BCM IRB will review reportable events according to its policies. The BCM PI is responsible for notifying participating site PIs of the BCM IRB decision to all participating sites.

When an External IRB is Serving as the sIRB of Record
BCM will enter into a reliance agreement with the external IRB. If there is not a current reliance agreement or reciprocity agreement in place, BCM's preferred reliance agreement process should be used. A reliance agreement should be in place between BCM and the IRB of record. Please follow the instructions outlined regarding Submission Process. ***Note*:** The BCM PI makes all reports in accordance with the BCM policies and the policies of the external sIRB.

Related standard AAHRPP I.9

Scope of the IRB's Authority

Introduction	Date of Last Revision/Review: 01/13/21 This topic provides an explanation of the IRB activities and the IRB's authority in each activity.
Requirement	No official or committee of the College may permit the conduct of human subject research that has not been approved by an IRB designated by the College.
Empowerment	The IRB is empowered to take any action necessary to protect the rights and welfare of human subjects participating in research at the College.
Authority of the College	Research that has been approved by an IRB designated by the College remains subject to any additional review deemed appropriate by the President or Board of Trustees. The College retains the authority to prohibit conduct of research within its facilities or by its employees or agents that the College deems not to be in its best interests.
IRB activities	This table describes how the IRB manages human subject protection through its activities:

When …	Then …
The IRB considers it necessary to protect human subjects and assure compliance with applicable laws and regulations	The IRB has the authority to observe and monitor the respective institution's human subject research to whatever extent it desires. For more information, see: • Reporting and Assessing Compliance Concerns • Suspension or Termination of IRB Approval • Independent Verification from Other Sources • "Consent Monitoring" in Other Considerations for Informed Consent
The IRB determines a situation has serious problems, especially in instances of serious or continuing non-compliance	The IRB may suspend or terminate the enrollment and ongoing involvement of human subjects in research as it determines necessary for the protection of those subjects For more information, see: • Reporting and Assessing Compliance Concerns • Suspension or Termination of IRB Approval

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Scope of the IRB's Authority, Continued

IRB activities (continued)

This table describes how the IRB manages human subject protection through its activities (continued):

When …	Then …
A situation of serious or continuing non-compliance exists	The IRB may do any of the following to protect the rights and welfare of research subjects, for example: • Disqualify an investigator from conducting a particular research project or research altogether at the College • Require education and training in the ethics and regulations of human subject research • Take any other reasonable corrective actions deemed appropriate • **For VA research**, promptly report the situation to the local VA facility research Office. The local Research Office will report to the regional Office of Research Oversight of the Veterans Health Administration. For more information, see Reporting and Assessing Compliance Concerns
The IRB assesses investigator research files	The IRB requests that Research Compliance Services conduct the assessment and provide a follow-up report to the IRB. For more information, see Research Compliance Services Responsibilities.
Any component of the College or investigator desires to add a new site to an existing IRB-approved protocol	The component or investigator must submit the request with all required materials to the IRB.

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Scope of the IRB's Authority, Continued

IRB activities (continued)

This table describes how the IRB manages human subject protection through its activities (continued):

When …	Then …
Any reports, audit findings, or correspondence to or from any regulatory agency regarding the protection of human subjects in research in which s/he is involved are received by any person • Conducting research within any component of the College • Acting as an employee or agent of the College, regardless of location	• This person must promptly provide the IRB with copies of those reports, audit findings, or correspondence. ***Example***: A report from OHRP or FDA • The IRB reviews such correspondence to determine if action is needed to protect human subjects. • The IRB notifies the College's Legal Counsel and Compliance Officer of any such reports.
The IRB or any IRB member requires access to College Officials	The IRB or any IRB member may bring any matter directly to the attention of the Human Subject Signatory Official, Compliance Officer, or Legal Counsel when warranted.
Research is **not** conducted in either of these conditions: • By an employee or agent of the College • At a component of the College	The research is **not** considered research at the College.
The IRB is asked to accept responsibility for review and oversight of such non-College research	The IRB can do so only with: • A written agreement of the Human Subject Signatory Official, specifying its being conducted in accordance with applicable regulatory requirements • A written agreement specifying the responsibilities of – The non-College investigator and non-College institution – The College and the Baylor College of Medicine and its IRBs
The IRB is designated for review of research under Assurance of another institution (non-wholly owned or controlled by Baylor College of Medicine)	• The IRB can do so only with the written agreement of the Human Subject Signatory Official and in accordance with applicable regulatory requirements. • Any such designation must be accompanied by a written agreement specifying the responsibilities of the College and its IRB under the other institution's Assurance. **Authority** The IRB has no authority over or responsibility for research conducted at other institutions in the absence of such a written agreement.

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Scope of the IRB's Authority, Continued

IRB activities (continued)

This table describes how the IRB manages human subject protection through its activities (continued):

When …	Then …
A BCM PI conducts industry sponsored research	BCM requires all industry sponsored and funded research protocols to be submitted to a commercial IRB. See Submission Process for a list of commercial IRBs on which BCM PIs may rely as well as instructions for reliance submissions in the BCM BRAIN system.
Research is conducted in multiple sites and follows Department of Defense (DOD) regulations and requirements	A formal agreement between the organizations involved in the research is required in order to specify the roles and responsibilities of each party. The PI will submit this agreement document with the research protocol submission to the BCM IRB. See U.S. Department of Defense Research for a description of this procedure.
Research involves more than one institution, each institution is responsible for safeguarding the rights and welfare of human subjects ***Example***: Industry-sponsored multi-site studies	• The BCM IRB must review research in which BCM meets the definition of being "engaged," even if no subjects are enrolled at BCM or affiliated institutions. • If no subjects are enrolled at BCM or its affiliates, the BCM IRB generally does not review the consent form to be used at the outside institution.

Related standards AAHRPP I.1.A, I.1.B, I.1.C, I.1.D, I.3, I.5.D, II.2.H

Process of Setting up the IRB

Introduction

Date of Last Revision/Review: 01/28/19

This topic discusses how the College sets up the IRB with its accountability and authority.

Institution's requirement

No official or committee of the College may permit the conduct of human subject research that has not been approved by an IRB designated by the College.

Description

An Institutional Review Board (IRB) is an appropriately constituted group that has been formally designated to review and monitor research involving human subjects.

Accountability

Any IRB designated by the College derives its institutional authority from and is ultimately accountable to the Board of Directors (or Trustees).

Setup process

This table describes the IRB setup process:

Stage	Description
1	The Human Subject Signatory Official: • Nominates IRB members to the President and Academic Council of the College for approval and appointment to the IRBs according to the policies for appointments to Standing Committees of the College • Files a written Assurance of protection for human subjects, designating the IRB
2	The DHHS Office for Human Research Protections (OHRP) approves the Assurance.
3	The Human Subject Signatory Official oversees the development and implementation of Institutional policies governing the College's designated IRBs, all human subject research, and all investigators and research personnel at the College.
4	The Human Subject Signatory Official establishes additional reporting or communication relationships between the IRB and other officials or other committees, including the Board of Directors (or Trustees), as deemed appropriate.
5	The Human Subject Signatory Official oversees implementation of a research compliance monitoring process that provides monitoring reports, as appropriate, to the College's Signatory Official, Legal Counsel, Compliance Officer, and IRB Chairperson.
6	The Human Subject Signatory Official establishes and maintains policies to ensure that the College's Signatory Official, Legal Counsel, Compliance Officer, and IRB Chairperson are promptly notified regarding: • Any unanticipated problem involving risks to subjects or others • Any serious or continuing non-compliance with IRB requirements by research investigators • Any for-cause suspension or termination of IRB approval For more information see, Chapter 3, Section E, Reviews After Approval

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Process of Setting up the IRB, Continued

Setup process (continued)

This table describes the IRB setup process (continued):

Stage	Description
7	The Human Subject Signatory Official ensures that the IRB is provided with sufficient resources, meeting space, and staff to support the IRB's review and record keeping responsibilities. ***Reference***: DHHS regulations at 45 CFR 46.108(a)(1)
8	The Human Subject Signatory Official ensures that the IRB functions independently, has access to legal counsel and is free from undue influence.

Related standards

AAHRPP I.1.B, I.1.C, I.1.D, I.2, I.5

Responsibilities of Administrators

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides the responsibilities of the Administrators for the research teams regarding protection of human subjects.

Responsibilities by position

This table lists the responsibilities for protection of human subjects:

Position	Responsibilities
Board of Trustees	Have ultimate authority for the oversight and monitoring of the College Policies including Human Research Protections. ***Conflicts of interest***: To avoid any conflicts of interest in the research area, the IRB reports through the Institutional Official to the Board of Trustees. ***Access***: These persons have direct access to the Board if needed to fulfill the College's responsibilities for protecting human research subject: • Institutional Official • Chief Compliance Officer • IRB Chairpersons
IRB	Prepare an informational report to the Board of Trustees annually
Human Subject Signatory Official	• Is an Officer of the College (Institutional Official) • Assures Federal Research Oversight Agencies that the College complies with all Federal regulations governing the protection of human research subjects ***Reference***: See the next topic Oversight of the IRB by the Human Subject Signatory Official for more detail.
Human Protections Administrator	• Is the Director of Research Compliance-IRB • Is delegated day-to-day oversight of the College's human research protection program under the FWA by the FWA Signatory Official

Related standards

AAHRPP I.1.B, I.1D

Oversight of the IRB by the Human Subject Signatory Official

Introduction

Date of Last Revision/Review: 09/05/25

This topic discusses the responsibilities of oversight of the Human Subject Signatory Official regarding the operation of the IRB.

Requirement

The Human Subject Signatory Official is responsible for compliance oversight and review of the College's systemic protections for human subjects.

Responsibilities

The Human Subject Signatory Official designates the Institutional Review Board (IRB) to review the College's human subject research.

Delegation

The Human Subject Signatory Official may delegate the day-to-day responsibility for the review and oversight activities as s/he deems appropriate.

Oversight

The review and oversight responsibilities for human subject research activities include but are not limited to the following:

- Overseeing the operation and administration of the IRB and determining that the IRB functions in accordance with the assurances provided in compliance with all Federal, State, and local laws and regulations that govern human subject protection in the conduct of research with and with input from the Compliance Officer and (as warranted) in consultation with Legal Counsel
- Conducting compliance monitoring and auditing site visits to review IRB and Principal Investigator documentation periodically and determine compliance with assurances, OHRP, and FDA requirements.
- Preparing reports to the Board of Directors (or Trustees) as appropriate.
- Requiring corrective action or forwarding any matter to the Board of Directors (or Trustees) should a component of the College fail to take appropriate corrective action to address any confirmed compliance deficiencies, if warranted
  Note: The Compliance Officer also has the authority.
- Reviewing Institutional policies, IRB and Research Investigator manuals, and educational materials periodically to determine if they are maintained and updated appropriately
- Participating in regulatory inquiries and correspondence with regulatory authorities concerning protection of human research subjects

Communication

The Human Subject Signatory Official oversees communication as follows:

- Maintains open channels of communication among all parties involved in the human subject protection process at the College
- Ensures notification of OHRP and FDA of such incidents in accordance with applicable Federal regulations through coordination with the College's Legal Counsel, Compliance Officer, and IRB Chairperson

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Oversight of the IRB by the Human Subject Signatory Official, Continued

Quality Improvement Planning

The Human Subject Signatory Official/designee periodically assesses the quality, efficiency, and effectiveness of the human research protection program upon identification of previously unidentified risks to the integrity of the program or as a part of an ongoing routine assessment.

The goal of this program is to continually assure that the human research protection program is fulfilling its duties and to identify areas of improvement in response to changes in the regulatory environment or internal processes.

The Human Subject Signatory Official, together with the Executive Director of Research Compliance and Director of Research Compliance, establish measures of quality, efficiency, and effectiveness and make improvements based upon outcomes measures.

Outcomes measures will be evaluated and described by using appropriate statistical methods and may include:

- Time frames:
  – From submission to protocol approval,
  – The IRB uses in reviewing the protocol, and
  – The investigator uses to respond to requests for modifications
- Numbers of protocol submissions
- Distribution of submissions across the six IRBs
- Efficiencies benchmarked with peer institutions
- Appropriateness of assignment to full board or review by expedited procedures
- Documentation of IRB review:
  – Of FDA-regulated research
  – Research involving prisoners as subjects
  – Of research in emergency settings
- Timeliness of completion and quality of IRB minutes
- Satisfaction and suggestions from chairs and members
- Measures of member attendance, meeting projected attendance confirmation from members, and quorum loss

Quality assessment/audits

The Human Subject Signatory Official designee may audit these records:

- IRB files
- Subject records
- Investigator research files
- Regulatory materials

Staff in support of the Human Research Protection Program may carry out these assessments as designees of the Human Subject Signatory Official.

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Oversight of the IRB by the Human Subject Signatory Official, Continued

Quality Improvement	Upon review of these quality assessments, the Human Subject Signatory Official, together with the Executive Director of Research Compliance, the Director of Research Compliance-IRB, IRB Chairs and others, as requested, may develop plans for improvement. Most commonly such improvements will require changes to IRB procedures, submission materials and re-education of members, including staff. Identified areas of improvement are then reassessed at the discretion of the Human Subject Signatory Official, Executive Director of Research Compliance, or the Director of Research Compliance-IRB. See also Reporting and Assessing Compliance Concerns and Chain of Reporting.
Related standards	AAHRPP I.1.B, I.1.D, I.5, I.5.A, I.5.B

Protection of the IRB from Undue Influence

Introduction

Date of Last Revision/Review: 04/20/11

This procedure describes the way individuals report undue influence by the institution over the IRB and how the organization responds to attempts to unduly influence the IRB.

Authority

The IRB exercises its authority as follows, without undue influence by the organization (including the Institutional Official), regarding research activities:

- Reviews
- Approves
- Requires modifications (to secure approval)
- Disapproves

Report of concern

Concerns of undue influence by the institution are reported as follows:

Step	Action
1	Any individual, whether an IRB member, research subject, or other is encouraged to report any concern that the institution is exerting undue influence over the IRB's deliberations and determinations regarding human subject research.
2	The report may be made to any one of the following: • IRB Chair/Staff • Director of Research Compliance-IRB • Research Compliance Services • Associate Dean for Research Assurances • Compliance Helpline at 713-961-3547
3	Any of the above who receive a report of a concern are to forward the report to the institution's Compliance Officer.

Response to concern

Responses to concerns of undue influence by the institution are handled as follows:

Step	Action
1	The Compliance Officer is responsible for directing an official assessment of the concern and developing any corrective action as necessary.
2	A positive finding of undue influence is reported to the President, and the Institutional Official, for enforcement of corrective action.
3	Corrective action may include disciplinary action up to and including dismissal from employment.

Related standard

AAHRPP I.1.B, I.5.C

Responsibilities of Investigators and Their Research Staff

Introduction

Date of Last Revision/Review: 01/13/21

This topic provides the responsibilities of the investigators and their research staff on the research teams.

Notification responsibility

Researchers at every level are responsible for notifying the IRB within 48 hours of non-compliance with applicable regulatory requirements or determinations of the IRB of which they become aware, whether or not they themselves are involved in the research. Researchers may also notify the College's Human Subject Signatory Official, Compliance Officer, or Legal Counsel directly of any compliance concerns they may have.

Questions, concerns, and suggestions of researcher and research staff

Questions, concerns, and suggestions relating to the Human Research Protections Program at BCM may be conveyed to any of the following:

- IRB Chair/Staff
- Director of Research Compliance-IRB
- Research Compliance Services
- Associate Dean for Research Assurances
- Institutional Official
- Compliance Helpline at 713-961-3547
- IRB Helpline at 713-798-6970; irb@bcm.edu

For additional information, see Protection of the IRB from Undue Influence.

Reliance on external IRBs

BCM Investigators conducting research reviewed by an external IRB must:

- Be appropriately qualified
- Have completed the BCM required human subjects protections training for conducting research. This training must be completed every three years as a continuing education requirement.
- Continue to comply with all other BCM policies related to human subjects research
- Comply with all of the external IRB's policies and procedures related to human subject research

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Responsibilities of Investigators and Their Research Staff, Continued

Responsibilities by position

This table lists the responsibilities by position on the team:

Position	Responsibilities
Principal investigators	• Obtain *all* approvals necessary for the conduct of any study (including, but not limited to, IRB approval) prior to conducting the research • Implement the research as IRB approved • Bear direct responsibility for protecting every research subject, including protocol design which must minimize risks to subjects while maximizing research benefits • Comply with the findings, determinations, and requirements of the IRB • Obtain *all* the necessary approvals from entities external to the College, when research is conducted in collaboration with affiliated institutions, or outside organizations. The BCM IRB may request documentation that such approvals have been obtained. • Register all Applicable Clinical Trials in which the PI meets the definition of the Responsible Party as defined by Clinical Trials.gov. Provide website updates during the course of the study and enter study results after the study is completed. • Must: – Complete the BCM required human subjects protections training. This training must be completed every three years as a continuing education requirement. – Ensure that all Co-Investigators engaged in human research, or research conducted under their direction; have completed the BCM required human subjects protections training. This training must be completed every three years as a continuing education requirement. ***Reference***: See the topic Principal investigators for more details.

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Responsibilities of Investigators and Their Research Staff, Continued

Responsibilities by position (continued)

This table lists the responsibilities by position on the team (continued):

Position	Responsibilities
Other members of the research team (Co-Investigators)	• Protect human subjects • Comply with all IRB determinations and procedures • Complete the BCM required human subjects protections training • Adhere rigorously to all protocol requirements • Inform investigators of all adverse reactions or unanticipated problems involving risks to subjects or others • Oversee the adequacy of the informed consent process • Take whatever measures are necessary to protect the safety and welfare of subjects
Research Subjects	• Make every effort to comprehend the information researchers present to them so that they can make an informed decision about their participation in good faith • Make every reasonable effort to comply with protocol requirements and inform the investigators of unanticipated problems while participating ***Withdrawal***: Subjects always have the right to withdraw their participation in research at any time and for any reason without penalty or loss of benefits to which they would otherwise be entitled.

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Responsibilities of Investigators and Their Research Staff, Continued

Required training

Human Research Subject Protections

BCM provides human subjects protections training through the Collaborative Institutional Training Initiative (CITI) website. The minimum initial training requirement for all researchers is to complete one of the following CITI tracks (or an equivalent human subjects research protections course):

- Biomedical Research – Basic/Refresher
- Social-Behavioral Research – Basic/Refresher
- Biomedical Refresher 101
- Biomedical Refresher 200
- Biomedical Refresher 201
- Social & Behavioral Research Refresher 101
- Social & Behavioral Research Refresher 201

HIPAA

BCM also provides HIPAA training through the Collaborative Institutional Training Initiative (CITI) website. All researchers (described above) are required to complete the "Health Information Privacy and Security (HIPS) for Biomedical" or "Health Information Privacy and Security (HIPS) for IRB Members", as applicable. The "Health Information Privacy and Security (HIPS) for Biomedical" or "Health Information Privacy and Security (HIPS) for IRB Members" require the following modules to be completed:

- Basics of Health Privacy
- Health Privacy Issues for Clinicians
- Health Privacy Issues for Researchers
- Basics of Information Security, Part 1
- Basics of Information Security, Part 2
- Research Privacy & Security Training (BCM & Texas)

For instructions, see FAQs: On-Line Training.

For VA Research

All individuals who are subject to VA requirements are required to complete training in the ethical principles on which human research is to be conducted before they may participate in research involving human participants in accordance with requirements specified by ORD; the local site can require additional training.

Monitoring for compliance with training requirements

Investigators are assuring the IRB at the time of protocol submission that all applicable study team members will have completed their required human subject protections training prior to them engaging in any human subject research activities.

Any concern of non-compliance identified through the IRB's routine monitoring procedures will begin the IRB review process at this step.

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Responsibilities of Investigators and Their Research Staff, Continued

Other team members	The other team members, in addition to the principal investigators and Human Subject Signatory Official include: • Co-investigators • Study coordinators • Nurses • Research assistants • All other research staff
Related standards	AAHRPP I.1.B, I.1.C, I.1.D, I.1.E, I.5.A, I.5.C, I.5.D, III.1.A, III.1.D, III.2.A, III.2.C

PI and Research Personnel Responsibilities Regarding Research Materials

Date of Last Revision/Review: 04/29/22

What are research materials?

Research materials may include any of the following:

- Chemical compounds
- Drugs or other substances
- Tissue specimens (from humans or animals)
- Cultures of infectious substances (infectious to humans and/or animals)
- Plant pathogens and plant materials
- Genetically modified organisms
  Examples: Transgenic mice, plants, drosophila, *C. elegans*
- Cell lines, plasmids, and vectors

Responsibilities

Below are important compliance responsibilities that **may** be associated with research materials:

Step	Action
1	Work with recombinant or synthetic nucleic acid molecules, including bench, animal, plant, and human gene transfer, must be pre-approved by the Institutional Biosafety Committee (IBC) at ibc@bcm.edu or 713-798-6966
2	Work with biohazardous materials, including human blood, tissues, cells and cell lines as well as hazardous chemicals or agents may require review by the Office of Environmental Safety (OES). • For biohazardous materials questions, contact biosafety@bcm.edu or 713-798-6616 • For hazardous chemical questions, contact wdavis@bcm.edu or 713-798-3851
3	Work with human blood, tissues, cells and cell lines may require review by the BCM Institutional Review Board (IRB) at irb@bcm.edu or 713-798-6970
4	Work with live vertebrate animals must be pre-approved by the BCM Institutional Animal Care and Use Committee (IACUC) at iacuc@bcm.edu or 713-798-6966
5	Coordinate the health and well-being of research animals with the Center for Comparative Medicine (CCM) at ccm@bcm.edu or 713-798-4486

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PI and Research Personnel Responsibilities Regarding Research Materials, Continued

Responsibilities (continued)

Below are important compliance responsibilities that **may** be associated with research materials (continued):

Step	Action
6	Ensure that any BCM proprietary rights in the research materials are protected prior to shipping or transferring research materials by using a Material Transfer Agreement (MTA) when applicable. For information contact mta@bcm.edu or 713-798-1297. To determine whether an MTA is necessary, the investigator should consider whether: • There is a concern about competition in the same research area • The published material may have commercial value If the answer to one or both above is "yes", then an MTA may be appropriate. With respect to protection of potential intellectual property: • If the investigator believes that the materials generated have commercial value, the investigator should contact the BCM Ventures, bcmventures@bcm.edu or 713-798-4886, at the early stages of development and before publication • The investigator together with BCM Ventures will determine whether intellectual property protection is warranted See the table below to determine when it is needed to have an MTA in place before the transfer:

MTA is Needed	No MTA Needed	Transfer Only with Permission from the Provider
Mouse models	Reagents covered under a multi-site grant transferred within/between the grant recipients **(Excluding Mouse Models)**	Reagents that are not developed at BCM
Human derived samples	Reagents covered under a subcontract	Reagents received under an MTA or a similar contract from another institution
Unpublished materials		For the reagents not developed at BCM or by BCM investigators: Before transferring reagents to a third party, the PI and Sponsored Programs need written permission from the provider institution and the provider scientist.
Concerns with publication protection		
Concerns with intellectual property protection		
Concerns with specialized handling of the reagents		

PI and Research Personnel Responsibilities Regarding Research Materials, Continued

Responsibilities (continued)

Below are important compliance responsibilities which **may** be associated with research materials (continued):

Step	Action
7	Shipping Training must be completed by all personnel who ship or transport (see Biosafety Manual, Chapter 18 on Transportation) human or animal specimens of a research or clinical nature, biohazardous materials (including select agents) or hazardous chemicals. For information, contact the Office of Environmental Safety: • Click here to register for the class on Shipping Biological Samples • For information concerning transport or shipping of biological materials contact biosafety@bcm.edu or 713-798-6616. **Reference:** BCM IATA Manual • For information on shipping hazardous chemicals, contact wdavis@bcm.edu or 713-798-3851
8	Export control laws that regulate export of sensitive technologies, software, biological agents, and related data and services may also apply. These laws require that licenses be obtained for exports of these sensitive items unless an exemption exists. Whenever it is planned to send samples to organizations in other countries, check that both the material and the recipient are allowable. For information, contact Research Compliance Services oor-rcs@bcm.edu. Additional information can be found on federal websites such as the: • Commerce Department – Bureau of Industry and Security Export Administration Regulations (BIS EAR) • International Traffic and Arms Regulations (ITAR) • Office of Foreign Assets Control (OFAC)

Principal Investigators

Introduction

Date of Last Revision/Review: 05/12/20

This topic describes the function of the Principal Investigators regarding their request for IRB approval for research.

Compliance

Principal Investigators must ensure that:

- The research is conducted at all times in compliance with all applicable Federal, State, and local regulatory requirements and with the determinations of the IRB.
- The investigator has reviewed the College's FWA, this Human Research Protections Manual, DHHS Regulations for Protection of Human Research Subjects, relevant FDA regulations, and the Belmont Report.

IRB review and approval

Principal Investigators must ensure that:

- All human subject research which they conduct at the College or its components or as employees or agents of the College has received prospective review and approval by the IRB.
- Continuing IRB review and approval of the research are secured in a timely fashion.
- No changes in approved research are initiated without prior approval of the IRB (these should be submitted in BRAIN), except where necessary to eliminate apparent immediate hazards to subjects, and no research may be continued beyond the IRB-designated approval period.
- The IRB is notified promptly regarding:
  – Any injuries or unanticipated problems involving risks to subjects or others
  – Any serious adverse events experienced by subjects
  – Any adverse events reported to the study sponsor
  – Any non-compliance with applicable regulatory requirements or determinations of the IRB of which they become aware

For more information see Chapter 3, Section E, Reviews After Approval

Informed consent

The principal investigator must be responsible for the adequacy of both the informed consent document and the informed consent process, regardless of which members of the research team actually obtain and document consent.

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Principal Investigators, Continued

Records

Principal Investigators must ensure that:

- A final report is made to the IRB and to the sponsor in a timely manner after the completion or discontinuance of a research project
- Complete and accurate records are maintained regarding all communications with the IRB, the sponsor, and any Federal Agency, and such records are made available to the College's Human Subject Signatory Official and Compliance Officer immediately upon request.
- All study information (including study results) is up-to-date on the ClinicalTrials.gov website for Applicable Clinical Trials in which the PI is the Responsible Party. Through its website the BCM Office of Clinical Research provides guidance and registration information.
- **For VA research**, an entry is placed in the progress notes of the subject's medical record when the:
  – Subject is admitted to VA medical facility as in-patient
  – Subject is treated as outpatient at VA medical facility; or
  – When research procedures or interventions are used in or may impact the medical care of the research subject at a VA medical facility.

Related standards

AAHRPP I.1.B, I.1.D, I.5.D, II.2.E, II.3.F, III.1.A, III.1.D, III.2.C

IRB Special Relationships

Introduction

Date of Last Revision/Review: 04/29/25

This topic summarizes special relationships, including the protection education program, relationship to sponsors, review fees, and privacy board functions.

Human subject protection education program

The College is required under its OHRP-approved FWA to have a plan to provide education about human subject protections for research investigators and IRB members and staff.

The Human Subject Signatory Official is responsible for developing and implementing an education plan, and shall determine the education requirements needed for the College's personnel to participate in the conduct of human subject research and for IRB members and staff to be designated.

Relationship of the IRB to IND/IDE sponsors

No written notifications of IRB decisions are provided to sponsors by the IRB.

The Principal Investigator serves as the communications link between the IRB and the Sponsor for this purpose.

For FDA-regulated test articles, such linkage is agreed to by the sponsor and principal investigators when they sign the FDA Form 1572, Statement of Investigator.

IRB review fees

The Human Subject Signatory Official may authorize the IRB to collect reasonable fees for initial review and continuing review of sponsored research.

The Signatory Official reviews the fee schedule periodically to determine if the fee is market-based and adequate when considering the time and resources consumed in performing such reviews.

Privacy board functions and determinations

The IRB is designated to serve as the Privacy Board.

References: HIPAA, 45 CFR 164.501, 164.508, 164.512(i)

For VA research, the IRB Privacy Board shall include additional consideration related to HIPAA, and special laws related to protection/use of veterans' information, including Privacy Act of 1974, 5 U.S.C. 552A; VA Claims Confidentiality Statute, 38 U.S.C. 5701; Confidentiality of Drug Abuse, Alcoholism and Alcohol Abuse, Infection with Human Immunodeficiency Virus (HIV), Sickle Cell Anemia Medical Records, 38 U.S.C. 7332; and Confidentiality of Healthcare Quality Assurance Review Records, 38 U.S.C. 5705.

Functions include review and determinations of requests for Waiver or Alteration of Authorization to use or disclose Protected Health Information in Research.

Reference: Please refer to the College's separate policies and procedures on research privacy under HIPAA.

Research using external IRBs

BCM Investigators participating in research reviewed by an external IRB must comply with BCM's Conflict of Interest policy.

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IRB Special Relationships, Continued

Concerns or Complaints about IRB determinations

Investigators who have concerns or complaints about IRB determinations may bring these concerns to the IRB Chair or the Associate Dean for Research Assurances. These individuals may advise the investigator on ways to comply with IRB requirements, and may consider ways to improve services offered to investigators by the IRB and Office of Research. These activities will not unduly influence the IRB or undermine its independence.

Coordination with Offices/Committees/ Affiliate Institutions

The following table indicates IRB coordination between other Offices, Committees, and Affiliate institutions:

Offices	Descriptions
General Counsel	The IRB, Research Compliance administration, and Research Compliance services communicate regularly with committed members of the Office of the General Counsel on issues related to: • State and Federal law • Interpretations of the regulations • Correspondence with federal oversight agencies • Development of necessary agreements ***Examples***: IRB Memoranda of Understanding, Unaffiliated Investigator Agreements
Office of Communications & Community Outreach	The IRB, and Research Compliance Administration communicate regularly with members of the Office of Public Affairs on issues related to: • Community outreach • Involvement in research • Language understandable to subjects • Media inquiries • Research recruitment materials Members of the Office of Public Affairs serve as members of the IRB. The BCM Office of Communications & Community Outreach maintains a variety of mailing lists to target specific audiences and publications. Using the internet and multimedia opportunities, the BCM Office of Communications & Community Outreach distributes information about research findings, research participation opportunities, and new programs *via* traditional press releases, Facebook, Twitter, and related digital media targeted to specific audiences of the communities served by BCM. In addition to ongoing evaluation of the dissemination of information related to research at the College and affiliate institution leadership level, the human research protection program leadership periodically evaluates the delivery of web-based content regarding considerations before volunteering to participate in research.

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IRB Special Relationships, Continued

Coordination with Offices/Committees /Affiliate Institutions (continued)

The following table indicates IRB coordination between other Offices, Committees, and Affiliate institutions (continued):

Offices (cont.)	Descriptions
Sponsored Programs	The Office of Sponsored Programs relies on the BCM IRB review and level of risk to negotiate indemnification agreements with clinical research sponsors and to assure appropriate approvals to all sponsoring agencies.

Committees	Descriptions
Conflict of Interest	The BCM IRB: • Relies on the Research Conflict of Interest Committee (RCOIC) to review, make recommendations, and if applicable, manage Financial Conflicts of Interest (FCOI) as well as Institutional Conflicts of Interest (ICOI) • Will not approve protocol submissions without reviewing investigators' management plans for FCOI or ICOI **Individual Investigator Conflicts of Interest** • The IRB reviews the plan to manage financial interests of the investigators so they do not adversely affect participant protections or the credibility of the programs designed to protect human subjects • Financial conflicts of interest of an investigator may be managed, for example, through divestiture, or by assigning responsibilities for the research to the investigator who does not hold financial conflicts of interest • In addition, the IRB may require disclosure of financial conflict to the subjects. Unless there is no conflict or the management plan is complete divestiture the protocol will go back to the IRB for a final decision on approval.

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IRB Special Relationships, Continued

Coordination with Offices/Committees /Affiliate Institutions (cont.)

The following table indicates IRB coordination between other Offices, Committees, and Affiliate institutions (continued):

Committees (cont.)	Descriptions
Conflict of Interest (continued)	**Institutional Conflicts of Interest** • The IRB must be informed when the College has: – An active management role in the business which funds the research, or – Intellectual property rights in the product being tested, and/or – An Institutional Leader with direct responsibility for human subject research who holds a significant financial interest in the commercial research sponsor or the investigational product • The Office of Research receives reports on institutional financial interests from BCM Ventures and BCM Technologies (BCMT) through BRAIN • Institutional Leaders disclose their financial interests at least annually • When an investigator selects as a funding source one of the businesses in which BCM or its Institutional Leader has a financial interest, the investigator is notified through BRAIN of the institutional relationship, and that the protocol requires additional review by the Research Conflict of Interest Committee (RCOIC) • The RCOIC reviews the Institutional Conflict of Interest and proposes a plan to manage the conflict as it relates to the proposed research, so that it does not adversely affect participant protections. The plan is forwarded to the IRB. • The IRB reviews the plan recommended by the RCOIC and may impose additional requirements (including, but not limited to, the appointment of an independent DSMB, information about the interest being included in the consent form, or moving the research to another site) to protect human subjects and to ensure the objectivity of the research • The IRB has the final authority to decide whether the financial interest and its management, if any, allows the research to be approved. The BCM RCOI Research Compliance team members on behalf of the RCOIC monitors approved FCOI and ICOI management plans on a regular basis to ensure compliance. Reports of findings are made to the IRB and the RCOIC for review and deliberation.

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IRB Special Relationships, Continued

Coordination with Offices/Committees/ Affiliate Institutions (cont.)

The following table indicates IRB coordination between other Offices, Committees, and Affiliate institutions (continued):

Committees (cont.)	Descriptions
General Clinical Research Center	Research conducted at the General Clinical Research Center (GCRC) must be reviewed and approved by the GCRC Advisory Committee (GAC) prior to initiating the research activity on GCRC premises. GCRC research protocols may be submitted to the GAC and the BCM IRB concurrently.
Institutional Biosafety	**Institutional Biosafety Committee (IBC)** • Human Gene Transfer • Research involving the deliberate transfer of DNA (or DNA or RNA derived from recombinant DNA) into one or more human subjects requires initial and continuing review by the IBC • The BCM IRB will not review submissions requiring approval from the IBC until the IBC has reviewed and approved the protocol • SAEs that occur in these protocols require reporting to the IBC and the BCM IRB • IBC approval is documented in the files of each of the committees **Radiation Safety Committee (RSC)** • RSC of the IBC provides local review, as delegated by the Food and Drug Administration (FDA), of all human subject protocols using radioactive material • The RSC approval is documented in the files of each of the committees

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IRB Special Relationships, Continued

Coordination with Offices/Committees /Affiliate Institutions (cont.)

The following table indicates IRB coordination between other Offices, Committees, and Affiliate institutions (continued):

Affiliates	Descriptions
Investigational Drug Services	Investigational Drug Services (IDS) are available at each of the BCM Affiliate Hospitals. • Pharmacists dispensing investigational drugs for inpatient research protocols verify that the: – Protocol has current IRB approval – Patients signed an IRB-approved consent form prior to dispensing the drug • Specific procedures for each IDS are available to BCM investigators and are maintained as a link in the BCM IRB website
Affiliate Institutions	The IRB maintains its protocol files, findings, actions, and correspondence within the electronic Biomedical Research Assurance and Information Network (BRAIN). • Memoranda of Understanding between the IRBs and the Affiliate Hospitals designate personnel who may access these BRAIN files for research planned to be conducted at their sites. • Notifications of approvals as well as compliance concerns are further communicated among the IRB Administration Office and the Affiliate Hospitals

Related standards AAHRPP I.1.B, I.1.D, I.4.B, I.4.C, I.5.C, I.6.A, I.6.B, II.1.C, II.3.C.1, II.3.D, III.1.B

Section B
IRB Structure and Membership

Overview

Introduction

Date of Last Revision/Review: 01/28/19

This section focuses on the structure of the IRB and the members of the Board.

Accountability

The IRB is ultimately accountable to the Board of Trustees.

Appointment

The Human Subject Signatory Official nominates IRB members to the President and Academic Council of the College for approval and appointment to the IRBs according to the policies for appointments to Standing Committees of the College.

Composition

In accordance with DHHS and FDA regulations, the College's IRBs are comprised of persons from various disciplines and departments, including non-scientific members, and community representatives not otherwise affiliated with the College.

When the IRB reviews research involving categories of subjects that are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged, consideration shall be given to the inclusion of one or more individuals on the IRB among its reviewers who are knowledgeable about and experienced in working with these categories of subjects.

For VA Research: IRBs reviewing VA regulated research should also consider including a Veteran or Veteran's representative.

The Director of Research Compliance-IRB, Executive Director of Research Compliance, and the Associate Dean for Research Assurances will review the IRB rosters to evaluate their composition with respect to scientific expertise, experience in working with children, adults unable to consent, prisoners, and other vulnerable populations. In addition, opportunities to include all types of people to serve on the IRB will be sought on an ongoing basis.

Qualifications

The College's IRB members must:

- Have sufficient expertise to review the broad range of research in which the College commonly becomes involved
- Be knowledgeable about all relevant regulatory requirements
- Remain impartial and objective in their reviews

In this section

This section covers the following topics:

- Appointment of IRB Members, Length of Service, and Duties
- IRB Chairperson
- Evaluation of IRB Members and Chairpersons
- Alternate IRB Members
- Consultants to the IRB

Related standards

AAHRPP I.1.D, I.4.C, II.1.A, II.1.D

Appointment of IRB Members, Length of Service, and Duties

Introduction

Date of Last Revision/Review: 09/05/25

This topic discusses the members of the IRB, covering their terms and duties.

Appointment

The Human Subject Signatory Official nominates IRB members to the President and Academic Council of the College for approval and appointment to the IRBs according to the policies for appointments to Standing Committees of the College.

For VA research, at least two VA representatives are appointed to each IRB that reviews VA research by the VA facility Medical Center Director in writing.

Terms

Each member serves a one-year term. Any member's term may be extended for an additional one-year term without limitation.

For VA members

Appointment procedures for ex officio, non-voting members are made according to local SOPs and any other applicable VA requirements. Voting members of VA IRBs and VA representatives to external IRB(s) of Record and the VA Central IRB are appointed for a period of up to three years. They may be re-appointed to new terms of up to three years without a break in service at the end of each term.

***Note*:** There is not a maximum number of terms for IRB members as long as the composition of the IRB meets all requirements.

Candidates

Candidates for membership on the IRB may be recommended to the President by any of the following:

- IRB Chairperson
- IRB members
- Department Chairpersons
- IRB administrative staff
- Officials of the College or its components that conduct human subject research

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Appointment of IRB Members, Length of Service, and Duties, Continued

VA representation

Each IRB that reviews VA research shall include at least two VA-compensated employees as voting members as follows:

- Each VA member must be salaried by the VA at least 1/8th
- The VA members must serve as full members; this includes reviewing non-VA research matters coming before the IRB
- Special IRB membership is required for research using subjects who are mentally disabled or with impaired decision-making capacity (includes at least one expert in that area of research, may use ad hoc member(s) as necessary).

***Exceptions*:** Research and Development administration officials are prohibited from serving as voting members of the IRB but may serve as nonvoting ex officio members. This includes, but is not limited to the:

- Associated Chief of Staff (ACOS)
- Administrative Officer (AO) or Director of Research Operations (DRO)

The VA Research Compliance Officer (RCO) may serve as a nonvoting consultant, as needed to the IRB. The RCO may not serve as a voting or nonvoting member of the IRB. The RCO may attend meetings of the IRB when needed and invited by the Chairperson of the IRB to present or discuss compliance matters.

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Appointment of IRB Members, Length of Service, and Duties, Continued

Qualifications

This table describes the qualifications of the members of the IRB:

Type	Qualification
Scientist members	• Any individual who has had substantive training or experience in a scientific discipline (i.e., behavioral or biomedical) or in a scientific method should be considered a scientist • May have had experience and expertise in human subject research • Are recruited from among the College's faculty and staff as well as the community
Non-scientific members	• May not be construed as a scientist by training, education, or vocation • Are recruited from among the College's faculty and staff and from the community • May also be unaffiliated members • Generally are members that are regarded to represent the general perspective of research participants
Un-affiliated members	• These members or members of their immediate family may have no affiliation with the College, other than their service on the IRB • May also be non-scientific members • Generally are members that are regarded to represent the general perspective of research participants

Competing business interests

Personnel responsible for business development activities of the College may not serve as members of the IRB.

General makeup

Every effort is made to select personnel from a variety of disciplines, which represent the types of research proposals submitted for review and approval.

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Appointment of IRB Members, Length of Service, and Duties, Continued

IRB members

The IRB membership is comprised of these persons:

- At least five members including at least one of each:
- Whose primary expertise is in a scientific area
- Whose primary concerns are in non-scientific areas
- Who is not otherwise affiliated with the College and who is not part of the immediate family of a person who is affiliated with the College or other institutions for which the IRB is the designated IRB
- Who represents the general perspective of research participants

  ***Note*:** The non-scientific member, the unaffiliated member, and the member representing the general perspective of research participants may be the same person or may be represented by two or three persons.
- Persons with varying backgrounds to promote complete and adequate review of research activities commonly conducted at the College and institutions for which the IRB is the designated IRB
- Members whose training, background, and allied health professionals occupation are within a behavioral or biomedical research discipline should be considered a scientist, while members whose training, background, and occupation are outside of a behavioral or biomedical research discipline should be considered a nonscientist.

Other member requirements

The IRB membership must meet these other requirements:

- Persons who are sufficiently diverse relative to race, gender
- Include sufficiently qualified persons through their experience and expertise (professional competence)
- Persons with diverse cultural background and sensitivity to community attitudes so as to promote respect for the IRB's advice and counsel in safeguarding the rights and welfare of human subjects
- When the IRB reviews community-based participatory research that involves community members in the research process, the design, implementation of the research, and the dissemination of the results, IRB members or consultants with expertise in this area may be consulted for the review.
- For research funded by the National Institute on Disability and Rehabilitation Research (Department of Education regulated) that purposefully requires inclusion of children with disabilities or individuals with impaired decision-making capacity as research participants, the IRB must include in its review at least one person primarily concerned with the welfare of these research participants
- Persons able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable law, and standards of professional conduct and practice
- Persons who are knowledgeable about and experienced in working with the categories of subjects that are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

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Appointment of IRB Members, Length of Service, and Duties, Continued

Expectations of members	Members are expected to meet these requirements: • Vote to approve, require modifications to secure approval, table, or disapprove research submitted to the IRB. • Attend IRB meetings on a regular basis • Serve as primary reviewers for research as assigned • Serve as team reviewers for research as assigned • Participate in the discussion on all research discussed at convened meetings • Conduct expedited reviews on behalf of the IRB when so designated by the IRB Chairperson
Attendance monitoring	The IRB office will monitor the IRB meeting attendance to assure that: • Overall attendance rate for any one IRB has an unaffiliated member present for 10 of the 12 IRB meetings for the year; and • Overall attendance rate for any one IRB having a member who represents the general perspective of research participants present for 10 of the 12 IRB meetings for the year
Reasons for removal	Any member of the IRB may be removed by the President: • For failure to perform the duties of an IRB member, including failure to attend at least 80% of the IRB meetings held within any 12-month period • For scientific misconduct, conflict of interest, or argumentative behavior such that review of research by the IRB is made difficult or impossible
Applicable regulations	The applicable membership requirements for the IRB are from the DHHS regulations at 45 CFR 46.107**,** FDA regulations at 21 CFR 56.107 and VA policies.
Related standards	AAHRPP I.1.D, I.4.C, I.6.B, II.1.A, II.1.B, II.1.C, II.1.D, II.1.E, II.2.A, II.2.C

IRB Chairperson

Introduction

Date of Last Revision/Review: 06/24/24

This topic discusses the responsibilities and duties of the IRB Chairperson.

Qualification

The IRB has a Chairperson who is well-informed concerning regulations relevant to the involvement of human subjects in research.

Appointment

The Human Subject Signatory Official nominates the IRB Chairperson to the President and Academic Council of the College for approval and appointment to the IRBs according to the policies for appointments to Standing Committees of the College.

Term

The IRB Chairperson serves a one-year term, renewable for consecutive one-year terms without limitation.

Conducting a meeting

The Chairperson of the IRB conducts each meeting in an orderly manner as follows:

- Chairs the meeting
- Conducts business so that each proposal is fairly and completely reviewed
- Sees that the IRB reaches a decision on the disposition of each proposal
- Ensures that these decisions are communicated to the individuals who submitted the proposal

Duties

The IRB Chairperson has these duties:

- Utilize expedited review procedures to review and approve research in accordance with DHHS and FDA regulations
- Appoint qualified IRB members to review and approve research utilizing expedited procedures in accordance with DHHS and FDA regulations
- Review responses from investigators, as needed and as delegated by the IRB in appropriate circumstances, to determine if they respond sufficiently to the IRB's concern to allow approval under expedited review procedures and without being returned to the fully convened IRB
- Review of board modifications from studies reviewed by the convened board to ensure board modification memos reflect the board’s intent
- Review of single patient expanded access use requests
- Sign correspondence on behalf of the IRB
- Conduct reviews of Event Reports for determinations of possible unanticipated Problems involving risks to subjects or others (UPIRSO) or Non-Compliance
- Participate in subcommittee reviews for Non-Compliance
- Review IRB policies and procedures at least annually to confirm current compliance with all Federal State, and local requirements for the protection of human subjects

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IRB Chairperson, Continued

Vice Chair	The Vice Chair acts as the Chair of the IRB when the chair is unavailable and holds the same authority and duties. The annual IRB member evaluation includes an evaluation of the IRB Vice Chair's performance by the IRB Chair. Feedback from this evaluation is provided to the Vice Chair.
Relieving/removal	The President may relieve an individual as IRB Chairperson for failure to fulfill the duties listed above. The President may remove the Chairperson from the IRB: • For failure to perform the duties of an IRB member, including failure to attend at least 80% of the IRB meetings held within any 12-month period • For scientific misconduct, conflict of interest, or argumentative behavior such that review of research by the IRB is made difficult or impossible
Related standards	AAHRPP I.1.D, I.6.B, II.1.A, II.1.B

Evaluation of IRB Members and Chairpersons

Introduction	Date of Last Revision/Review: 04/20/11 The performance of IRB members and chairpersons is evaluated periodically in order to ensure that overall IRB performance meets regulatory requirements and to provide members and chairs opportunities for professional development.
Who evaluates	Performance of IRB members and chairs is evaluated by the IRB staff, chairs and members in a constructive fashion.
Member evaluation criteria	Criteria for evaluation of members include: • Attendance at meetings • Completion of assigned reviews in a timely fashion • Assistance with additional items such as expedited review and event review • Working knowledge of applicable regulations
Chair evaluation criteria	Criteria for evaluation of chairs include the above as well as: • Superior knowledge of regulations and guidances • Willingness to consult with investigators regarding IRB issues • Demonstration of leadership in meetings and other settings
Performance evaluation	IRB Chairs evaluate new members mid-year after the appointment to the IRB and annually for all other members. The IRB Chairs and Institutional Official send a letter to all members who meet evaluation criteria.
Performance concerns	Throughout the appointment year, should concerns arise about performance, the member or Chair will be presented with the relevant information and will be asked to help create and implement a performance improvement plan. Those who continue to be unable to meet performance criteria may be removed from the IRB.
Related standards	AAHRPP I.1.D, I.5, I.5.B, I.6.B, II.1.A, II.1.B

Alternate IRB Members

Introduction	Date of Last Revision/Review: 01/13/21 The IRB, at its discretion, may recruit alternate members to substitute for regular members of the IRB.
Listed on roster	Alternate members must be listed on the IRB's official membership roster, which must specify which member (or members) the alternate is qualified to replace.
One alternate for one member	Although an alternate may be qualified to replace more than one regular member, only one such member may be represented by the alternate at any convened meeting.
Establishing a quorum	Alternate members are included in determining or establishing a quorum at meetings when their respective regular members are absent but not when those regular members are present. To ensure maintaining an appropriate quorum, the alternate's qualifications should be comparable to the primary member to be replaced.
Rights and duties	The following are rights and duties of alternate members: • Alternate members have voting rights except that they may not vote at meetings attended by their respective regular members. • Alternates that serve for a regular IRB member responsible for reviews of protocols receive and review the same materials that the regular IRB member normally receives. • The regular IRB member may provide his/her review without being present at the fully convened IRB meeting. • Procedures for appointment, terms of appointment, length of service, and duties are exactly as for regular IRB members.
VA alternates	VA alternate members must have qualifications similar to member qualification(s) of the primary member they replace.
Related standards	AAHRPP I.1.D, II.1.A

Consultants to the IRB

Introduction

Date of Last Revision/Review: 04/20/11

This topic discusses the use of consultants to help the IRB with special expertise.

Purpose

At its discretion, when the IRB does not feel it has the scientific or scholarly expertise required among its members to review a protocol, the IRB may recruit (non-voting) consultants.

Consultants, sometimes referred to as non-voting or *ex officio* members, may be present at the meeting or submit a written report to aid the IRB in conducting its duties.

Process for using a consultant

This table describes the process for using a consultant:

Stage	Description
1	When the IRB decides that the services of an outside consultant are required, the IRB Chair or one of the Vice-Chairs finds and recommends a consultant to the IRB Analyst.
2	The IRB Analyst or one of the IRB members contacts the proposed consultant via e-mail or telephone, asking them to serve as an independent consultant to the IRB.
3	Upon agreeing to be a consultant, the consultant is asked: • To review the protocol based on their expertise or specialty • To provide a written summary of the protocol and their assessment of the risks and benefits to subjects
4	The IRB Analyst • Enters the written summary into BRAIN in the feedback page with a notation that the feedback is from the consultant • Presents the written summary to the other IRB members before the meeting in which deliberations, discussion, and voting on that protocol are to take place
5	The consultant, if present, or the Chair presents the consultant's report during the meeting, and deliberations and discussion of the protocol are conducted before a final vote.
6	If there is no consensus among Board members regarding the consultant's report, additional consultants (including the original) may be asked to clarify the issues.
7	The minutes of the IRB meeting reflect that a consultant was required for the IRB deliberation, discussion, and final decisions on this protocol.

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Consultants to the IRB, Continued

Consultant restrictions

Consultants may not be:

- Voting members of the IRB, however, they may be ex officio members
- Included in determining or establishing a quorum at any IRB meeting
- Used as reviewers for any research study for which they have a conflict of interest

Types

This table describes the types of consultants to the IRB:

Type	Functions
Continuing Consultants	• Serve a fixed term and generally attend all IRB meetings • May have access to all documents submitted to the IRB • May participate in IRB deliberations and make recommendations to influence IRB determinations
Ad Hoc Consultants	• Serve on an as-needed basis and generally attend IRB meeting only when their special expertise is needed • May have access to all documents submitted to the IRB that are pertinent to the research under review • May participate in IRB deliberations and make recommendations to influence IRB determinations ***Reference***: See Independent Verification from Other Sources in Chapter 3, IRB Review, for the criteria for the use of a consultant.
Legal Counsel	• Appointed by the College's General Counsel to serve as a Continuing Consultant, non-voting member to the IRB • Advises the IRB as to fulfilling its function to protect the rights and welfare of human subjects

Related standards

AAHRPP I.1.D, I.1.F, II.1.B, II.1.D, II.1.E

Section C
IRB Administrative Support and Records

Overview

Introduction	Date of Last Revision/Review: 01/28/19 This section discusses the support staff and records needed for the IRB to meet its requirements.
Requirement	The College must provide its IRB with sufficient meeting space and staff to support the IRB's review and responsibilities. ***Reference***: DHHS regulations at 45 CFR 46.108(a)(1)
In this section	This section covers the following topics: • Organizational Structure • Responsibilities of the IRB Administrator and Other IRB Staff • IRB Record Requirements • IRB File Requirements • IRB Materials Submission Deadlines
Related standards	AAHRPP I.1.D

Organizational Structure

Introduction

Date of Last Revision/Review: 12/17/15

This topic describes the organizational structure of the IRB and its support staff.

Requirement

The College is required to have a plan to provide education about human subject protections for IRB members and staff.

Reference: OHRP Assurance (FWA)

Responsible official

The Human Subject Signatory Official has responsibility for establishing and maintaining systems for the protection of human subjects in research conducted within the College or by its employees or agents.

To this end, the Human Subject Signatory Official ensures that sufficient resources, including meeting space and staff, are provided to support the IRBs' review and responsibilities.

Reporting lines and supervision

The reporting lines and supervision for the IRB organization follow:

- The Director of Research Compliance-IRB reports to and takes direction from the IRB Chairperson regarding human subject protection issues.
- The Director of Research Compliance-IRB reports to the College's Executive Director of Research Compliance for administrative purposes.
- IRB Professional Staff and IRB Support Staff report to the Director of Research Compliance-IRB.

Competing business interests

Personnel responsible for business development activities of the College may not be involved with the day-to-day operations of the IRB.

Staff training and development

This table lists the initial requirements for the training and professional development of the IRB staff:

Position	Requirement
IRB Chairperson	• Must complete the initial educational module available on the OHRP website • Must complete the BCM required human subjects protections training for IRB members. This training must be completed every three years as a continuing education requirement. • Are strongly encouraged to attend: – National or regional human subject protection conferences on a periodic basis – Continuing education opportunities in the College or neighboring institutions ***Expenses***: Resources to do so will be provided.

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Organizational Structure, Continued

Staff training and development (continued)

This table lists the initial requirements for the training and professional development of the IRB staff (continued):

Position	Requirement
IRB Analysts	• Must complete the BCM required human subjects protections training for IRB members. This training must be completed every three years as a continuing education requirement. • Are strongly encouraged to become Certified IRB Professionals or Certified IRB Administrators • Are expected to attend: – National or regional human subject protection conferences on a periodic basis – Continuing education opportunities in the College or neighboring institutions • Additional requirements: May be established as deemed necessary by the Human Subject Signatory Official ***Expenses***: Resources to do so will be provided.
Director of Research Compliance-IRB	• Must complete the BCM required human subjects protections training for IRB members. This training must be completed every three years as a continuing education requirement. • Is strongly encouraged to become Certified IRB Professionals or Certified IRB Administrators • Is expected to attend: – National or regional human subject protection conferences on a periodic basis – Continuing education opportunities in the College or neighboring institutions ***Additional requirements***: May be established as deemed necessary by the Human Subject Signatory Official ***Expenses***: Resources to do so will be provided.
IRB Support Staff	• Must complete the BCM required human subjects protections training for IRB members. This training must be completed every three years as a continuing education requirement. • Are encouraged to take advantage of other educational opportunities as they are made available

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Organizational Structure, Continued

Staff training and development (continued)

This table lists the initial requirements for the training and professional development of the IRB staff (continued):

Position	Requirement
New IRB members	• Must complete the BCM required human subjects protections training for IRB members. This training must be completed every three years as a continuing education requirement. • Must complete a new member orientation and training session on the regulations and guidance that govern the IRB review of human research • Have the opportunity to observe several IRB meetings before they are assigned studies as a Primary or Team Reviewer
Department of Defense (DOD) training requirements	There may be specific DOD educational requirements or certification required of the IRB when reviewing DOD regulated research. The Principal Investigator is responsible for assuring that the IRB Office is notified of DOD funding or DOD regulated activity through IRB submission of the IRB Protocol Summary (New, Amendment or Continuing Review) and will provide specific information or guidance from the DOD funding program officer or DOD research contact. The Director of Research Compliance-IRB will inform the IRB staff, IRB chairperson, and IRB members-of these requirements when appropriate. See U.S. Department of Defense Research.
Required human subjects protections training for IRB members and staff	There are several options for investigators to meet the training requirement for the protection of human subjects in research. Courses such as the NIH Office of Extramural Research free tutorial on "Protecting Human Research Participants" and the Office of Human Research Protections On-line Tutorial both meet the institutional requirement to meet the human subjects protections education requirement. BCM also provides human subjects protections training through the Collaborative Institutional Training Initiative (CITI) website. The minimum initial training requirement for all IRB Chairpersons, all IRB members, and all IRB staff is to complete the CITI track for IRB Members - Basic/Refresher - Basic Course. For instructions, see FAQs: On-Line Training.
Monitoring for compliance with training requirements	Completion of the required training will be monitored annually for existing members at the start of the academic year. New appointments will complete training as part of IRB member orientation.

Related standards AAHRPP I.1.D, I.1.E, II.1.C

Responsibilities of the IRB Administrator and Other IRB Staff

Introduction

Date of Last Revision/Review: 04/20/11

This topic discusses the responsibilities of those persons who support the IRB members.

Requirement

The IRB Administrator (Director of Research Compliance-IRB), with the appropriate assistance of other IRB Analysts and Support Staff, is responsible for ensuring that the IRB functions are accomplished in a professional fashion that complies with all relevant regulatory requirements.

Responsibilities

This table lists the responsibilities by area of responsibility:

Area	Responsibilities
General	Maintaining quality control of IRB support functions
Initial review	• Conducting a limited pre-review of incoming applications to ensure completeness and as otherwise directed by the IRB • Conducting a limited pre-review of proposed informed consent documents to ensure that they are written at a level that is easily understandable for prospective subjects and is written in a language that prospective subjects are likely to understand ***Example***: English, Spanish
Before meetings	• Assisting new IRB members in completing orientation procedures and meeting required education standards • Scheduling IRB meetings • Distributing pre-meeting materials with sufficient time to allow IRB members an opportunity to review them in preparation for the meeting • Tracking the progress of each research protocol submitted to the IRB
Communication	• Serving as a resource for investigators on general regulatory information and providing guidance about forms, submission procedures, and general research related issues • Facilitating communication between investigators and the IRB • Drafting reports and correspondence to research investigators on behalf of the IRB or IRB Chairperson regarding the status of the research, including conditions for initial or continuing approval of research and responses to reports of adverse events or unanticipated problems • Assisting in evaluation, audit, and monitoring of human subject research as directed by the IRB and the Human Subject Signatory Official

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Responsibilities of the IRB Administrator and Other IRB Staff, Continued

Responsibilities (continued)

This table lists the responsibilities by area of responsibility (continued):

Area	Responsibilities
Records	• Maintaining the official roster of IRB members • Compiling the minutes of IRB meetings in compliance with regulatory requirements • Securely and properly archiving all IRB records • Maintaining a computerized database for tracking purposes and logging incoming information into the database • Maintaining all IRB documentation and records in accordance with regulatory requirements • **For VA research,** make available approved IRB minutes (non-redacted) regarding VA research to the VA Research and Development Committee through the VA Research Office

Other staff responsibilities

Under the direction and supervision of the Director of Research Compliance-IRB, other IRB staff:

- Are responsible for documenting that IRB activities and determinations fully satisfy all regulatory requirements
  Requirement: Such staff must have a detailed, working knowledge of relevant regulatory requirements.
- Assist in the administration of the IRB

Related standards

AAHRPP I.1.D, I.5

IRB Record Requirements

Introduction

Date of Last Revision/Review: 01/13/21

This topic discusses the requirements for records to maintain the IRB reviews.

Procedures requirement

Requirement
The College must implement written policies and procedures to govern the operations and direct the activities of its IRB.

Implementation
This Human Research Protections Manual addresses that requirement, based on Federal regulations.

Document flow procedures

The Director of Research Compliance-IRB is responsible for developing and implementing procedures for efficient document flow.

Findings and determinations

IRB records include documentation of all IRB findings and determinations.

References:

- As required under DHHS and FDA human subject protection regulations
- As recommended by official (written) OHRP and FDA guidance

IRB records defined

At a minimum, IRB records must include all information:

- Required under DHHS and FDA regulations at 45 CFR 46.115 and 21 CFR 56.115, respectively
- Recommended by official (written) OHRP and FDA guidance

File organization

IRB files are organized such that the following information may be readily accessed:

File	Contents
General	• Written IRB Operating Procedures • Research (Protocol) Tracking System • Current and Past IRB Membership Rosters • Training Records • IRB Research Application (Protocol) Files

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IRB Record Requirements, Continued

File organization (continued)

IRB files are organized such that the following information may be readily accessed (continued):

File	Contents
For VA Research	IRB records include: • Copies of all correspondence between the IRB and the Research and Development Committee • Unexpected adverse events submitted to the IRB • Protocol violations submitted to the IRB • A resume for each IRB member • Research records include, but are not limited to, IRB Committee records, records of all observations, participant recruitment activities, other data relevant to the investigation, progress notes, research study forms, surveys, questionnaires, and other documentation regarding the study. • For research subject to the 2018 Requirements, the rationale for an expedited reviewer's determination that particular research appearing as a category on the expedited review list is more than minimal risk, and therefore not eligible for expedited review; • Documentation specifying the responsibilities that the VA facility and an organization operating as the VA facility's IRB of Record each will undertake to ensure compliance with the requirements of this directive, such as an MOU or an IRB Authorization Agreement or IRB reliance agreement.
Review results	• Documentation of Exemptions from DHHS regulations • Documentation of Exemptions and Exceptions from FDA regulations • Documentation of Expedited Reviews • Documentation of IRB Findings and Review Category for the Involvement in Research of Pregnant Women, Fetuses, Neonates, Prisoners, and Children • Documentation of IRB Findings and Justifications for Waiver of Informed Consent and Waiver of Documentation of Informed Consent • Information for All Approved Research Addressing Each of the Eight Criteria for Approval under DHHS regulations at 21 CFR 56.111 and 46 CFR 46.111
After review documentation	• Documentation of Convened IRB Meetings -Minutes • Documentation of Review by Another Institution's IRB • All Correspondence to and from the IRB • Adverse Event Reports, exceptions, deviations, unanticipated problems

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IRB Record Requirements, Continued

Record retention

IRB records (in print or electronically) are retained by the IRB for no less than three years, and research records are retained by the College for no less than three years after the completion of the research.

Reference: Federal regulations at 21 CFR 56.115(b) and 45 CFR 46.115(b)

For Department of Defense (DOD) regulated research, submitting records to the DOD for archiving may be required.

See U.S. Department of Defense Research.

For VA research

- Required records, including the researcher's research records, must be retained for a minimum of six years but may be retained longer if required by other federal regulations or sponsor archive requirements.
- Codes or keys linking participant data to identifiers must be retained as part of the research record for at least six years.
- If a protocol is cancelled without participant enrollment, IRB records are maintained for at least three years after cancellation.

Access

All IRB records are kept secure in locked filing cabinets or locked storage rooms with limited access.

- Ordinarily, access to IRB records is limited to the following:
  – IRB Chairperson
  – IRB members
  – IRB staff
  – Human Subject Signatory Official
  – Compliance Officer
  – Officials of Federal and State regulatory agencies, including OHRP and FDA
- Research investigators are provided reasonable access to files related to their research.
- All other access to IRB records is limited to those who have legitimate need for them, as determined by the IRB Chairperson

For VA Research

The Research and Development Committee has access to all VA IRB records.

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IRB Record Requirements, Continued

IRB membership rosters

All IRB membership rosters include at least the following information:

- Names of IRB members
- Names of alternate members and the corresponding regular member(s) for whom each alternate may serve
- Earned degrees and specialties of each member and alternate, if applicable, sufficient to describe each member's chief anticipated contribution to IRB deliberations
- The representative capacity of each member or alternate as:
  – Scientist or non-scientist
  – Affiliated or non-affiliated
  – Representative of a vulnerable population
- Indications of experience of members sufficient to describe each member's chief anticipated contributions to the IRB deliberations
- Any employment or other relationship with the College or its components

Changes

Any changes in IRB membership are reported as required by applicable OHRP guidance.

Voting and Non-Voting Members

Voting members include: Chairpersons, Vice-Chairpersons, Members, the Director of Research Compliance-IRB, and Alternate members when substituting for regular members.

Non-voting members include: Alternate members when not substituting for regular members, ex officio members (i.e. consultants such as compliance personnel, biological safety officer, and radiation safety officer).

Education and training records

The College is required under its OHRP FWA to have a plan to provide education about human subject protections for research investigators and IRB members and staff.

- The IRB maintains accurate records listing research investigators, IRB members, IRB staff and research staff that have fulfilled the College's human subject protection training requirements.
- Such records are available for review by the Human Subject Signatory Official as a part of compliance monitoring activities and include documentation of completion of the requirements.

Reference: For the specific requirements, see Staff training and development on an earlier topic.

Related standards

AAHRPP I.1.B, I.1.D, I.1.E, II.1.E, II.5.A, II.5.B

IRB File Requirements

Introduction

Date of Last Revision/Review: 03/23/15

This topic discusses the files required to support the IRB reviews.

IRB research application (protocol) files

The IRB maintains a separate file for each research application (protocol) that it receives for review.

Retention
Such files are kept for a period not less than three years after closure.

For VA Research, files must be kept indefinitely until there is a disposition scheduled approved by the National Archives and Records Administration (NARA) and are published in VHA RCS 10-1.

File contents

Each IRB research application (protocol) file contains at least the following materials:

Classification	Materials
IRB approval review	• The IRB Research Application (Protocol) • Documentation of type of IRB review • The IRB-approved informed consent document, with the beginning and ending dates of the current approval period clearly displayed on at least the first page • Copies of all research proposals reviewed and scientific evaluations of the proposed research, if any • Applications for Federal support, if any • Sponsor or cooperative group protocols and sample informed consent documents, if any • Advertising or recruiting materials, if any
Changes	• Applications for protocol amendments or modifications • Continuing review progress reports and related information • **For VA research**, the progress report must include: – The number of participants considered as members of specific vulnerable populations, or – An assurance that all serious or unexpected adverse events had been reported as required
Special challenges	• Reports of unanticipated problems involving risks to subjects or others • Reports of injuries to subjects and adverse events occurring within the College or its components (or involving its employees or agents) and reported to any regulatory agency • Reports of external adverse events and safety reports received from sponsors or cooperative groups

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IRB File Requirements, Continued

File contents (continued)

Each IRB research application (protocol) file contains at least the following materials (continued):

Classification	Materials
Continuing review and monitoring	• Data and Safety Monitoring Board (DSMB) reports, if any • Results of any internal quality control and monitoring activities, if any • All IRB correspondence to and from research investigators, government agencies, data monitoring boards, or sponsors • All other IRB correspondence related to the research • Documentation of all IRB review and approval actions, including initial and continuing convened (full) or expedited IRB review • Documentation of type of IRB review
Upon completion	• Documentation of Project Closeout (The IRB administratively closes and returns to the principal investigator any new research application when additional information requested by the IRB is not submitted within a 60-day period.) • Documentation of statements of significant new findings provided to subjects

IRB database

The Human Subject Signatory Official provides the IRB with access to a centralized IRB research (protocol) tracking database.

Database information

The database includes at least the following information:

- Title of the research (protocol)
- Name of Principal Investigator
- Funding source (if any)
- Date of initial approval
- Date of most recent continuing approval
- End of current approval period
- Type of review (expedited or convened review)
- Current status
  Examples: Under Review, Approved, Suspended, Closed

Related standards

AAHRPP I.1.D, II.2.D, II.5.A

IRB Materials Submission Deadlines

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides the deadlines for submitting materials to the IRB.

Goal

The goal of the IRB is to assist investigators in designing and implementing research that embodies the utmost concern for subjects' safety, dignity, privacy, and autonomy.

Communication with IRB members

With the goal in mind, it is fully acceptable to discuss one's research with IRB members before submission or at any time during the IRB review, approval, or oversight process.

- Advice and discussion improves quality and serves the goals of both the IRB and the investigator.
- IRB staff is also available to assist investigators by answering questions.

Location of forms

The College provides an online protocol submission system (BRAIN) to facilitate submission of materials to its IRB.

Deadlines

This table lists the deadlines regarding IRB reviews and determinations:

Review Type	Deadline
Initial full (convened) Review	Protocol deadlines can be obtained from the Institutional Review Board website.
Continuing Review	May extend no more than 365 days after the convened meeting at which the research was last approved ***Requirement***: The IRB is required to conduct substantive and meaningful continuing review of research not less than once per year.
Continuing Review, expedited	May extend no more than 365 days after the expedited review at which the research was last approved
Determinations for full (convened) reviews	Ordinarily in writing within 7 business days after its meeting
Determinations for expedited reviews	Ordinarily in writing before the meeting date for which the protocol was assigned

Related standards

AAHRPP I.1.D, II.2.C

Chapter 3
IRB Reviews

Table of Contents

Overview for IRB Reviews

Section A Initial Review
- Overview
- Determination of Human Subjects Research
- Initial Review for Exemptions
- Exempt Review Category of Research
- Exempt Emergency Use of a Test Article
- Expedited Review of Research
- Categories of Expedited Review of Research

Section B Convened Full Board Review
- Overview
- Conduct of a Convened Meeting
- Primary and Team Reviewer System
- Research Materials
- Conflicts of Interest in IRB Review
- Minutes of an IRB Meeting
- Actions Taken at the IRB Meeting
- How an IRB Determination Is Provided

Section C Criteria for Approval of Research
- Overview
- Approval Criteria
- Risks Are Minimized
- Psychological, Social, Economic, and Legal Harms
- Equitable Selection of Subjects
- Informed Consent of Subjects
- Other Considerations for Informed Consent
- Safety Monitoring
- Independent Verification from Other Sources
- Location of Research

Section D Confidentiality of Data
- Overview
- Protecting the Privacy of Subjects and Confidentiality of Data
- Additional Confidentiality Safeguards
- Confidentiality of Data Sets
- Confidentiality with Data or Tissue Banks
- Research Involving Epidemiology
- Genetic and Family Research
- Research Involving Deception or Withholding of Information

Continued on next page

Table of Contents

Section E Reviews After Approval
- Overview
- Initial and Continuing Review by the Convened IRB
- Continuing Review Deadline Issues
- Changes in Previously Approved Research
- Suspension or Termination of IRB Approval
- Event Reporting Required of Principal Investigators
- IRB Review of Event Reports for Determination of (UPIRSO) Unanticipated Problems Involving Risks to Subjects or Others
- Reporting and Assessing Compliance Concerns
- Chain of Reporting

Overview for IRB Reviews

Introduction	Date of Last Revision/Review: 04/20/11 This chapter provides the information needed for all types of IRB reviews.
Types of reviews	The IRB has responsibility for three types of reviews: • Initial review in which the IRB chair or designee determines that the research is either exempt from IRB review or meets the requirements for expedited review • Full board review in which all members meet and discuss the request • Continuing review in which the IRB meets to review ongoing research
Reporting responsibility	Whether involved in the research or not, all employees and agents of Baylor College of Medicine and its affiliates are required to notify the IRB if they become aware of any non-compliance with human subject regulatory requirements or with the determinations of the IRB.
In this chapter	This chapter covers the following sections: • Section A: Initial Review • Section B: Convened Full Board Review • Section C: Criteria for Approval of Research • Section D: Confidentiality of Data • Section E: Reviews After Approval
Related standards	AAHRPP I.1.D, I.5.D, II.2.A, II.2.B, II.2.C, II.2.D, II.2.E, II.2.F, II.2.G, II.2.H

Section A
Initial Review

Overview

Introduction	Date of Last Revision/Review: 04/20/11 This section focuses on the initial review of proposed research to determine the best path for the review.
When to begin	When the Primary Investigator submits the request for an IRB review via BRAIN, the IRB Chairperson or designee reviews the request to determine whether the proposed activities constitute research involving human subjects, meet exemption criteria, and whether expedited review is appropriate. If the Primary Investigator has included this information in the request, the IRB must verify that the research meets the criteria.
In this section	This section covers the following topics: • Determination of Human Subjects Research • Initial Review for Exemptions • Exempt Review Category of Research • Exempt Emergency Use of a Test Article • Expedited Review of Research • Categories of Expedited Review of Research
Related standards	AAHRPP I.1.A, I.1.D, II.2.A, II.2.B, II.2.E

Determination of Human Subjects Research

Introduction

Date of Last Revision/Review: 12/05/23

The determination of whether activities constitute research involving human subjects/participants requires a sophisticated level of understanding of the applicable regulations.

After reviewing applicable policy and guidance, Investigators are responsible to assure that all human subjects research is prospectively reviewed by the BCM IRB.

Who verifies

When there is doubt about whether or not a proposed activity meets the regulatory definition of Human Subjects Research, Investigators should seek guidance from the IRB office as to when to submit a summary of activities for a determination of research involving human subjects.

The IRB office determination of whether the activities meet the regulatory definitions for research involving human subjects/participants will be made by one of the following:

- The IRB Chairperson
- An experienced member of the IRB
- Another qualified professional designated by the Human Subject Signatory Official following appropriate training
- ***Note*****:** BCM investigators at affiliated institutions must be aware of and comply with the institutions' requirements. For example, proposed QI activities to be conducted at Harris Health must receive a determination from the IRB prior to the start of the project.

Required information to be submitted

In reviewing human subject research determinations, the investigator must supply enough information to the reviewer to ascertain whether or not the proposed activities meet the regulatory definitions of human subjects research.

Documentation

Documentation of the verified determination consists of the reviewer's written concurrence in the IRB Research Review File that the activity described in the Investigator's Application does or does not satisfy the definition of the human subject research. The investigator proposing the activities will receive a notification stating the determination.

The justification for and the criteria for the determination that a proposed research protocol does not constitute human subjects research, and that 45 CFR 46 does not apply to the research, will be documented in the IRB records.

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Determination of Human Subjects Research, Continued

Examples of human subjects research

In addition to traditional biomedical studies, the IRB must review and approve research involving:

- Data collected through intervention or interaction with individuals. Intervention includes physical procedures (*e.g.,* drawing blood) as well as research on individual or group characteristics or behavior (*e.g.,* perception, cognition, motivation, identity, language, communication, and cultural beliefs or practices)
- Human beings used to test devices, products or materials that have been developed through research
- Survey, interview, oral history, focus group, program evaluation, evaluation of human factors, or quality assurance methodologies
- Private information that can be readily linked to an individual, even if the information was not collected specifically for the study in question
- Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens
- Bodily materials (such as cells, blood or urine, tissues, hair or nail clippings) if the materials are identifiable when received by the PI, even if these materials were not collected by the Baylor College of Medicine investigator

ALL research involving human subjects conducted by faculty, staff, or students (including undergraduate honors theses, masters' theses, and doctoral dissertations) must be reviewed and approved by the appropriate IRB before the activity begins**.**

Case reports

Case reports or case series describing interesting observations on three or fewer patients do not meet the definition of research as a systematic investigation designed to contribute to generalizable knowledge. Therefore, the IRB does not review or approve such reports.

Case series including more than three patients will be considered research and will require IRB review and approval prior to the conduct of the research.

Even though a case series of three or fewer patients does not constitute research, it is still subject to HIPAA rules. Investigators therefore may be required to de-identify all data disclosed (as defined by HIPAA) or to obtain patient authorization to disclose private health information.

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Determination of Human Subjects Research, Continued

Activities that are deemed NOT to be research	For purposes of 45 CFR 46.102(I), the following activities are deemed not to be research: 1) Scholarly and journalistic activities (*e.g.,* oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected. (2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. –Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). –Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters). (3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes. (4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. *Written,* or *in writing,* for purposes of this part, refers to writing on a tangible medium (*e.g.,* paper) or in an electronic format.
Activities that may meet the federal definition of "research" but not constituting human subjects research	In analyzing whether a particular activity is research involving human subjects, it is important to focus on what is being obtained by the investigators. If the investigators are not obtaining either data through intervention or interaction with living individuals, identifiable private information, or identifiable biospecimens, then the research activity does not involve human subjects.
Regulations and Guidance	45 CFR 46, 21 CFR 50, Guidance on Research Involving Coded Private Information or Biological Specimens, OHRP, August 10, 2004
Related standards	AAHRPP I.1.A, I.1.D, I.1.D, I.1.A, II.2.D, II.2.E

Initial Review for Exemptions

Introduction

Date of Last Revision/Review: 01/13/21

The determination of whether human subject research activities are exempt from the Federal regulations requires a sophisticated level of expertise and is not left to individual investigators proposing the activities. BCM reserves the right to suspend or terminate IRB approval of research approved with a limited IRB review.

Who verifies

All exemptions claimed for proposed human research activities conducted at the College or by its employees or agents must be reviewed to determine if they meet the regulatory criteria for exempt research involving human subjects/participants as well as the ethical standards of the College. Exemption of these research activities must be verified by one of the following:

- The IRB Chairperson
- An experienced member of the IRB
- Another qualified professional designated by the Human Subject Signatory Official following appropriate training

Exception: The emergency use of a test article

Required information

In reviewing exemption requests, the investigator must supply enough information to the reviewer to ascertain whether the claimed regulatory exemption criterion genuinely applies.

Documentation

Documentation of the verified exemptions consists of the reviewer's written concurrence in the IRB Research Review File that the activity described in the Investigator's Application for Exempt Research satisfies the conditions of the cited exemption category. The investigator proposing the activities will receive a notification stating the determination.

For VA research, exemption determinations shall be communicated to the investigator and the VA Research and Development Committee through the VA Research Office.

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Initial Review for Exemptions, Continued

Regulations

The categories of exempt research are stipulated in the Federal Policy (Common Rule) and in DHHS regulations at 45 CFR 46.104(d).

***Note*:** The College, however, only grants one of the eight exemptions to research that is specifically covered under 45 CFR 46.104(d)(5). All other categories of exemption under the Common Rule are reviewed by the IRB using expedited procedures.

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 which are designed to study, evaluate, improve or otherwise examine:

- Public benefit or service programs
- 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.

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.

Related standards

AAHRPP I.1.A, I.1.D, II.2.A, II.2.B, II.2.C

Exempt Review Category of Research

Introduction

Date of Last Revision/Review: 03/04/21

Some research is exempt from further IRB review. Exemption waives only the need for further review and does not negate the need for the consent of subjects where applicable.

Changes to exempt research

Any change to exempt research can compromise its exempt status under the regulations and must be reviewed by the IRB office as a new abbreviated protocol submission referencing the assigned protocol number for the previous exempted version.

No expiration of exempt research

The IRB does not require continuing review of exempt research. Investigators must assure that the research is conducted ethically and without changes that may compromise its exempt status.

Regulations and category of exemption

The categories of exempt research are stipulated in the Federal Policy (Common Rule) and in DHHS regulations at 45 CFR 46.104(d).

***Note*:** The College, however, only grants one of the eight exemptions to research that is specifically covered under 45 CFR 46.104(d)(5). All other categories of exemption under the Common Rule are reviewed by the IRB using expedited procedures.

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 which are designed to study, evaluate, improve or otherwise examine:

- Public benefit or service programs
- 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.

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.

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Exempt Review Category of Research, Continued

Regulations and category of exemption (continued)	***Note*:** The following criteria must be satisfied to invoke the exemption for research and demonstration projects examining "public benefit or service programs": • The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act) • The research or demonstration project must be conducted pursuant to specific federal statutory authority • There must be no statutory requirement that the project be reviewed by an Institutional Review Board (IRB) • The project must not involve significant physical invasions or intrusions upon the privacy of participants • Concurrence from the funding agency ***Note:*** This category may be applied to research involving children, *pregnant women, fetuses, and neonates*. This category may NOT be applied to research involving prisoners or to FDA-regulated research.
VA research	Research determined to be exempt requires approval by the R&D Committee. Continuing review approval for exempt research is not required by the R&D Committee for continuing review following initial approval. However, continuing review by R&D is needed, per VHA Directive 1200.05, if the exempt research is under the oversight of another subcommittee (e.g., Safety Review Subcommittee).
Related standards	AAHRPP I.1.A , I.1.D, II.2.A, II.2.B, II.2.C

Exempt Emergency Use of a Test Article

Introduction

Date of Last Revision/Review: 04/20/11

This topic discusses the use of a test article in an emergency situation. See FDA Infosheet.

Note: Exempt emergency use of a test article does NOT refer to use of individual patient INDs, see Treatment INDs and IDEs.

Institutional requirements

All emergency uses of test articles conducted at the College or by its employees or agents must be compliant with the FDA regulations and must be reported to the IRB as required.

All emergency uses of test articles conducted at the College or by its employees or agents reported to the IRB will be reviewed by an individual knowledgeable of FDA regulations to determine if they complied with the FDA regulations. Additionally, the individual will determine if the emergency use did not meet the DHHS definition of research under the Federal Policy and the DHHS Subpart A, Definitions.

The Director of Research Compliance-IRB, in consultation with the IRB Chair or another qualified professional designated by the Human Subject Signatory Official will make this determination.

For more information regarding the reporting, see After any emergency use of a test article.

Types of exemptions

There are two types of exemptions that arise regarding the emergency use of a test article:

Types:	Description: The emergency use of an investigational drug, device, or biologic is permitted …
Without IRB approval but with informed consent	On a human subject in a life-threatening or severely debilitating situation on a one-time basis per institution without IRB review and approval in which all of the specific conditions listed below are met. In an emergency use situation without IRB review and approval, the investigator or treating physician should ensure and document that ALL of the following conditions are met before proceeding with the use of the test article: • A human subject is in a life-threatening situation, and, • No standard acceptable treatment is available, and, • There is insufficient time to obtain IRB approval, and • Informed consent from the subject or legally authorized representative will be obtained prior to the emergency use. ***Note*:** This emergency use must not meet DHHS definition of research under the Federal Policy and the DHHS Subpart A Definitions. See FDA Infosheet. ***Reference*:** FDA regulations at 21 CFR 56.102(d) and 21 CFR 56.104 (c), 45 CFR 46.102(d)

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Exempt Emergency Use of a Test Article, Continued

Types of exemptions (continued)

There are two types of exemptions that arise regarding the emergency use of a test article (continued):

Types:	Description: The emergency use of an investigational drug, device, or biologic is permitted …
Without IRB approval and without informed consent	Without IRB review and approval and without informed consent where the investigator and an independent physician who is not otherwise participating in the clinical investigation certify in writing all of the specific conditions listed below are met. Even in an emergency use situation without IRB review and approval, the investigator is required to obtain informed consent from the subject or the subject's legally authorized representative. The only exception is if both the investigator and a physician that is not otherwise participating in the clinical investigation (the treatment and medical care of the subject with the test article) certify in writing that ALL of the following conditions have been met for the emergency use of the test article without informed consent: • The subject is confronted by a life-threatening situation necessitating the use of the test article, and, • Informed consent cannot be obtained because of an inability to communicate with the subject or obtain legally effective consent from the subject, and, • Time is not sufficient to obtain consent from the subject's legally authorized representative, and, • No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life. ***Note 1*:** If in the investigator's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. ***Note 2*:** This emergency use must not meet DHHS definition of research under the Federal Policy and the DHHS Subpart A Definitions. ***Reference*:** FDA regulations at 21 CFR 50.23

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Exempt Emergency Use of a Test Article, Continued

After any emergency use of a test article	The emergency use must be reported to the IRB within 5 working days. This notification or report to the IRB must contain the following information: • Short background of the patient and his/her condition • Description of the emergency and the use of the investigational drug, device, or biologic • Statement confirming that EACH one of the required four conditions for the emergency use were met • Statement confirming that EACH one of the required four conditions for emergency use without informed consent were met (if consent was not obtained prior to the emergency use) • Statement that no new use of the investigational drug, device, or biologic will occur without prior IRB review and approval ***Important***: Such reporting must not be construed as IRB approval for the emergency use. ***Note***: Data obtained from an emergency use of a test article cannot be used in prospectively planned research that would meet the DHHS definition of research under the Federal Policy and the DHHS Subpart A Definitions.
Documentation	The IRB staff is responsible for maintaining the documentation of emergency use in the IRB records.
Clarification of the term: **Compassionate Use**	For studies involving investigational drugs, "Compassionate Use" is often meant to refer to the emergency use situations discussed earlier. "Compassionate use" sometimes refers to use of an unapproved agent obtained under an individual patient IND (also called single patient IND); see FDA Infosheet. Legality: "Compassionate use" is not a term that appears in the FDA or DHHS regulations or the Common Rule. The FDA regulations do not provide for expedited IRB approval in emergency situations. Therefore, "interim," "compassionate," "temporary" or other terms for an expedited approval process are not authorized. "Compassionate use" situations should not be confused with the Humanitarian Use Device (HUD) Exemption. ***Reference***: See Humanitarian Device Exemptions.
More information	For more information, see the following topics in Chapter 5, IRB Review of FDA-Regulated Research: Investigational Drugs, Devices, and Biologics: • Emergency Use of a Test Article Without IRB Review • Emergency Use of a Test Article Without Informed Consent
Related standards	AAHRPP I.1.D, I.7.C, II.2.D, II.2.E

Expedited Review of Research

Introduction

Date of Last Revision/Review: 01/13/21

This topic discusses the expedited path for a review of the research.

When applicable

The IRB reviews research through an expedited procedure if either:

- The research constitutes a minor change in previously approved research during the period for which approval is authorized (see Changes in Previously Approved Research) or
- The research activities present no more than minimal risk to human subjects and involve only procedures listed in one or more of the Categories of Expedited Review of Research authorized by 45 CFR 46.110 and 21 CFR 56.110 as published in the November 9, 1998 DHHS-FDA list of research eligible for expedited IRB review 63 FR 60353-60356 and 60364-60367, unless the reviewer determines that the study involves more than minimal risk
- Research for which limited IRB review is a condition of exemption. See Exempt Review Category of Research
- 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
- The expedited review procedure may not be used for classified research involving human subjects
  ***Note*:** The VA does not conduct classified research involving human subjects.
- 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

Reference: DHHS regulations, the Federal Policy (Common Rule), and FDA regulations

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Expedited Review of Research, Continued

IRB review	Under an expedited review procedure, the IRB Chairperson, an experienced voting IRB member or a group of experienced voting IRB members (serving as a subcommittee) designated by the Chairperson may: • Review and approve the research on behalf of the IRB • Review and approve the research on behalf of the IRB requiring modifications (to secure approval) • Request additional information • Forward the application to the fully convened IRB when, in the opinion of the expedited reviewer(s), the research does not meet the expedited review criteria described above in the When applicable section. ***Note***: Experienced IRB member is an IRB member that has participated in at least one IRB training session and 16 IRB meetings (typical two-year service with 75% attendance). The IRB Chairperson informs the IRB staff responsible for the support of the IRB who the designated reviewers are for the expedited review process for items to be reviewed by that IRB.
Disapproval of research	The expedited reviewer may not disapprove any research activity. The research activity may be disapproved only after review by the fully convened IRB.
Requirements	For initial or continuing reviews conducted by expedited review: • The designated voting IRB member should receive all of the materials listed in the section Research Materials • The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review.
Documentation of expedited review	Documentation for expedited reviews is maintained in IRB records and includes the category and circumstances that justify using expedited procedures. The IRB staff keeps all IRB members advised of research that has been approved under expedited procedures by providing a list of the research approved by expedited procedures to the IRB members. **For VA research**, expedited determinations shall be communicated to the investigator and the VA Research and Development Committee through the VA facility Research Office.
Re-review request	At the request of any IRB member, the fully convened IRB may re-review any research that has been approved using expedited review procedures if, in the opinion of the expedited reviewer(s), the research does not meet the expedited review criteria described above in the When applicable section. The re-review is conducted in accordance with the IRB's usual non-expedited procedures.
Related standards	AAHRPP I.1.D, II.2.C-E, II.2.E.1, II.2.E.2, II.2.E.3

Categories of Expedited Review of Research

Introduction

Date of Last Revision/Review: 04/20/11

This topic lists the categories of research that can use expedited procedures.

Criteria

The IRB may utilize expedited procedures for the initial or continuing review of research that is both of the following:

- Has no greater than minimal risk
- Falls within the FDA/DHHS-specified expedited review categories
  Reference: 63 FR 60353-60356 and 60364-60367, November 9, 1998
- The categories in this list apply regardless of the age of subjects, except as noted
- Categories one (#1) through seven (#7) pertain to both initial and continuing IRB review

Important

These categories do **not** apply to research involving prisoners.

Categories

This table lists the categories of research that can use expedited procedures:

Expedited Category	Description
#1	Clinical studies of drugs and medical devices only when condition one of the following is met: • Research on drugs for which an investigational new drug application is not required. Exception: 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. ***Reference***: 21 CFR Part 312 • Research on medical devices for which one of the following applies: – An investigational device exemption application is not required. ***Reference***: 21 CFR Part 812 – 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, to occur no more frequently than 2 times per week in an 8-week period, as follows: • From healthy, non-pregnant adults who weigh at least 110 pounds. ***Amount drawn***: May not exceed 550 ml • From other adults and children, 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 ***Amount drawn***: May not exceed the lesser of 50 ml or 3 ml per kg

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Categories of Expedited Review of Research, Continued

Categories (cont) This table lists the categories of research that can use expedited procedures (continued):

Expedited Category	Description
#3	Prospective collection of biological specimens for research purposes by non-invasive means. ***Dental examples***: • Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction • Permanent teeth if routine patient care indicates a need for extraction • 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 ***Mouth/nose area examples***: • Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue • Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings • Sputum collected after saline mist nebulization ***Labor examples***: • Placenta removed at delivery • Amniotic fluid obtained at the time of rupture of the membrane before or during labor ***Other examples:*** • Excreta and external secretions (including sweat) • Hair and nail clippings in a non-disfiguring manner

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Categories of Expedited Review of Research, Continued

Categories (cont) This table lists the categories of research that can use expedited procedures (continued):

Expedited Category	Description
#4	Collection of data through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, ***Exclusions***: Procedures involving x-rays or microwaves **Medical devices** • 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***: • 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 • Weighing or testing sensory acuity • Magnetic resonance imaging • Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography • Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual

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Categories of Expedited Review of Research, Continued

Categories (cont) This table lists the categories of research that can use expedited procedures (continued):

Expedited Category	Description
#5	Research involving materials, such as data, documents, records, or specimens, that have been collected or will be collected solely for non-research purposes ***Examples***: Medical treatment or diagnosis **Clarification** The intent of the drafters was to define two categories here, each appropriate for expedited review: • Research involving materials that have already been collected (for any previous research or non-research purpose) at the time when the research is proposed • Research involving materials that will be collected in the future (prospectively) for a non-research purpose Prospective studies are designed to observe outcomes or events, such as diseases, behavioral outcomes, or physiological responses that occur subsequent to identifying the targeted group of subjects, proposing the study, and initiating the research. ***Note***: A prospective study using materials (data, documents, records, or specimens) that will exist in the future because they will be collected in the future (after the research has been proposed and initiated) for some purpose unrelated to the research, such as routine clinical care, would qualify for this expedited review category ***Examples***: Clinical observations, medical treatment, or diagnosis occurring in a non-research context would qualify for these expedited criteria. However, data to be collected prospectively for the research (by procedures only to be conducted for the research) would not qualify for this expedited category.
#6	Collection of data from voice, video, digital, or image recordings made for research purposes

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Categories of Expedited Review of Research, Continued

Categories (cont) This table lists the categories of research that can use expedited procedures (continued):

Expedited Category	Description
#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 For Department of Defense (DOD) regulated research: Surveys and/or questionnaires performed on DOD personnel must be submitted by the PI, reviewed, and approved by the DOD after the research protocol is reviewed and approved by the IRB. If there are any changes to the surveys and/or questionnaires required by the DOD, the PI is required to submit these surveys and/or questionnaires with the changes to the IRB for review and approval prior to implementing them. See U.S. Department of Defense Research.
#8	Continuing review of research previously approved by the convened IRB where the status of the research is described by at least one of the following: (a) Where all the following apply: – The research is permanently closed to the enrollment of new subjects – All subjects have completed all research-related interventions – 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 (c) Where the remaining research activities are limited to data analysis ***Note*:** For a multi-center protocol, an expedited review procedure may be used by the IRB at a particular site whenever the conditions of category #8 (a), (b), or (c) are satisfied for that site. However, with respect to category #8(b), while the criterion that "no subjects have been enrolled" is interpreted to mean that no subjects have ever been enrolled at a particular site, the criterion that "no additional risks have been identified" is interpreted to mean that neither the investigator nor the IRB at a particular site has identified any additional risks from any site or other relevant source.

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Categories of Expedited Review of Research, Continued

Categories (continued)

This table lists the categories of research that can use expedited procedures (continued):

Expedited Category	Description
#9	Continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories 2 through 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

Related standards

AAHRPP I.1.D, II.2.C, II.2.D, II.2.E, II.2.E.1, II.2.E.2, II.2.E.3

Section B
Convened Full Board Review

Overview

Introduction

Date of Last Revision/Review: 04/20/11

This section discusses the IRB review by the convened full board.

Requirement

All human subject research conducted at the College or by its components must be reviewed and approved by an IRB designated by the Human Subject Signatory Official.

No human subject research may be initiated or continued at the College or any of its affiliates or by any of its employees or agents without prior approval of an IRB officially designated under the College FWA.

In this section

This section covers the following topics:

- Conduct of a Convened Meeting
- Primary and Team Reviewer System
- Research Materials
- Conflicts of Interest in IRB Review
- Minutes of an IRB Meeting
- Actions Taken at the IRB Meeting
- How an IRB Determination Is Provided

Related standards

AAHRPP I.1.D, II.2.D, II.2.E

Conduct of a Convened Meeting

Introduction

Date of Last Revision/Review: 04/20/11

This topic describes the conduct of a convened meeting of the IRB.

Quorum requirements

The IRB conducts initial and continuing reviews of all non-exempt research that do not meet expedited criteria at fully convened IRB meetings.

In order to have a quorum for a fully convened IRB meeting:

- At least one member whose primary concerns are in non-scientific areas must be present
- A majority of the members must be present
- The Director of Research Compliance-IRB is responsible for making the determination of whether an IRB meeting is appropriately convened with a quorum and when the convened IRB meeting loses quorum.

For research to be approved, it must receive the approval of a majority of those members present.

Reference: Per Federal regulations, the Federal Policy (Common Rule) for the Protection of Human Subjects, and FDA regulations

For VA research

If the research involves an FDA regulated article, a licensed physician must be present.

At least one voting VA IRB member must be present during review of VA research.

Timing and scheduling of IRB meetings and agenda items

Each IRB will have a regularly scheduled meeting each month. The IRB meeting schedule will be communicated in advance to the IRB members for the purpose of each member's attendance planning to fulfill membership requirements.

Each IRB meeting should last only as long as necessary to efficiently carry out the important IRB business of protocol review as well as any education that requires the presence of the full committee. For this purpose, the IRB staff and the IRB Chairperson may limit the number of agenda items accordingly to the time frames of the planned members' attendance.

Telephonic/video conferencing

IRB members may participate in convened IRB meetings via telephonic and video conferencing in accordance with applicable guidance from FDA and OHRP.

Discussion

All IRB members are afforded full opportunity to discuss each research proposal during the convened meeting.

Related standards

AAHRPP I.1.D, II.1.A, II.2.C, II.2.D, II.2.E

Primary and Team Reviewer System

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides a description of the Primary and Team Reviewer System for an IRB review of human research.

Primary/Team Reviewers

The IRB utilizes the Primary and Team Reviewer System to assist in the initial and continuing review of research by the convened IRB.

The Primary and Team Reviewers are considered to be the lead reviewers for research proposals assigned to them. All IRB members are expected to review the materials provided to them in order to make an informed decision regarding the research at the convened meeting.

***Note**:* Renewals and amendments may be reviewed by a single primary reviewer.

References: In accordance with FDA and OHRP guidance

Assignment

The IRB Analyst assigns protocols in BRAIN upon receipt of a complete set of IRB application materials:

- To one primary and at least two team reviewers based on their scientific and scholarly expertise
- Also, if there are no members with the required scientific and scholarly expertise, to a consultant with the required scientific and scholarly expertise
- Approximately 7-10 days before the meeting date when that protocol is to be discussed and voted upon

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Primary and Team Reviewer System, Continued

Responsibilities

The Primary Reviewers:

- Are thoroughly versed in all details of the research
- Conduct an exhaustive review of the research using all submitted materials
- Contact individual investigators for clarification as needed before the convened meeting or ask the IRB staff to seek this clarification from the investigator
- Fill out the appropriate Primary Reviewer forms by preparing a brief summary of the protocol to the Board Comments section as follows:
  - This written summary will be added to the minutes for that meeting.
  - The summary must include the discussion basis for the approval of the research, requiring changes in (approved with modifications or tabled) the research protocol; or disapproving the research protocol.
  - The summary may include a pre-meeting motion based on the review of the protocol.
- Lead the discussion of the proposed research at the convened meeting of the IRB giving a brief summary of the protocol and facilitating any discussion prompted by the summary and the comments available at the meeting with the assistance of the Chairperson

Note: The primary reviewer typically makes the motion to approve, request modifications in, table, or disapprove the research protocol.

Team Reviewers:

- Are thoroughly versed in all details of the research
- Conduct an exhaustive review of the research using all submitted materials
- Contact individual investigators for clarification as needed before the convened meeting or ask the IRB staff to seek this clarification from the investigator
- Fill out the appropriate Team Reviewer forms
- Assist in leading the discussion of the proposed research at the convened meeting of the IRB and facilitating any discussion prompted by the summary and the comments available at the meeting with the assistance of the Chairperson

Note: In the absence of the primary reviewer at the meeting, the secondary reviewer of the protocol will be asked to present the findings.

Use of subcommittees

The IRB may utilize subcommittees to support IRB review activities. The IRB Chairperson may appoint subcommittees:

- To perform expedited reviews
- To fulfill the duties of Primary and Team reviewers
- On an ad hoc basis to perform additional functions as needed

Related standards

AAHRPP I.1.D, II.1.E, II.2.C, II.2.D, II.2.E

Research Materials

Introduction

Date of Last Revision/Review: 04/20/11

This topic describes the required research materials for an IRB review.

Access to research file

Except for unusual circumstances, at least one week before the convened meeting, the complete IRB file for all research to be discussed during the meeting is provided to all IRB members for their review in BRAIN, and the entire IRB file is present in the meeting room during the meeting.

Reason: To provide sufficient time for all IRB members to review each proposed project before the meeting so they can discuss each project adequately and determine the appropriate action during the convened review. All IRB members are expected to review the materials provided to them in order to make an informed decision regarding the research at the convened meeting.

Continued on next page

Research Materials, Continued

Materials IRB members review

The following table lists the materials IRB members review depending on their role and the type of submission they are reviewing:

Type of submission	*Primary members review (full board and expedited)*	*Team members review (full board and expedited if applicable)*	*All other members review (full board)*
Initial Submissions	• The complete protocol • A protocol application • A proposed informed consent document • Grant application(s) • Investigator's brochure (if one exists) • Recruitment materials, including advertisements intended to be seen or heard by potential subjects • Financial interests disclosure and proposed management plan • For HHS-supported multicenter clinical trials, the IRB should receive and review a copy of the HHS-approved sample informed consent document and the complete HHS-approved protocol, if they exist	• The complete protocol • A protocol application • A proposed informed consent document • Grant application(s) • Investigator's brochure (if one exists) • Recruitment materials, including advertisements intended to be seen or heard by potential subjects • Financial interests disclosure and proposed management plan • For HHS-supported multicenter clinical trials, the IRB should receive and review a copy of the HHS-approved sample informed consent document and the complete HHS-approved protocol, if they exist	• Protocol application (of sufficient detail to make the determinations required under HHS regulations at 45 CFR 46.111) • The proposed informed consent document • Any recruitment materials, including advertisements intended to be seen or heard by potential subjects • The complete documentation is available to all members for review
Continuing Review Submissions	• The complete protocol • A protocol application • Modifications previously approved by the IRB • A protocol application • A renewal application describing the progress of the research • Financial interests disclosure and proposed management plan • A copy of the current informed consent document	• The complete protocol • A protocol application • Modifications previously approved by the IRB • A protocol application • A renewal application describing the progress of the research • Financial interests disclosure and proposed management plan • A copy of the current informed consent document	• A protocol application • A renewal application describing the progress of the research • A copy of the current informed consent document • The complete documentation is available to all members for review

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Research Materials, Continued

Materials IRB members review (continued)

The following table lists the materials IRB members review depending on their role and the type of submission they are reviewing (continued):

Type of submission	*Primary members review (full board and expedited)*	*Team members review (full board and expedited if applicable)*	*All other members review (full board)*
Amendments	• A summary of the proposed amendment(s) • The complete protocol with proposed revisions • Modifications previously approved by the IRB • A protocol application • A copy of the current informed consent document with proposed revisions • The complete documentation is available to all members for review	All changed documents	All changed documents
	Source: Office for Human Research Protections (OHRP), Department of Health and Human Services, Guidance on Written IRB Procedures, July 11, 2002		

Meeting documentation

The minutes of IRB meetings will document separate deliberations, actions, and votes for each protocol undergoing initial review by the convened IRB.

Confidentiality of IRB reviews, files, and records

All research materials submitted by the Principal Investigator for review are reviewed by the IRB and archived in a manner that maintains the confidentiality of the documents related to all the participants of the research team, sponsor, and all research subjects.

Related standards

AAHRPP I.1.D, II.2.C, II.2.D, II.2.E

Conflicts of Interest in IRB Review

Introduction

Date of Last Revision/Review: 12/14/15

This topic discusses conflict of interest and members of the IRB.

Requirement

No IRB member, or consultant to the IRB, may participate in the IRB's initial or continuing review of any protocol in which the member has a conflicting interest, except to provide information requested by the IRB.

Conflicts of interest can be either financial or non-financial.

The IRB shall ensure that steps are taken to manage, reduce, eliminate potential/real conflicts of interest i.e. financial, role (investigator/patient relationships), or institutional.

IRB members (including the chairperson, and any consultants solicited for review) who have conflicting interests, or an immediate family member with a conflicting interest, are required to disclose such interests and to recuse and absent themselves from the: review of, deliberations on, quorum counts for, and votes on the relevant protocol.

Documentation: Such recusals and absences are recorded in the IRB meeting's minutes and the same procedures apply to expedited review of research.

Applicability

This procedure applies to all of the following types of IRB reviews and determinations:

- Protocols reviewed using the expedited procedures
- Protocols reviewed by the fully convened IRB
- Reviews of potential unanticipated problems involving risks to subjects or others
- Assessments of concerns of non-compliance with regulations, laws, College policies and procedures, and requirements of the IRB

Discussion

While many IRB members also conduct research, it remains their ongoing responsibility to disclose any conflicting interests to appropriate institutional officials and to recuse and absent themselves appropriately from any IRB deliberations on which they may be conflicted.

For this reason, IRB members are required to declare a conflict of interest and recuse and absent themselves from deliberation and voting on that agenda item.

Related standards

AAHRPP I.1.D, I.6.A, II.1.B, II.1.C, II.1.D, II.2.C, II.2.D, II.2.E, Disclosure of Outside Interests Policy #31.2.01

Minutes of an IRB Meeting

Introduction

Date of Last Revision/Review: 01/13/21

This topic provides an overview of the documentation requirements for the minutes of the IRB meeting. All IRB determinations are in feedback in BRAIN.

Important: Specific action documentation is covered in the next topic.

Contents overview

The meeting minutes are a record of the following specific information:

- Attendance
- Member and consultant recusals and absences due to conflicts of interest
- Quorum requirements
- Actions taken by the IRB on the initial or continuing review of research
  Examples:
- Review of protocol or informed consent modifications or amendments
- Unanticipated problems involving risks to subjects or others
- Adverse event reports
- Reports from sponsors, cooperative groups, or DSMBs
- Reports of continuing non-compliance with the human subject regulations or IRB determinations
- Suspensions or terminations of research
- Protocol-specific votes for any action involving the review of research protocols
- Separate votes for other IRB actions
- Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document
- The basis for requiring changes in or disapproving research
- Summary of controverted issues and their resolution
- Required IRB findings and determinations
- The IRB's determination of and the rationale for a device's significant or non-significant risk determination
- Records must include the rationale for conducting continuing review on research that otherwise would not require continuing review.
- Records must include the rationale for an expedited reviewer's determination that research appearing on the expedited review list is more than minimal risk.
- Records must include documentation specifying the responsibilities that a relying organization and an organization operating an IRB each will undertake to ensure compliance with the requirements of the Common Rule.

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Minutes of an IRB Meeting, Continued

Contents overview for VA research

For VA research (in addition to the above):

- Once the IRB approves the minutes, they may not be altered
- Research approved contingent on specific minor conditions by the chair or designee are documented in the minutes of the first IRB meeting that takes place after the approval
- If VA research includes vulnerable population subjects, all determinations in VA regulations shall be met. The IRB documents in the minutes or IRB records, the findings required by VA regulations.
- IRB minutes must be submitted to the research and development committee in a timely manner. When relying on an affiliate IRB, the affiliate may either provide unredacted copies of minutes, or provide redacted minutes but allow VA personnel, including ORO and the local VA research office staff, research compliance officer, and members of the research and development committee to review unredacted minutes within two days of a request.

Attendance

IRB minutes list attendance as follows:

- Names of members present
- Names of absent members
- Names of alternates attending in lieu of specified (named) absent members (alternates may substitute for specific absent members only as designated on the official IRB membership roster)
- Names of non-voting members and consultants present
- Name of investigators present
- Names of guests present

Attendance via teleconference

Members may be present via audio (telephone) or audio-visual teleconference with the meeting minutes indicating that these members:

- Are present via teleconference
- Received all pertinent information before the meeting
- Were able to participate actively and equally in all discussions

Continued on next page

Minutes of an IRB Meeting, Continued

Quorum standard	IRB minutes include a statement of Quorum Requirements based on the following standard: • A majority of the IRB members (or their designated alternates), including at least one member whose primary concerns are in nonscientific areas, must be present to conduct a convened meeting. • For research to be approved, it must receive the approval of a majority of those members present at the meeting • Members present via audio (telephone) or audio-visual teleconference count in the quorum **<u>For VA research</u>** • At least one voting VA IRB member must be present during review of VA research • A licensed physician must be part of the quorum for the review of VA regulated research utilizing any FDA-regulated test article
Quorum documentation	IRB minutes include documentation of quorum and votes for each IRB action by recording votes as follows: • Total number voting • Number voting for • Number voting against • Number abstaining
Roster listing	An individual who is not listed on the official IRB membership roster may not vote with the IRB and does not contribute to the quorum.
Conflict of interest	Members recusing and absenting themselves due to conflicting interests may not be counted toward quorum requirements (may not be counted among those voting or abstaining).
Related standards	AAHRPP I.1.D, II.1.D, II.2.C, II.2.D, II.2.E, II.5.B

Actions Taken at the IRB Meeting

Introduction

Date of Last Revision/Review: 11/12/20

This topic provides the documentation in the minutes for the actions taken at the IRB meeting, including the following:

- Requirement
- Notification of investigators
- IRB review summary
- Disapproval/controverted issues
- Findings and determinations
- Actions after meeting
- IRB Protocol Approval Dates

Requirement

IRB minutes include all actions taken by the convened IRB and the votes underlying those actions.

Notification of investigators

These actions are also provided in writing to investigators in the form of a memorandum from the IRB which includes, at minimum, the following information (where appropriate):

- Investigator's name
- Title of study
- IRB number
- Approval date
- Continuing review interval
- Changes to the materials submitted in order to secure approval

Note: The Human Subject Signatory Official is provided a written summary of all the IRB's actions in the form of IRB meeting minutes after they are approved by the IRB.

Continued on next page

Actions Taken at the IRB Meeting, Continued

IRB review summary

This table describes the actions the IRB may take to be documented in the minutes:

When the research is …	Then …
Approved as submitted with no changes/additional changes required	The research may proceed.
Approved with modifications	• Such minor changes must be clearly delineated by the IRB so the investigator may simply concur with the IRB's stipulations. • Such minor changes require the review and approval of a designated voting IRB member. • The research may proceed after the required changes are verified and the protocol approved by the designated reviewer.
Tabled	The research may proceed only after the same fully convened IRB has reviewed and approved: • The required substantive changes to the research • Additional substantive information that was lacking in the application
Disapproved	The IRB has determined that the research cannot be conducted at the College or by its employees or agents. Reasons for the decision are included.
Reviewed by the VA Research and Development (R&D) Committee after IRB approval, requiring changes/modifications	The changes/modifications by the VA R&D Committee shall be re-approved by the IRB.

Disapproval/ controverted issues

The minutes of IRB meetings include:

- The basis for requiring changes in or disapproving research
  Result: This information is also provided in writing to the investigator, who is given an opportunity to respond in person or in writing.
- A summary of the discussion of all controverted issues and their resolution

Continued on next page

Actions Taken at the IRB Meeting, Continued

Required IRB findings and determinations

The following specific IRB findings and determinations are documented in IRB meeting minutes, including protocol-specific information justifying each finding or determination:

Action	Description
Risk	The level of risk of the research
Approval period	The approval period for the research, including identification of research that warrants review more often than annually
Verification needed	Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research
Waiver of informed consent	• Justification for waiver or alteration of informed consent, addressing each of these 4 criteria that the IRB must find and document: – The research involves no more than minimal risk to subjects. – The waiver or alteration will not adversely affect the rights and welfare of subjects. – The research could not practicably be carried out without the waiver or alteration. – Whenever appropriate, the subjects will be provided with additional pertinent information after participation. – That the research could not practicably be carried out without using identifiable information in an identifiable format (when applicable) – That the research could not practicably be carried out without using identifiable biospecimens in an identifiable format (when applicable) ***Reference***: 45 CFR 46.116(d) • Justification for waiver of the requirement for written documentation of consent ***Reference***: 45 CFR 46.117(c)
DHHS-supported research	Justification for approval of research involving: • Pregnant women, human fetuses and neonates ***Reference***: The criteria specified under Subpart B of the DHHS human subject regulations • Prisoners ***Reference***: The categories and criteria specified under Subpart C of the DHHS human subject regulations ***Certification***: The IRB Chairperson is responsible for providing certification of the IRB's findings to OHRP.
• DHHS-supported research • FDA-regulated research	Justification for approval of research involving children ***References***: The categories and criteria specified under Subpart D of the DHHS or FDA human subject regulations ***Notification***: The IRB Chairperson is responsible for providing notification to OHRP of the IRB's findings concerning research requiring review by a panel of experts.

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Actions Taken at the IRB Meeting, Continued

Required IRB findings and determinations (continued)

The following specific IRB findings and determinations are documented in IRB meeting minutes, including protocol-specific information justifying each finding or determination (continued):

Action	Description
Special protections	Special protections warranted in specific research projects for groups of subjects who are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, regardless of source of support for the research. **For VA research** When including pregnant women, all determinations found in VA policies must be met. When involving mentally disabled/impaired decision-making capacity, the following requirements must be met: • IRB membership shall include at least one expert in the area of research (may use ad hoc member(s) as necessary) • Specific determinations must be assessed, met and documented in writing
Emergency setting	Justification for approval of research planned for an emergency setting ***References***: • The criteria specified under the special 45 CFR 46.101(i) DHHS waiver • The FDA exception at 21 CFR 50.24.
Other items	Any IRB discussions or determinations regarding any other items on which the IRB takes formal action including: • Unanticipated problems involving risks to subjects or others • Serious adverse events

Actions after meeting

The IRB Chairperson ordinarily implements protocol approvals and other IRB actions immediately following the IRB meeting at which the action took place and need not wait for the approval of the minutes.

Continued on next page

Actions Taken at the IRB Meeting, Continued

IRB protocol approval dates

Follow these steps to determine approval and expiration dates for each type of protocol review:

Types of Review	Dates
Full board	For all full board reviews: • Approved: Date of **approval** • Expires: 1 year from date of **meeting** For outright approvals: • Approved: Date of **meeting** • Expires: 1 year from date of **meeting**
Expedited	If approval is PRIOR to the meeting date: • Approved: Date of **approval** • No expiration date required. Principal Investigator check-in with the HRP/IRB Office in 5 years If approval is on or after the meeting date: • Approved: Date of **approval** • No expiration date required. Principal Investigator check-in with the HRP/IRB Office in 5 years

Related standards

AAHRPP I.1.D, II.2.C, II.2.D, II.2.E, II.4.A, II.4.B, II.5.B

How an IRB Determination Is Provided

Introduction

Date of Last Revision/Review: 04/20/11

This topic discusses how an IRB determination is provided.

No overrule permitted

No committee or official of the College may set aside or overrule a determination by the IRB to disapprove or require modifications in the College's human subject research. No committee or official of the College may permit the conduct of human subject research that has not been approved by an IRB officially designated by the College

Reasons for reconsideration

The IRB reconsiders a decision when the basis for the appeal is new information not previously considered by the IRB

Protocol review authority

A protocol approved by the IRB may be subject to further review and approval or disapproval by officials of the College, officials of Affiliated institutions, or officials of institutions where research will be conducted. However, those officials cannot approve a protocol that has been disapproved by the IRB.

Process

This table describes the appeal process:

Stage	Description
1	The IRB notifies the investigators and the College in writing of its decision to approve or disapprove the proposed research activity or of modifications required to secure IRB approval of the research activity.
2	Does the IRB decide to disapprove a research activity? • If ***yes***, it shall: – Include in its written notification a statement of the reasons for its decision – Give the investigator an opportunity to respond in person or in writing • If ***no***, the approval process is complete.
3	The investigator responds in person or in writing. ***Important***: Details are available at Reasons for reconsideration earlier in this topic.
4	The IRB evaluates the investigator's response in reaching its final determination.

Related standards

AAHRPP I.1.C, I.1.D, II.2.C, II.2.D, II.2.E

Section C
Criteria for Approval of Research

Overview

Introduction	Date of Last Revision/Review: 04/20/11 This section focuses on the criteria for IRB approval of research.
Regulations	These DHHS regulations delineate specific criteria for the approval of research: • 45 CFR 46.111, FDA regulations at 21 CFR 56.111 • Federal Policy (Common Rule at Section 111)
In this section	This section covers the following topics: • Approval Criteria • Risks Are Minimized • Psychological, Social, Economic, and Legal Harms • Equitable Selection of Subjects • Informed Consent of Subjects • Other Considerations for Informed Consent • Safety Monitoring • Independent Verification from Other Sources • Location of Research
Related standards	AAHRPP I.1.D, II.2.B, II.2.C, II.3.A, II.3.B, II.3.C, II.3.F, II.4.A, II.4.B

Approval Criteria

Introduction

Date of Last Revision/Review: 01/13/21

This topic provides a summary of the criteria for approval by the IRB.

Approval requirements

The IRB determines that all of the following requirements are satisfied before approving proposed research:

- Risks are minimized:
  - By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
  - Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes,
- Risks to participants are reasonable in relation to both the anticipated benefits and the importance of the knowledge that might reasonably be expected to result
- The selection of subjects is equitable
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, unless appropriately waived under the federal regulations
- Informed consent will be appropriately documented, unless appropriately waived under the federal regulations
- The research includes adequate provisions for monitoring data to ensure the safety of subjects
- The research includes adequate provisions to maintain the confidentiality of data and protect the privacy of subjects
- The research includes adequate additional protections to safeguard the rights and welfare of subjects who may be vulnerable to coercion or undue influence
- Financial interests of the investigator do not adversely affect subject protections or the credibility of the human research protection program
- Financial interests of the College do not adversely affect subject protections or the credibility of the human research protection program
- For purposes of conducting the limited IRB review required by §46.104(d) (2) and (3), the IRB will make the determination required by §46.111(a)(7)

Related standards

AAHRPP I.1.B, I.1.D, I.6.B, II.2.C, II.2.D, II.2.E, II.3.A, II.3.B, II.3.C, II.3.E

Risks Are Minimized

Introduction

Date of Last Revision/Review: 01/28/19

This topic discusses research with minimized risk in the protocol.

Requirement

The IRB must consider the overall level of risk to subjects in evaluating proposed research.

In general, the regulations require that the IRB distinguish research that is "greater than minimal risk" from research that is "no greater than minimal risk."

Possible benefits

Under specific circumstances, research that is "no greater than minimal risk" may be eligible for:

- Expedited review
- Waiver or alteration of informed consent requirements
- Waiver of the requirement to obtain written documentation of consent

Definition: Minimal risk

"Minimal risk means that the probability and magnitude of harm or discomfort in the research are not greater in and of themselves than those encountered in daily life or during the performance of routine physical or psychological examinations or tests."

Reference: Under Federal regulations at 45 CFR 46.102(i), 21 CFR 50.3(k), and 56.102(j)

Procedures review

This table lists the procedures review process for risk minimizing:

Stage	Description
1	The investigator indicates the proposed risk category at the time of submission of each protocol to the IRB.
2	The IRB determines that risks are minimized by using procedures that are consistent with sound research design and do not expose subjects to unnecessary risks. ***Acceptable risks***: • Procedures commensurate with the experiences of the proposed subject • Procedures already employed for diagnosis and treatment of proposed subjects • No expectation of death or injury due solely to research intervention ***Example***: Whenever appropriate, the research should utilize procedures already being performed on the subjects for diagnostic or treatment purposes.
3	The IRB reviews the research according to the IRB review criteria and affirms or requires the change of the risk category.

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Risks Are Minimized, Continued

Research plan

The IRB considers the research plan, including the research design and methodology, to determine that there are no flaws that would place subjects at unnecessary risk:

When the research …	Then the IRB …
Design presents unnecessary or unacceptable risks to subjects without commensurate benefits to the subjects or to others	Cannot ethically approve for the research to proceed
Project is adequately designed and thus subjects protected	Reserves the authority to seek opinions from consultants on proposed research and its design
Design does not meet requirements	May determine that proposed research must be re-designed to protect the rights and welfare of human subjects as follows: • Enhance subject autonomy • Maximize benefits • Reduce risks • Select subjects equitably • Minimize undue influence or coercion

Research team qualifications and necessary resources

The IRB considers the qualifications of the research team.

- Clinicians are expected to maintain appropriate professional credentials and licensing privileges.
- Investigators are automatically screened, in accordance with the BCM Office of Risk Management process, for FDA debarment, disqualification, or suspension under Title 21 CFR 1404. The appropriate institutional authority is notified when applicable.
- Members of the research team must possess:
  – Professional and educational qualifications to conduct the research project and to protect the rights and welfare of subjects
  – Necessary resources to conduct the research project and to protect the rights and welfare of subjects

Related standards

AAHRPP I.1.D, I.1.F, I.2, II.2.C, II.2.D, II.2.E, II.3.A, II.4.A, III.1.C

Psychological, Social, Economic, and Legal Harms

Introduction	Date of Last Revision/Review: 01/28/19 When evaluating research, the College carefully examines not only the risk of physical harm but also the risk of psychological, social, and legal harms
Approval requirement	To approve research, the IRB must determine that the risks of the research are reasonable in relation to the anticipated benefits (if any) to subjects and to the importance of the knowledge that may reasonably be expected to result.
Risks to participants	The IRB considers: • The potential for participants to experience stress, anxiety, guilt, or trauma that can result in genuine psychological harm • The risks of criminal or civil liability or other risks that can result in serious social, economic, or legal harm ***Examples***: Damage to financial standing, employability, insurability, reputation; stigmatization; and damage to social relationships • The risk of harm to "non-target" individuals when information is being collected on living individuals in addition to the primary "target" subjects
Risk of information collection	The collection of any identifiable private information or identifiable biospecimens about any living individual constitutes human subject research. ***Solution*:** The IRB may require additional protections, study redesign, or the informed consent of "non-target" individuals (unless the requirement for informed consent can be waived).
Review criteria	To mitigate such harm, the IRB reviews proposed research for: • Appropriate preventive protections and debriefings • Adequate disclosure of risks in the informed consent information • Mechanisms to protect the confidentiality and privacy of persons participating in the research
Risk analysis	The IRB develops its risk/benefit analysis by evaluating the most current information about the risks and benefits of the interventions involved in the research in addition to information about the reliability of this information. The IRB considers only those risks that result from the research and not long range effects of applying the knowledge gained in the research. ***Example***: Public policy implications
Related standards	AAHRPP I.1.D, I.1.F, I.2, II.2.C, II.2.D, II.2.E, II.3.A, II.4.A, III.1.C

Equitable Selection of Subjects

Introduction

Date of Last Revision/Review: 03/23/15

This topic discusses the equitable selection of subjects for research.

Approval requirement

To approve research, the IRB must determine that the selection of subjects is equitable.

In making an assessment about whether selection of subjects is equitable the IRB takes into account the following:

- Purposes of the research
- Setting in which the research would be conducted
- Whether prospective subjects would be vulnerable to coercion or undue influence
- Selection (inclusion/exclusion) criteria
- Subject recruitment and enrollment procedures
- The influence of payments to subjects

Inclusion/exclusion criteria

The IRB carefully examines inclusion and exclusion criteria and recruitment procedures to determine that the burdens and benefits of the research are being distributed equitably.

Inclusion of minorities requirement

It is a requirement of the College that females and members of minority groups and their sub-populations should be included in all biomedical and behavioral research projects involving human subjects unless compelling scientific justification is provided that inclusion is inappropriate with respect to health of the subjects or the purpose of the research.

Inclusion of females requirement

The IRB remain mindful of the desirability of including both males and females as research subjects and do not permit the arbitrary exclusion of persons of reproductive potential. Exclusion of such persons must be fully justified and based on sound scientific rationale.

Inclusion of children

In June 1996, the American Academy of Pediatrics and the NIH held a joint workshop concerning the participation of children in clinical research with the following outcome.

- There is valid concern that treatment modalities developed based on research conducted on adults without adequate data from children are being used to treat children for many diseases or disorders.
- Participants in the workshop concluded that there is a sound scientific rationale for including children in research.

For VA research:

Research involving children must-be reviewed carefully by the IRB for its relevance to VA and must not be greater than minimal risk. The VA medical center Director must approve participation in the proposed research that includes children. The IRB must have the appropriate expertise to evaluate any VA research involving children.

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Equitable Selection of Subjects, Continued

Department of Defense regulated research

For research regulated by the Department of Defense, there are specific requirements related to the recruitment of U.S. military personnel to minimize undue influence.

See U.S. Department of Defense Research for more information.

IRB review

The IRB considers the following issues when reviewing research involving selection criteria of subjects:

When the research involves …	Then …
Adults as subjects	• The IRB must determine that legally effective informed consent must be sought and obtained from each prospective subject or the subject's legally authorized representative unless informed consent requirements can be waived or altered under Federal regulations. ***Reference***: See 45 CFR 46.116 and 21 CFR 50.20. • Any such waiver or alteration must be consistent with applicable Federal and State laws and regulations. **For VA research** • The legally authorized representative must be selected in accordance with VA regulations • It is prohibited to enter non-veterans into VA-approved research studies when there are sufficient veterans available to complete the research
Children as subjects	• The IRB must determine that the permission of the child's parent(s) or guardian(s) and the assent of the child must be sought and obtained. ***Reference***: In accordance with Subpart D of the HHS and FDA human subject regulations at 45 CFR 46.408 and 21 CFR 50.55, respectively • Any waiver or alteration of assent requirements must be consistent with applicable Federal and State laws and regulations. ***Reference***: See Chapter 6 for details about children as subjects.

Related standards

AAHRPP I.1.D, I.1.G, II.2.C, II.2.D, II.2.E, II.3.A, II.3.C, II.4.A, II.4.B, III.1.E

Informed Consent of Subjects

Introduction

Date of Last Revision/Review: 01/18/19

This topic discusses the informed consent of subjects in research when informed consent is required and not waived.

When to seek and obtain consent

Investigators must seek prospective consent of research subjects (or their legally authorized representative) prior to the research subjects' participation in the research activities. Informed consent should be obtained only under circumstances that minimize the possibility of coercion or undue influence and that provide the parent(s), guardian(s), subject, or legally authorized representative with sufficient opportunity to consider whether or not the subject will participate.

***Exception*:** When the PI accesses, obtains, uses, or records identifiable information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects under 45 CFR 46.116(g).

Exception to prospective consent for screening, recruiting, or determining eligibility

The Common Rule revised in January 2018 eliminates the requirement for the IRB to either waive consent or to ensure that a prospective consent process will be used for researchers to access, obtain, and record identifiable private information or identifiable biospecimens for the purpose of screening, recruiting, and determining the eligibility of prospective subjects for a research study.

An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

- The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative
- The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens

***Reference*:** 45 CFR 46.116(g)

Language considerations

This table provides guidelines regarding the language for information for informed consent, permission, and assent documents:

Characteristic	Information for informed consent, permission, and assent must …
Understandable	Be presented in language that is understandable to the subject, legally authorized representative, parent(s), or guardian(s)
Exculpatory language	Not include any exculpatory language through which either: • The subject is made to waive or appear to waive any of the subject's legal rights • The Investigator, the sponsor, the College, or its employees or agents are released from liability for negligence, or appear to be so released

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Informed Consent of Subjects, Continued

References	See Chapter 4 for details on requirements regarding informed consent. See Chapter 6 for the requirements for permission and assent relative to the involvement of children in research.
Related standards	AAHRPP I.1.D, II.2.C, II.2.D, II.2.E, II.4.A, II.4.B, II.3.F, III.1.F

Other Considerations for Informed Consent

Introduction

Date of Last Revision/Review: 01/13/21

This topic discusses other considerations for informed consent and monitoring.

Consent monitoring

In considering the adequacy of informed consent, permission, and assent procedures, the IRB may require special monitoring of the process by an impartial observer (consent monitor) to reduce the possibility of coercion and undue influence.

The principal investigator or the IRB may request a consent monitor from Research Compliance Services.

When to use consent monitoring

Such monitoring may be particularly warranted:

- Where the research presents significant risks to subjects or if subjects are likely to have difficulty understanding the information to be provided
- As a corrective action where the IRB has identified problems associated with a particular Investigator or a research project

Additional protections in Informed Consent

In considering the adequacy of informed consent, permission, and assent procedures, the IRB may require that Investigators include a waiting period within the process or employ devices such as audiovisual aids or tests of comprehension.

Recruitment requirement

Recruitment procedures must be designed so that informed consent, permission, and assent are given freely, and coercion and undue influence are avoided.

For VA Research

- Researchers are required to ensure appropriate telephone contact with participants. This pertains to contacting the participant by telephone. Research team members are prohibited from requesting social security numbers by telephone.
- The researcher ensures that the research team makes initial contact with the prospective participant in person or by letter prior to initiating any telephone contact, unless there is written documentation that the participant is willing to be contacted by telephone about the study in question or a specific kind of research (e.g., if the prospective participant has diabetes, the participant may indicate a desire to be notified of any diabetes-related research studies). Any initial contact must provide a telephone number or other means that the prospective participant can use to verify the study constitutes VA research.
- Researchers ensure that in later contact, the research team begins telephone calls to the participant by referring to previous contacts and, when applicable, the information provided in the consent document, and ensuring that the scope of telephone contacts with the participant is limited to topics outlined in IRB-approved protocols and consent documents.

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Other Considerations for Informed Consent, Continued

VA research

If the VA researcher does not personally obtain informed consent, the researcher must delegate this responsibility in writing (e.g., by use of a delegation letter) to research staff sufficiently knowledgeable about the protocol and related concerns to answer questions from prospective participants, and about the ethical basis of the informed consent process and protocol.

- If the researcher contracts with a firm (e.g., a survey research firm) to obtain consent from participants, collect private individually identifiable information from human participants, or be involved in activities that would institutionally engage the firm in human participants research, the firm must have its own IRB oversight of the activity. In addition, the Privacy Officer (PO) must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.
- The researcher must ensure that all original or digitalized signed and dated informed consent documents are maintained in the researcher's research files, readily retrievable, and secure.
- Trainees (including students, residents, and fellows of any profession), including VA employees, from schools with an academic affiliation agreement consistent with current VHA policy, may serve as members of research teams, but not serve as principal researcher within a VA facility. Trainees may use data or human biological specimens that have been collected within VA for clinical, administrative, or research purposes only when:
  - The study has been approved by the local VA medical facility, and IRB, when appropriate;
  - A researcher sufficiently experienced in the area of the trainee's research interest is serving as principal researcher or co-principal researcher and is responsible for oversight of the research and the trainee.

Evaluation

The IRB must know who the subjects will be, what incentives are being offered, and the conditions under which the offer will be made.

Advertisements

The IRB reviews advertisements and recruitment incentives associated with the research that it oversees including reproductions of the final copy of printed advertisements to evaluate the relative size of type used and other visual effects and final audio/videotape prepared for broadcast.

The IRB reviews research recruitment advertising to ensure that advertisements do not:

- State or imply a certainty of favorable outcome or other benefits beyond that outlined in the approved consent document and the protocol;
- Promise "free medical treatment" when the intent was only to say participants would not be charged for taking part in the investigation; or
- Emphasize the payment or the amount to be paid, by such means as larger or bold type, or include any exculpatory language.

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Other Considerations for Informed Consent, Continued

FDA-regulated advertisements	For FDA-regulated research, the IRB reviews advertising to ensure that advertisements do not: • Make claims, either explicitly or implicitly, about the drug, biologic or device under investigation that are inconsistent with FDA labeling • Make claims that the research procedures are safe or effective for the purposes under investigation or are known to be equivalent or superior to other drug, biologic, or device; • Use terms, such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational • Allow compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing
Limited information	Any advertisement to recruit subjects should be limited to the information the prospective subjects, legally authorized representatives, parents, or guardians need to determine eligibility and interest.
Items to include	When appropriately worded, the following items may be included: • The name and address of the clinical Investigator and research institution • The condition under study and the purpose of the research • In summary form, the criteria that will be used to determine eligibility for the study • A brief list of participation benefits, if any • The time or other commitment required of the subjects • The location of the research and the person or office to contact for further information

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Other Considerations for Informed Consent, Continued

Payments for research participation	The IRB reviews any proposed payments to research subjects (or their parents, guardians, or legally authorized representatives) associated with the research that it oversees to assure that: • Payment of subjects is prohibited for participation in research when the research: – Is integrated with a patient's medical care – Makes no special demands on the subject beyond those of usual medical care • Applications include the amount and schedule of all payments • Credit for payment accrues as the study progresses and is not contingent upon the subject completing the entire study • Payments are not to be of such an amount as to result in coercion or undue influence on the decision to participate or continue participation • Payments are not to be provided on a schedule that results in coercion or undue influence on the decision to participate or continue participation • Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn • All information concerning payment, including the amount and schedule of payments, is set forth in the consent document
Payments for Department of Defense research participation	For research regulated by the Department of Defense, there are specific requirements related to the recruitment of U.S. military personnel to minimize undue influence. See U.S. Department of Defense Research for more information.
Indemnity and liability provisions	Subjects in research at the College may not be asked to waive or appear to waive any of their legal rights.
Finder's fees and bonus payments	Finder's fees, payment in exchange for referrals of potential participants; and bonus payments designed to accelerate recruitment tied to the rate or timing of enrollment, are strictly prohibited. ***Note*:** Payments are defined as monetary and non-monetary payment, and can include gifts, travel, or the expectation that these payments will be made in the future. See definition of "Financial Interest" in Disclosure of Outside Interests Policy #31.2.01.
Related standards	AAHRPP I.1.C, I.1.D, II.2.C, II.2.D, II.2.E, II.3.C, II.3.C.1, II.4.A, II.4.B, II.3.F, III.1.E-F, III.2.B

Safety Monitoring

Introduction

Date of Last Revision/Review: 04/20/11

This topic discusses safety monitoring regarding IRB reviews.

Safety monitoring plan

To approve research, the IRB must determine that, where appropriate, the research plan makes adequate provision for monitoring the data to protect the safety of subjects.

- For research in which risks are substantial or greater than minimal, and for research in which reports of serious harms are expected, a detailed description of the data and safety monitoring plan should be submitted to the IRB as part of the proposal.
- This plan should contain procedures for reporting adverse events.

For Sponsored Research:

The contract or funding agreement for the research protocol must describe in detail the plan for monitoring the data and safety of participants and the timeframes of reporting to the Principal Investigator routine and urgent reports generated by the data and safety monitoring plan. This may be accomplished through an appendix of the clinical protocol to the contract or funding agreement or any other document that fulfills this requirement.

The Principal Investigator is responsible for submitting the plan and these reports to the IRB for review.

Risk monitoring

Monitoring should be commensurate with the size and complexity of the study.

- The establishment of data safety monitoring boards (DSMBs) is usually required for Phase 3 and randomized Phase 2 clinical trials involving interventions that entail potential risk to the participants.
- For some early phase studies that involve potentially high risks or vulnerable populations, a DSMB may be appropriate.
- For many Phase 1 and non-randomized Phase 2 trials, independent DSMBs are not necessary, but a monitoring plan must be established. For these studies, continuous close monitoring by the investigator may be appropriate.

Essential elements of monitoring plans

The essential elements of all data and safety monitoring plans include:

- Monitoring the progress of the trial and the safety of participants
- Ascertaining that all adverse events are properly reported
- Reporting any suspension of the trial to sponsors
- Assuring data accuracy and protocol compliance

Reference: NIH Policy for Data and Safety Monitoring, release date June 10, 1998

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Safety Monitoring, Continued

Alternative	In lieu of requiring that safety monitoring information be submitted directly to the IRB, the IRB may rely on a current statement from a duly constituted DSMB/DMC indicating the following: • It has reviewed: – Study-wide adverse events – Interim findings – Any recent literature that may be relevant to the research • It has determined that continuation of the research is justified
For Department of Defense regulated research	For DOD regulated research, the data and safety monitoring plan must adhere to DOD requirements. See U.S. Department of Defense Research for more details of this requirement.
Related standards	AAHRPP I.1.D, I.8.C, II.2.C, II.2.D, II.2.E, II.3.B, II.4.A, II.4.B, III.1.C

Independent Verification from Other Sources

Introduction	Date of Last Revision/Review: 04/20/11 This topic discusses independent verification from other sources, including consultants.
Reason	The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that the IRB utilize sources other than the investigator to verify independently that no material changes or other problematic events have occurred during the IRB-designated approval period.
Determining factors	The IRB considers the following factors in determining which studies require such independent verification: • The probability and magnitude of anticipated risks to subjects • The likely medical condition of the proposed subjects • The probable nature and frequency of changes that may ordinarily be expected in type of research proposed • Prior experience with the principal investigator and research team • Any other factors that the IRB deems relevant
Requirements	In making determinations about independent verification, the IRB: • May prospectively require that such verification take place at predetermined intervals during the approval period • May retrospectively require such verification at the time of continuing review
Related standards	AAHRPP I.1.D, II.2.C, II.2.D, II.2.E, II.3.A, II.4.A, II.4.B

Location of Research

Introduction

Date of Last Revision/Review: 04/13/15

Permission to conduct clinical research on the premises of any institution, location or site (hereafter referenced as location) is subject to permission from that location.

Permissions may range from a letter of approval from the head of that location to multiple committee and departmental reviews as well as their own designated IRB. It is the Principal Investigator's responsibility to obtain permission to conduct research from the location before proceeding, regardless of BCM IRB approval status.

IRB determination

The IRB must determine that appropriate human subject research assurance has been provided for each site listed and that there is an adequate plan to manage the information among the sites related to participant protections including reporting unanticipated problems, protocol modifications, and interim results.

When research is conducted in other nations, the PI will provide with the protocol submission a contact person on the international IRB or Ethics Committee to serve as a reviewing Consultant to the BCM IRB.

Tables

The tables below describe how the Principal Investigator indicates locations to conduct research within BRAIN:

When the Principal Investigator plans to conduct research at BCM location(s)…	
Add In the protocol application in BRAIN, Section A6a	Baylor College of Medicine
	This addition will: Add the BCM name on consent form(s). ***Note***: signature by the department chair or center and BCM IRB approval grants permission for conduct at BCM. However, investigators must be aware of interdepartmental procedures regarding research
When the Principal Investigator plans to conduct research at affiliated institution(s)…	
Add In the protocol application in BRAIN, Section A6a :	The affiliated institution where the research will be conducted. Each institution has its own internal processes for review and approval for research to begin beyond IRB approval. Contact the research office of that institution to determine additional requirements.
	This addition will: • Allow the human protections administrators of the affiliates to view protocols in BRAIN that have received BCM IRB review. • Add the institutions name on consent form(s).
Contact the affiliate institution research office	To comply with the requirements of that institution. **For VA regulated research:** All international research must also be approved explicitly in a document signed by the VA medical facility Director, except for Cooperative Studies Program activities which must be approved by the CRADO.

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Location of Research, Continued

Tables (continued) The tables below describe how the Principal Investigator indicates locations of research within BRAIN (continued):

When the Principal Investigator named on the BCM IRB protocol application: • **Is serving as the investigator/sponsor, or** • **As the coordinating site, or** • **Has overall responsibilities for the multi-site research, AND** **has permission to conduct research at other locations…**	
Add In the protocol application, Section A6a and A6b:	Any other location from which the investigator has obtained permission or approval to conduct research. Add the location, the IRB name (if applicable) and the contact information of an IRB or Ethics Committee (EC) member from that location that will serve as a consultant to the BCM IRB for the review of the protocol. This PI will provide in the research protocol submission to the BCM IRB the following: • Confirmation of the qualifications of the local researchers and staff for conducting research in that country • The plans for: – Post-approval monitoring – Handling complaints – Handling non-compliance – Reporting and handling unanticipated problems involving risks to subjects or others – Consent process and documentation of consent addressing any language issues – Coordination and communication with the local IRB or EC • Any local laws, regulations, customs, and practices that must be followed due to Department of Defense regulations (if applicable) The consultant reviewer from the local IRB or EC will conduct for the BCM IRB the initial and continuing reviews of the BCM research protocol submission including the review of amendments.
Contact the IRB office at irb@bcm.edu	If the location is not found in the drop down menus in BRAIN

Related standard AAHRPP I.3, II.2.C, II.2.D, II.2.E, II.2.H

Section D
Confidentiality of Data

Overview

Introduction

Date of Last Revision/Review: 04/20/11

This section focuses on confidentiality of data in research.

In this section

This section covers the following topics:

- Protecting the Privacy of Subjects and Confidentiality of Data
- Additional Confidentiality Safeguards
- Confidentiality of Data Sets
- Confidentiality with Data or Tissue Banks
- Research Involving Epidemiology
- Genetic and Family Research
- Research Involving Deception or Withholding of Information

Related standards

AAHRPP I.1.A, I.1.D, II.2.D, II.3.D, II.3.E

Protecting the Privacy of Subjects and Confidentiality of Data

Introduction

Date of Last Revision/Review: 01/13/21

This topic discusses requirements for adequate provisions to protect the privacy of subjects and the confidentiality of data.

Approval requirement

To approve research, the IRB must determine that, where appropriate, there are adequate provisions to protect the privacy of subjects and the confidentiality of data.

Privacy requirements

Does the research involve observation or intrusion in situations where the subjects have a reasonable expectation of privacy? Would reasonable people be offended by such an intrusion? Can the research be redesigned to avoid the intrusion?

Identifiable information or identifiable biospecimens may not generally be obtained from private (non-public) records without the approval of the IRB and the informed consent of the subject, even for activities intended to identify potential subjects who will later be approached to participate in research.

Confidentiality requirements

To prevent a breach of confidentiality that potentially could harm subjects, it is important to protect individually identifiable private information (including identifiable biospecimens) when it has been collected.

When identifiable information or identifiable biospecimens linked to individuals will be recorded as part of the research design, the IRB requires that adequate precautions will be taken to safeguard the confidentiality of the identifiable information or biospecimens.

Safeguarding methods

Among the available methods for safeguarding confidentiality are:

- Coding of records
- Statistical techniques
- Physical or computerized methods for maintaining the security of stored data

For Department of Energy (DOE) research:

- Researchers are required to follow the DOE requirements for the protection of personally identifiable information of subjects
- A data protection plan that addresses all the required elements on the DOE Checklist should be completed and submitted with the protocol

Considerations

In reviewing protections, the IRB:

- Considers the means to answer the research question that is the least intrusive to the research subjects
- Considers the nature, probability, and magnitude of harm that likely would result from a disclosure of collected information or biospecimens outside the research
- Evaluates the effectiveness of proposed techniques to keep information confidential in determining the adequacy of confidentiality protections
  ***Examples*:** Coding systems, encryption methods, storage facilities, access limitations, or anonymizing the data

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Protecting the Privacy of Subjects and Confidentiality of Data, Continued

VA considerations	When the VA conducts a study that is protected by a Certificate of Confidentiality, the following health record documentation provisions apply: • For studies that do not involve a medical intervention (e.g., observational studies, including interview and questionnaire studies), no annotation may be made in the health record • For studies that involve a medical intervention, a progress note entry should indicate: • An individual has been enrolled in a research study • Any details that would affect the subject's clinical care • The name and contact information for the investigator conducting the study • Subjects' informed consent forms and HIPAA authorization documents are not to be included in the health record • Investigators should work with the research office in their facility to assure that when Veterans are enrolled in a study protected by a Certificate of Confidentiality, they are not simultaneously enrolled in other interventional studies unless it is absolutely clear that this enrollment does not raise safety issues. • For studies which will include information about the participant's participation in the participant's VHA medical record, information must be given to the prospective participants as part of the informed consent process.
Related standards	AAHRPP I.1.D, II.2.D, II.3.D, II.3.E, III.2.C

Additional Confidentiality Safeguards

Introduction	Date of Last Revision/Review: 11/18/19 This topic discusses additional safeguards for confidentiality in research.
Certificates of Confidentiality	Where research involves the collection of highly sensitive information about individually identifiable subjects, the IRB may determine that special protections are needed to protect subjects from the risks of investigative or judicial processes. In such situations, the IRB may require that an Investigator obtain a DHHS Certificate of Confidentiality (CoC).
Description	The CoC protects against the involuntary release of sensitive information about individual subjects for use in Federal, State, or local civil, criminal, administrative, legislative, or other legal proceedings.
Conditions not protected	The CoC does not do either of the following: • Prohibit voluntary disclosure of information by an Investigator, such as voluntary reporting to local authorities of child abuse or of a communicable disease • Protect against the release of information to DHHS or FDA for audit purposes
Conditions specified	The IRB requires that these conditions for release be stated clearly and explicitly in the informed consent document.
Website references	Information concerning Certificates of Confidentiality can be obtained from any of the following websites: http://www.niaaa.nih.gov/grant-funding/management-reporting/certificates-confidentiality-niaaa-specific-protecting-identity https://researchstudies.drugabuse.gov/faq.html http://www.cancer.gov/clinicaltrials/conducting/certificates-of-confidentiality https://www.nhlbi.nih.gov/grants-and-training/policies-and-guidelines/certificates-of-confidentiality
For vulnerable subjects	To approve research, the IRB must determine that, where appropriate, additional safeguards have been included to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence. ***Examples***: Children, prisoners, persons with impaired decision-making capacity, or economically or educationally disadvantaged persons Details about protections for vulnerable subjects are provided in Chapter 6.
Special reviewers	When the IRB reviews research involving vulnerable subjects, the IRB will include among its reviewers persons who are knowledgeable about and experienced in working with these vulnerable subjects.
Related standards	AAHRPP I.1.D, II.2.D, II.3.D, II.3.E

Confidentiality of Data Sets

Introduction

Date of Last Revision/Review: 01/28/19

This topic discusses the confidentiality of data sets used in research.

Data set review

This table shows how the use of data sets is reviewed by the IRB:

When …	Then the use of the data sets …
The data sets are publicly available, whether or not they contain sensitive, identifiable information, or identifiable biospecimens ***Example***: Available to the general public, with or without charge	May be exempt from IRB review.
Large, existing data sets containing identifiable private information, or identifiable biospecimens about living individuals	Requires IRB review. ***Result***: The IRB must determine whether the information can be used without additional informed consent from the subjects.

Informed consent determination

This table describes how the IRB determines whether the identifiable information or identifiable biospecimens can be used without additional informed consent from the subjects:

When the IRB …	Then …
Examines the conditions of informed consent under which the data were originally obtained	It may be that the proposed research is permissible under the original terms of consent.
Considers whether it is permissible to waive the usual informed consent requirements in accordance with 45 CFR 46.116(d)	Many times, a waiver of consent is appropriate.
Determines that the research can proceed only if the Investigator obtains and uses data that have been made anonymous	• Codes and other identifiers are permanently removed from the data set before the data are sent to the Investigator. • The removal is accomplished in such a manner that neither the Investigator nor the source maintaining the data set can re-establish subjects' identities.

Related standards

AAHRPP I.1.D, II.2.A, II.2.B, II.2.D, II.3.D, II.3.E

Confidentiality with Data or Tissue Banks

Introduction

Date of Last Revision/Review: 01/28/19

This topic discusses confidentiality when using data banks or tissue banks in research.

Requirement

The investigator shall comply with any conditions determined by the repository IRB to be appropriate for the protection of subjects.

For VA research: If specimens will be banked, genetic testing done, or a commercial product developed, VA policy must be followed.

Repository

A data bank contains information about individuals and is also called a data repository.

A tissue bank contains biospecimens and often associated health information and is also called a tissue repository.

Note: The data in repositories (data and tissue) may be identifiable or not.

Tissue bank activities

Tissue Bank activities involve three components:

- The collectors of data or tissue samples
- The bank/repository storage and data management center
- The recipient investigators

IRB responsibility

Under a repository arrangement, the IRB:

- Formally oversees all elements of repository activity, setting the conditions for:
  – Collection
  – Secure storage
  – Maintenance
  – Appropriate sharing of the data and tissues with external investigators
- Determines the parameters for sharing data (information) and tissues (biospecimens) which are within the repository in a manner such that additional informed consent of subjects is or is not required

Reference: See Guidance on this topic on the OHRP Website.

Parameter agreements

Typically, these parameters involve formal, written agreements stipulating conditions as follows:

- The repository shall not release any identifiers to the investigator.
- The investigator shall not attempt to recreate identifiers, identify subjects, or contact subjects.
- The investigator shall use the data only for the purposes and research specified.

Related standards

AAHRPP I.1.D, II.2.C, II.2.D, II.3.D, II.3.E

Research Involving Epidemiology

Introduction

Date of Last Revision/Review: 04/20/11

This topic discusses the confidentiality of research involving epidemiology.

Description

Epidemiology research often:

- Makes use of sensitive, individually identifiable, private information (usually obtained from medical or other private records)
- Links this information with additional information obtained from other public or private records, such as employment, insurance, or police records
- Combines historical research with survey and interview research
- Uses community based participatory research and requires special protections and review concerns. IRBs can use OHRP's Institutional Review Board Guidebook for guidance in this type of review.

Privacy handling

This table describes how the IRB handles epidemiology studies that often present significant problems regarding both privacy and confidentiality:

Stage	Description: The IRB …
1	Considers privacy issues and must be satisfied that the research does not constitute an unwarranted invasion of the subjects' privacy
2	Seeks to establish that the Investigator has legitimate access to any identifiable information that is to be utilized ***Example***: If State disease registry information is to be utilized, the IRB needs to examine State law relative to the legitimate release of such information for research.
3	Examines mechanisms for maintaining the confidentiality of data collected when the privacy concerns have been resolved
4	Seeks to establish that confidentiality protections are appropriate to the nature and sensitivity of the information that has been obtained

Waiver request

Because epidemiology research typically requires very large numbers of subjects, epidemiology Investigators almost always request that the IRB waive the usual requirements for informed consent.

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Research Involving Epidemiology, Continued

Requirements	To approve such a waiver in epidemiology research, the IRB must find and document that the first three criteria at 45 CFR 46.116(d) for a waiver of informed consent have been met, specifically that: • The research presents no more than minimal risk to subjects. • The waiver will not adversely affect the rights and welfare of the subjects. • The research could not practicably be carried out without the waiver. ***Fourth requirement***: Usually does not apply ("whenever appropriate, the subjects will be provided with additional pertinent information after participation")
Related standards	AAHRPP I.1.D, I.4.C, II.2.C, II.2.D., II.3.D, II.3.E

Genetic and Family Research

Introduction	Date of Last Revision/Review: 01/28/19 This topic discusses confidentiality regarding genetic and family research.
Issues in genetic research	Information obtained through genetic research may have serious repercussions for the subject or the subject's family members. Genetic information can adversely affect an individual's insurability and employability. Therefore, the protection of privacy of the subjects and the confidentiality of information gathered for and resulting from genetic research is a major concern.
Approval requirement	The IRB will expect the Investigator to describe in detail how individual privacy of subjects will be protected and how the confidentiality of obtained information will be maintained.
Example	The IRB is particularly careful about approving research that appears to involve only a simple, minimal risk blood draw but then goes on to include or add a component involving genetic analysis. The addition of the genetic analysis can alter the level of risk.
Family history research	Family history research is a common technique used in Bio-Social and Bio-Behavioral Research. Family history research typically involves obtaining information from one family member (called a proband) about other family members.
Identification of subjects in proposed research	Issues arise as follows: • It is important to recognize the Federal regulations and the Common Rule include in the definition of human subject a living individual about whom an Investigator obtains “identifiable private information” and “identifiable biospecimens”. • The family members identified and described by the proband may be human subjects under the regulations if the Investigators obtain identifiable private information about them.
How IRB handles issues	The IRB must: • Determine whether family members are human subjects in such research • If so, consider the possible risks involved • Determine whether their informed consent is required or can be waived under the conditions specified at 45 CFR 46.116(d)
Compliance Requirement	All human subject research conducted at the College or by its employees or agents must comply with all applicable laws and regulations of the United States and the State in which the research is conducted, as well as with any local requirements.
Related standards	AAHRPP I.1.D, II.2.C, II.2.D, II.3.D, II.3.E

Research Involving Deception or Withholding of Information

Introduction	Date of Last Revision/Review: 04/20/11 This topic discusses the use of deception or withholding of information in research.
Description	Deception research involves certain research activities in which the subject is not told or is misled about the true purpose of the research. ***Examples***: Certain studies of group processes, contextual influences on cognition
Review attitude	The IRB reviewing research involving incomplete disclosure or outright deception must apply both common sense and sensitivity to the review.
IRB review	The IRB needs to be satisfied that: • The deception is necessary. • When appropriate, the subjects shall be debriefed. ***Example***: Debriefing may be inappropriate when the debriefing itself would present an unreasonable risk of harm without a corresponding benefit. • The proposed subject population is suitable.
IRB review criteria	Specifically, the IRB must find and document that all four of the following criteria have been satisfied: • The research presents no more than minimal risk to subjects. • The waiver or alteration shall not adversely affect the rights and welfare of the subjects. • The research could not practicably be carried out without the waiver or alteration. • Where appropriate, the subjects shall be provided with additional pertinent information after participation.
Waiver documentation	When determining to approve the use of deception under a waiver of informed consent, the IRB: • Should consider each criterion in turn • Documents that a waiver of the usual informed consent requirements is justified ***Reason***: The only way deception can be permitted • Documents specifically how the proposed research satisfies that criterion in the minutes of its meeting and in the IRB protocol file ***Reference***: Federal regulations and the Common Rule at 45 CFR 46.116(d)
Greater than minimal risk	The regulations make no provision for the use of deception in research that poses greater than minimal risks to subjects.
Reference	See Research Involving Deception in Chapter 4.
Related standards	AAHRPP I.1.D, II.2.C, II.2.D, II.3.D, II.3.E

Section E
Reviews After Approval

Overview

Introduction

Date of Last Revision/Review: 04/20/11

This section covers IRB actions and determinations that occur after the research request has been previously approved.

In this section

This section covers the following topics:

- Initial and Continuing Review by the Convened IRB
- Continuing Review Deadline Issues
- Changes in Previously Approved Research
- Suspension or Termination of IRB Approval
- Event Reporting Required of Principal Investigators
- IRB Review of Event Reports for Determination of (UPIRSO) Unanticipated Problems Involving Risks to Subjects or Others
- Reporting and Assessing Compliance Concerns
- Chain of Reporting

Related standards

AAHRPP I.1.D, II.2.C, II.2.D, II.2.E, II.2.F, II.2.G, III.2.D

Initial and Continuing Review by the Convened IRB

Introduction

Date of Last Revision/Review: 01/13/21

IRB actions for initial or continuing review of research include those listed below.

Standard frequency for continuing review

The IRB must conduct substantive and meaningful continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk but not less than once per year.

***Note*:** Continuing review must continue for protocols that remain active for long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants, and all participants have completed all research-related interventions. Continuing review must continue for protocols when the remaining research activities are limited to data analysis.

***Exception*:** Unless the IRB determines otherwise, continuing review of research is not required in the following circumstances:

- Research that falls into one or more of the categories appropriate for expedited review
- Research that has progressed to the point that it involves only one or both of the following which are part of the IRB-approved study:
  – Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
  – Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care

VA requirements

If a researcher does not provide continuing review information to the IRB or the IRB has not approved a protocol by the expiration date:

- The researcher must immediately submit to the IRB chair a list of research participants who could be harmed by stopping study procedures.
- The IRB chair determines within two business days whether participants on the list may continue participating in the research interventions or interactions.

More frequent reviews

The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that research be reviewed more often than annually.

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects.

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Initial and Continuing Review by the Convened IRB, Continued

Factors for frequency	The IRB considers the following factors in determining which studies require more frequent review: • The probability and magnitude of anticipated risks to subjects • The likely medical condition of the proposed subjects • The overall qualifications of the principal investigator and other members of the research team • The specific experience of the principal investigator and other members of the research team in conducting similar research • The nature and frequency of adverse events observed in similar research at this and other institutions • Any other factors that the IRB deems relevant
Protocol revisions, modifications, and amendments	Revisions, modifications, or amendments to a research protocol must be incorporated into the written protocol for continuing review: • This practice ensures that there is only one complete protocol with the revision dates noted on each revised page and the first page of the protocol itself. • This procedure is consistent with the procedure used for revised and approved informed consent documents, which then supersede the previous one.
Verification from sources	The IRB may seek verification from sources other than the investigators that no material changes have occurred since previous IRB review: • As part of routine assessments by Research Compliance Services on behalf of the IRB; • Research with higher levels of risk to subjects; • Projects conducted by investigators previously under an IRB corrective action plan; or • Concerns brought to the attention of the IRB. ***Reference***: See Reporting and Assessing Compliance Concerns

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Initial and Continuing Review by the Convened IRB, Continued

Review materials	These materials include: • The currently approved informed consent document • The proposed informed consent document • The IRB Continuing Review Application comprised of the following: – A summary of the research – A status report on the progress of the research – The number of subjects enrolled and withdrawn – A description of any unanticipated problems involving risks to subjects or others – A summary of adverse events – A summary of relevant recent literature – Other information considered relevant by the investigator • **For VA research**, the investigator submits to the IRB: – Gender and minority status of subjects entered into study – Number of subjects considered as members of specific vulnerable populations (does not require a detailing of the category) – An assurance that all serious adverse events and unexpected adverse events have been reported as required – See reference below for additional requirements
Distribution of materials	Except for unusual circumstances, at least one week before the convened meeting, each IRB member is provided with detailed continuing review materials sufficient to conduct substantive and meaningful reviews.
Documentation	The minutes of IRB meetings document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB as well as the protocol specific findings justifying those determinations.
Related standards	AAHRPP I.1.D, I.4.A, II.2.A-D, II.2.D.1, II.2.D.2, II.2.E, II.2.E.1-3, II.4.B, II.4.D

Continuing Review Deadline Issues

Introduction

Date of Last Revision/Review: 04/20/11

This topic discusses issues involved with deadlines for an IRB continuing review.

Important

The regulations permit no grace period to the one-year requirement for continuing review.

Expiration of approval period

The IRB is required to conduct substantive and meaningful continuing review of research not less than once per year.

- The IRB approval period for research may extend no more than 365 days after the convened meeting at which the research was last approved.
- No grace period and no exceptions to this one-year requirement are permitted.
- All research activities, including recruitment and data analysis, must stop.
- Research that continues after the approval period expires is research conducted without IRB approval.

Reference: See "Consequences of exceeding" below

Consequences of exceeding

When investigators exceed the one-year requirement for the continuing review, the following consequences occur:

- Research that continues after the approval period expires is research conducted without IRB approval.
  Note: All research activities, including recruitment and data analysis, must stop.
- The IRB automatically suspends the enrollment temporarily of new subjects in any ongoing expired research that does not receive continuing review and approval before the end of the stipulated approval period.
- Previously enrolled subjects may continue their involvement in expired research only where the IRB determines that continued involvement is in the best interest of the subjects.
- **For VA research**:
  – The IRB notifies investigators to immediately submit to an IRB chair a list of participants for whom stopping research activities would cause harm.
  – All research activities are to stop unless an IRB or IRB chair, in consultation with the VA Chief of Staff, finds that it is in the best interest of the subject to continue participation.
  – The IRB promptly reports the expiration of VA research to the:
  > Sponsoring agency (if any)
  > Private sponsor (if any)
  > Local VA facility Research Office
  >The VA facility will report the situation to the regional VA Office of Research Oversight

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Continuing Review Deadline Issues, Continued

Notification to investigators	The IRB notifies investigators in writing of its determinations in the form of a memorandum from the IRB which includes, at minimum, the following information (where appropriate): • Investigator's name • Title of the study • IRB project number • Reason(s) for suspension or termination
Conclusion	Since the research must be re-approved before the expiration deadline, investigators should ensure that the IRB receives continuing review information for an IRB meeting before the expiration date.
Related standards	AAHRPP I.1.D, II.2.C, II.2.D, II.2.D.2, II.2.E, II.2.G, II.3.A

Changes in Previously Approved Research

Introduction

Date of Last Revision/Review: 10/23/23

This topic discusses the review of proposed changes to research previously approved by the IRB.

Revisions, modifications, or amendments to a research protocol must be incorporated into the written protocol summary in BRAIN for review by the IRB.

This ensures that there is only one:

- Complete approved protocol summary with the revision dates noted on each revised page and the first page of the protocol itself
- Approved version of the protocol summary and informed consent document for a protocol at any given point in time

Review for regulatory approval criteria

The IRB reviews and determines that the changes to the previously approved research satisfy all of the approval criteria, as explained for expedited and convened IRB review (see Expedited Review of Research and all procedures in Section B Convened Full Board Review) before approving the proposed changes.

The IRB ensures that information relating to protocol changes will be provided to participants when such information may relate to the participant's willingness to continue to take part in the research.

Definitions

The table below defines the following terms:

Term	Definition
Amendment	The College defines an amendment to be any change to an approved protocol regardless of how minor it is. Investigators must report to the IRB planned changes in the conduct of the study, since these may affect the protection of human subjects.
Minor Change	The College defines a minor change to be one that makes **no substantial alteration** in **ANY** of the following: • The probability or magnitude of risks to subjects • The research design or methodology • The number of subjects enrolled in the research • The qualifications of the research team • The facilities available to support safe conduct of the research • The likelihood of subjects' willingness to participate • Any factor that might warrant convened review

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Changes in Previously Approved Research, Continued

Expedited procedure	The IRB may utilize expedited procedures to review a proposed change to previously approved research if it represents a minor change to be implemented during the previously authorized approval period, 45CFR46.110 (b)(2) and 21 CFR 56.110. ***Note*:** When a proposed change in a research study is not minor, then the IRB must review and approve changes at a convened meeting before changes may be implemented.
Exception requests	An exception is a planned deviation for a single occurrence. Exceptions are submitted via the amendment mechanism. Multiple exceptions of the same kind suggest a protocol modification is warranted. Each planned exception requires separate amendment submission and prospective IRB approval. An exception request should include the following: • A description of the exception including rationale; • Proposed date of the exception, declaration of time sensitivity and rationale; • Clarification as to why the action is a single occurrence and why the protocol does not require modification, or explanation that a future modification is planned; • Plans for communicating the exception to subject; • Assessment of increased risk involved in the exception; • Assessment of subject benefit from the exception; and • Assessment of impact of the exception on data integrity
Exception from prospective IRB review of amendments	The only exception to prospective IRB review of proposed changes to the research before their implementation is the rare circumstance in which a change is necessary to eliminate apparent immediate hazards to the research subjects. • In this case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with protection of human subjects • ***Critical note*:** Event Reporting Required of Principal Investigators or new information that may affect the risk/benefit assessment must be promptly reported to, and reviewed by, the IRB to ensure adequate protection of human subjects
Review of changes by the fully convened IRB	The IRB utilizes the Primary and Team Reviewer System to assist in the review of changes to previously approved research by the convened IRB, as described for initial and continuing review. Specific documents related to the changes to the previously approved research will be distributed to primary reviewers and to all other IRB members for review as described for initial and continuing review for discussion at the convened meeting.

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Changes in Previously Approved Research, Continued

VA regulated research	**For VA Research:** If a study team member is replaced by another individual and the IRB-approved protocol identifies the person by title and not name, a replacement by another individual with the same title is not a protocol change and so an amendment to the protocol is not needed.
Related standards	AAHRPP I.1.D, II.2.C, II.2.D, II.2.D.3, II.2.E, II.2.E.3, II.2.F, II.2.G, II.3.A

Suspension or Termination of IRB Approval

Introduction

Date of Last Revision/Review: 10/10/12

The topic discusses the suspension or termination of IRB approval.

Requirement

The IRB may vote to suspend or terminate approval of research that is not being conducted in accordance with IRB or regulatory requirements or that has been associated with serious unexpected problems or serious harm to subjects.

Considerations upon suspension

In making this determination, the IRB or the person temporarily suspending research must:

- Consider actions to protect the rights and welfare of currently enrolled subjects
- Consider whether procedures for withdrawal of enrolled subjects take into account their rights and welfare
  ***Examples*:** Making arrangements for medical care off a research study, transfer to another investigator, and continuation in the research under independent monitoring
- Consider informing current subjects of the termination or suspension
- Have any adverse event or outcome reported to the IRB

Clarifications

- The phrase *suspension or termination of IRB approval* does **not** include the permanent or temporary suspension of subject enrollment or participation in research that results solely from the expiration of the IRB approval period for the research.
- An administrative hold is a voluntary interruption of research enrollments and ongoing research activities by an appropriate facility official, research investigator, or sponsor and does not apply to interruptions of research related to concerns related to the safety, rights, or welfare of human research subject, research investigators, research staff, or others.

  An administrative hold must not be used to avoid reporting deficiencies or circumstances otherwise covered in federal regulations, VA policies, or other federal requirements governing research. An administrative hold is not the same as a suspension or termination of IRB approval.

Who implements temporarily

Where the IRB Chairperson determines that such action is necessary to protect the rights and welfare of subjects, the Chairperson may require an immediate, temporary suspension of enrollment of new subjects or of continued participation of previously enrolled subjects, pending review of the situation by the convened IRB.

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Suspension or Termination of IRB Approval, Continued

Notification

The IRB notifies the principal investigator orally and in writing of such suspensions or terminations and includes a statement of the reasons for the IRB's actions. For PIs conducting research reviewed by an external IRB, the BCM IRB also reports in writing to the external IRB:

- Any suspension related to the research project reviewed by the external IRB
- Any restriction of an investigator's research privileges that would affect the research project reviewed by the external IRB

Result: The investigator is provided with an opportunity to respond in person or in writing.

See Reporting and Assessing Compliance Concerns for details of the notification process.

See Chain of Reporting for timelines for reporting suspensions or terminations.

For VA research:

Suspension/termination of VA research by either the IRB or the VA Research and Development (R&D) Committee, and reasons for action, are communicated between the IRB and the VA.

See Chain of Reporting: VA Research.

Related standards

AAHRPP I.1.D, I.5.D, II.2.C, II.2.D, II.2.E, II.2.G

Event Reporting Required of Principal Investigators

Introduction

Date of Last Revision/Review: 06/19/23

This topic provides the reporting process for investigators to report events to the IRB.

Definition

Unanticipated Problems

Although federal regulations require prompt reporting to the IRB of any unanticipated problems involving risks to subjects or others, this phrase is not defined in either HHS or FDA regulations.

In January 2007, the Office for Human Research Protections (OHRP) released new guidance to assist IRBs in fulfilling this requirement. According to the guidance document OHRP considers unanticipated problems, in general, to include any incident, experience, or outcome that meets all of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given:
  - The research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and
  - The characteristics of the subject population being studied
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized

For VA research:

The terms "unanticipated" and "unexpected" refer to an event or problem in VA research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.

The phrase "related to participation in the research" means a logical sequence of cause and effect shows that the study procedures were the reason for the incident, experience, or outcome. The phrase "possibly related to participation in the research" implies a lesser degree of certainty about causality and refers to an incident, experience, or outcome for which there is some evidence to reasonably suggest a causal relationship between study procedures and the incident, experience, or outcome.

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Event Reporting Required of Principal Investigators, Continued

Definition (cont.)

In January 2009, the Food and drug Administration (FDA) released new guidance to assist IRBs in fulfilling this requirement.

According to the guidance document, FDA considers, in general, an adverse event observed during the conduct of a study to be an unanticipated problem involving risk to human subjects, and requires reporting to the IRB, only if it were unexpected, serious, and would have implications for the conduct of the study (e.g., requiring a significant, and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or investigator's brochure).

An individual adverse event occurrence ordinarily does not meet these criteria because, as an isolated event, its implications for the study cannot be understood.

Investigator reports

Principal investigators must report to the BCM IRB and the external IRB of Record (if applicable according to procedure) as soon as possible, but in all cases within 5 business days of any of the following events:

1) Event (including but not limited to on-site and off-site adverse event reports, injuries, side effects, breaches of confidentiality, deaths, or other problems) that occurs any time during or after the research study, which in the opinion of the principal investigator meets all of the elements a) through c) below:

   a) Suggests that the research places one or more participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized. A new or increased risk may be defined as one that requires some action (e.g., requiring a significant and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or investigator's brochure, modification of the consent process, or informing participants.)

   b) Unexpected/Unanticipated (in terms of nature, severity, or frequency given:
      - The research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and,
      - The characteristics of the subject population being studied

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Event Reporting Required of Principal Investigators, Continued

Investigator reports (cont.)

Principal investigators must report to the BCM IRB and the external IRB of Record (if applicable according to procedure) as soon as possible, but in all cases within 5 business days of any of the following events (continued):

c) Related or *possibly related* to the participation in the research procedures:
- *Possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research
- An event is "related to the research procedures" if in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures or if it is more likely than not that the event affects the rights and welfare of current participants

***Note*:** If an event, in the opinion of the principal investigator, does not meet ALL of the elements a) through c) above, the investigator is not required to make a prompt report to the IRB. However, such events may require reporting to the sponsor.

2) Changes made to the research protocol without prior IRB review to eliminate apparent immediate harm to a research participant(s)

***Note*:** For protocol deviations that do not require prompt reporting, at time of continuing review the investigator will inform the IRB of its own quality monitoring processes by which deviations were identified, and process changes to prevent unintended variances.

3) Other unanticipated event, incident, or problem that is related to the research and that indicates that participants or others might be at new or increased risks:
- Any event that requires prompt reporting to the IRB according to the research protocol or plan or the sponsor
- Any accidental or unintentional change to the IRB-approved research protocol (PI self-report of non-compliance) or plan that involved risks or has the potential to recur.
- Any publication in the literature, safety monitoring report, interim result, or other finding that indicates an unexpected change to the risks or potential benefits of the research. For example:
  - An interim analysis indicates that participants have a lower rate of response to treatment than initially expected
  - Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected
  - A paper is published from another study that shows that an arm of your research study is of no therapeutic value

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Event Reporting Required of Principal Investigators, Continued

Investigator reports (continued)

Principal investigators must report to the BCM IRB and the external IRB of Record (if applicable according to procedure) as soon as possible, but in all cases within 5 business days of any of the following events (continued):

4) Any complaint of a participant that indicates unanticipated risk or that cannot be resolved by the research team
5) Protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that placed one or more participants at increased risk, or has the potential to occur again
6) Any instance of non-compliance including PI self-reports
7) Any suspension or termination of research approval
8) Unanticipated adverse device effect (Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.)
9) Unauthorized disclosure of Protected Health Information (PHI) or breach of electronic security (these events should concurrently be reported to the BCM Privacy Officer and IT Security)

For Research Relying on an External IRB

- Before engaging in research, the Principal Investigator must be familiar with the external IRB's reporting requirements specified in the study related documents
- Investigators must promptly report any applicable event according to the external IRB of Record and BCM requirements and procedures. Also, a copy of this prompt report should be provided to the BCM IRB Office *via* email at the time of report to the external IRB of Record.

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Event Reporting Required of Principal Investigators, Continued

Investigator reports for VA research

Investigator reports for VA Research are handled as follows:

VA personnel must report within 5 business days of becoming aware of any *local* (i.e., occurring in the reporting individual's own facility) serious adverse event (SAE) or serious problem that is both *unanticipated, and at least possibly related to the research.* The Principal Investigator makes the initial determination of whether the event is unanticipated and related.

Within 5 business days after receiving written notification of an SAE that the PI considers at least possibly related, the IRB Chair or qualified IRB member-reviewer must determine and document whether any actions are warranted to eliminate apparent immediate hazards to subjects.

The IRB must review the incident and determination of the IRB Chair or qualified IRB member-reviewer at the next convened meeting and must determine and document that:

- The incident was serious and unanticipated and related to the research; or
- There is insufficient information to determine whether the incident was serious and unanticipated and related to the research; or
- The incident was not serious, and/or the incident was not unanticipated, and/or the incident was not related to the research.

Regardless of determination, the convened IRB must also determine and document whether any protocol or informed consent modifications are warranted.

If modifications are warranted, the convened IRB must determine and document whether or not investigators must notify or solicit renewed/revised consent from previously enrolled subjects; and if so, when such notification or consent must take place and how it must be documented.

The IRB must notify the VA Facility Director and the ACOS/R&D in writing within 5 business days after its convened meeting if:

- Actions were taken to eliminate apparent immediate hazards to subjects; or
- The IRB determined that the incident was serious and unanticipated and related to the research, or there was insufficient information to make the determination; or
- Protocol or informed consent modifications were warranted

Local Research Deaths: VA personnel must ensure oral notification to the Institutional Review Board (IRB) and ACOS/R&D (i.e., within one hour) immediately upon becoming aware of any local research death that is both unanticipated and related or possibly related to the research. VA personnel must also ensure that a follow-up written notification is provided to the IRB within one (1) business day of becoming aware of such a death.

The ACOS/R&D, or designee, must alert the VA medical facility Director and appropriate ORO workgroup by email or telephone within one (1) business day after receiving the initial oral notification and provide relevant information as requested.

Within one (1) business day after receiving written notification of the death, the IRB Chair or another qualified IRB voting member must assess and document whether any actions are warranted to eliminate apparent immediate hazards to subjects and, if so, initiate those actions.

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Event Reporting Required of Principal Investigators, Continued

Investigator reports for VA research (cont.)

Investigator reports for VA Research are handled as follows (continued):

The IRB must review the written notification, the immediate hazard assessment of the IRB Chair or other qualified IRB voting member, and the actions taken to date at its next convened meeting, not to exceed 30 calendar days after the date of written notification. ***Note*****:** *Incidents covered by this paragraph may call for immediate attention and require the IRB to convene an emergency session prior to its next scheduled meeting.*

The IRB must determine and document during this convened meeting the following:

- That the death was or was not unanticipated and related to the research or there is insufficient information to make a determination
- Whether modifications are warranted and
- Whether/when/how investigators must notify or solicit renewed consent from enrolled subjects, and if so, when such notification or consent must take place and how it must be documented.

The IRB must notify the VA Facility Director, the RCO, and the ACOS/R&D within 5 business days of determinations. The Facility Director must report to ORO within 5 business days after notification by the IRB.

If a VA investigator classifies a serious adverse event as "anticipated" in an unfounded manner this will constitute serious non-compliance.

In addition to the 9 reportable events above, VA research policies and procedures require principal investigators to report to the IRB as soon as possible, but in all cases within 5 business days any of the following events:

1) Any DMC, DSMB, or DSMC report describing a safety problem in the research
2) Interruptions of subject enrollments or other research activities due to concerns about the safety, rights, or welfare of human research subjects, research staff, or others
3) Any work-related injury to personnel involved in human research, or any research-related injury to any other person, that requires more than minor medical intervention (i.e., basic first aid), requires extended surveillance of the affected individual(s), or leads to serious complications or death.
4) Any VA National Pharmacy Benefits Management (PBM) Bulletins or Communications (sometimes referred to as PBM Safety Alerts) relevant to a VA research project.

Note**:** The local VA has its own procedures for ensuring that these reports are provided to investigators so that the PI may report them to the IRB.

5) Any sponsor analysis describing a safety problem for which action at the facility level may be warranted.

Note**:** Sponsor AE reports lacking meaningful analysis do not constitute "problems" under this paragraph.

6) Any unanticipated problem involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others

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Event Reporting Required of Principal Investigators, Continued

Investigator reports for VA research (continued)	**Investigator reports for VA Research are handled as follows** (continued)**:** 7) Any problem reflecting a deficiency that substantively compromises the effectiveness of a facility's human research protection or human research oversight programs. 8) Any unauthorized use, loss, disclosure, or data breach of VA sensitive information must be reported to the VA Privacy Officer and/or VA Information Security Officer and to the IRB upon discovery.
Other reports	The IRB will accept other reports of events where the principal investigator has evaluated the event but is still unsure whether the event should be reported.
IRB review of event reports	The IRB will review the event reports as specified in IRB Review of Event Reports for Determination of (UPIRSO) Unanticipated Problems Involving Risks to Subjects or Others
Related standards	AAHRPP I.1.D, I.4.A, II.2.C, II.2.D, II.2.E, II.2.F, II.2.G, II.2.H, II.3.B, III.2.D

IRB Review of Event Reports for Determination of (UPIRSO) Unanticipated Problems Involving Risks to Subjects or Others

Introduction

Date of Last Revision/Review: 04/28/23

This topic provides the procedures for the IRB's review of events required to be reported by investigators. The IRB reviews each to determine whether or not it is an unanticipated problem involving risks to subjects or others (UPIRSO).

IRB review of event reports

An experienced IRB member will review event reports submitted by investigators to determine whether the event is an UPIRSO:

- Was unanticipated/unexpected/unforeseen,
- Places a person or others at increased risk of harm than was previously known or recognized, and
- Was related to or possibly related to the research procedures.

If the experienced IRB member and IRB Chair/designee under the Primary and Team Reviewer System determines that an event does not meet the UPIRSO criteria, no further action is taken.

If the experienced IRB member and IRB Chair/designee believe that the event(s) report *may* meet the UPIRSO criteria, the event is reviewed under the primary reviewer system (see Primary and Team Reviewers, Research Materials). The IRB will determine whether each event is an UPIRSO.

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IRB Review of Event Reports for Determination of (UPIRSO) Unanticipated Problems Involving Risks to Subjects or Others, Continued

IRB review of VA event reports

For VA Research, the IRB reviews event reports as follows:

- Within 5 business days after a report of a serious unanticipated problem involving risks to subjects or others or of a local unanticipated SAE, the convened IRB or experienced IRB member must determine and document whether or not the event met each of the following criteria:
  – Serious, and,
  – Unanticipated, and,
  – Related to the research
- If the convened IRB or the experienced IRB member determines that the problem or event met each of the above three criteria, a simultaneous determination is required regarding the need for any action (e.g., suspension of activities; notification of subjects) necessary to prevent an immediate hazard to subjects.
- If the convened IRB or the qualified IRB member-reviewer determines that the problem or event is serious and unanticipated and related to the research, the IRB Chair or designee report the problem or event directly (without intermediaries) to the Facility Director within five business days after the determination.
- All determinations of the qualified IRB member-reviewer (regardless of the outcome) must be reported to the IRB at its next convened meeting, not to exceed 30 business days.
- If it was determined that the problem or event met each of the above three criteria, the convened IRB must determine and document whether or not a protocol or informed consent modification is warranted.
- If the convened IRB determines that a protocol or informed consent modification is warranted, the IRB must also determine and document:
  – Whether or not previously enrolled subjects must be notified of the modification and, if so,
  – When such notification must take place and how such notification must be documented.

IRB reports of UPIRSOs

If the IRB subcommittee determines that the report was indeed an UPIRSO, it follows the IRB procedures for communicating its determinations (see How an IRB Determination is Provided and Chain of Reporting).

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IRB Review of Event Reports for Determination of (UPIRSO) Unanticipated Problems Involving Risks to Subjects or Others, Continued

IRB actions	The IRB may take any of the following actions in response to post approval reports: • Modification of the protocol • Modification of the information disclosed during the consent process • Providing additional information to current participants (This must be done whenever the information may relate to the participant's willingness to continue participation) • Providing additional information to past participants • Requiring current participants to re-consent to participation • Alteration of the frequency of continuing review • Observation of the research or the consent process • Requiring additional training of the investigator • Notification of investigators at other sites • Termination or suspension of the research • Obtaining additional information • Taking no action
Related standards	AAHRPP I.1.D, I.4.A, II.2.C, II.2.D, II.2.E, II.2.F, II.2.G, II.2.H, II.3.B, III.2.D

Reporting and Assessing Compliance Concerns

Introduction

Date of Last Revision/Review: 09/05/25

In accordance with 45 CFR 46.103, the BCM Institutional Review Boards (IRBs) have the responsibility and authority to oversee the use of human subjects in research that is under their jurisdiction.

As part of the IRBs' oversight responsibilities, procedures exist for the "prompt reporting…of any serious or continuing non-compliance with the federal regulation" or institutional policies and "suspension or termination of IRB approval."

Scope

This procedure applies to all research activities of faculty, staff, students, or others who are involved in human subject research that fall under the jurisdiction of the BCM IRBs. For more information see, Scope of the IRB's Authority.

BCM IRBs will serve as the compliance oversight authority on behalf of BCM to assure safe and appropriate performance of research conducted under the review authority of an external IRB.

Definitions

The following table defines terms used in this procedure:

Terms	Definitions
Non-compliance	Conducting research involving human subjects in a manner that violates laws, federal regulations, policies, or institutional policies governing such research. ***Note*:** This includes the failure to comply with IRB determinations and the failure of the IRB to follow regulations. **For VA research:** This includes non-compliance with VA policies and Handbook requirements.
Serious non-compliance	Violations that have or pose a greater than minimal risk of harm or discomfort to research participants or others involved in the research. **For VA research:** A failure to adhere to the laws, regulations, or policies governing human research that may reasonably be regarded as: • Presenting a genuine risk of substantive harm to the safety, rights, or welfare of human research subjects or others, including their rights to privacy and confidentiality of identifiable private information • Presenting a genuine risk of substantive harm to the safety, rights, or welfare of research personnel who conduct research • Presenting a genuine risk of substantive harm to the health or welfare of animals used in research • Presenting a genuine risk of substantive reputational harm to VA; or • Substantively compromising a VA medical facility's Animal Care and Use Program (ACUP), Human Research Protection Program (HRPP), Research Safety and Security Program (RSSP), or research information security processes

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Reporting and Assessing Compliance Concerns, Continued

Definitions (con't.) The following table defines terms used in this procedure (continued):

Terms	Definitions
Continuing non-compliance	A pattern of non-compliance that has the potential to compromise human research protections. **For VA research:** Continuing non-compliance means repeated instances of non-compliance with applicable laws, regulations, policies, agreements, or determinations of a research review committee or the prolonged persistence of non-compliance occurring after its identification, awareness, or implementation of a corrective action intended to effectively resolve the non-compliance.
Reportable	The term "reportable" refers to an incident, event, or situation that must be reported under the requirements of an applicable regulatory or oversight entity.

Suspected non-compliance reporting process Below is a description of the reporting process for suspected non-compliance on the part of an investigator or research staff:

Questions	Answers
Who may report?	Reports can come from a number of different sources, including: • Investigators • Research personnel • Oversight committees/staff members • Research Compliance Officer of the VA • Subjects/family of subjects • Institutional personnel • The media • The public • Anonymous sources
Who do the reports go to?	Verbal or written reports may be made to either of the following: • Director of Research Compliance-IRB • Research Compliance Services (RCS)

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Reporting and Assessing Compliance Concerns, Continued

Suspected non-compliance reporting process (cont.)

Below is a description of the reporting process for suspected non-compliance on the part of an investigator or research staff (continued):

Questions	Answers
How is suspected non-compliance reported?	Since these types of reports may arrive in various formats (phone call, letter, email) there is not a requirement regarding specific information that must be reported. In most cases, the complainant is asked to submit the concern(s) in writing. **For VA research:** Within 5 business days of becoming aware of any non-compliance with applicable human research protection requirements, members of the VA research community are required to ensure that the apparent non-compliance has been reported in writing to the IRB. ***Note*:** The determination that non-compliance is "serious" or "continuing" rests with the IRB. The VA Research Compliance Officer (RCO) Reports non-compliance: Within 5 business days of identifying non-compliance based on an informed consent audit, regulatory audit, or other systematic audit of VA research, an RCO must make a complete report of the non-compliance to the IRB.

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Reporting and Assessing Compliance Concerns, Continued

Suspected non-compliance reporting process (cont.)

Below is a description of the reporting process for suspected non-compliance on the part of an investigator or research staff (continued):

Questions	Answers
How is suspected non-compliance reported? (cont)	An initial report of non-compliance based on an RCO informed consent audit, RCO regulatory audit, or other systematic RCO audit is required regardless of whether disposition of the matter has been resolved at the time of the report. **VA RCO Reports non-compliance:** The IRB reviews RCO reports of non-compliance not only to determine the serious or continuing nature of the PI's non-compliance, but also to assure that subjects' rights and welfare are adequately protected. In order for the IRB to review any RCO report of non-compliance, the IRB can ONLY receive complete reports. A complete report from the RCO should include ALL of the following: • PI name • Protocol: – IRB H# in BRAIN – Title – Risk category • Date of the: – Report – Audit • Type of audit • Brief protocol summary should include: – A statement if the protocol is still actively enrolling – Total number of subjects enrolled in the study to date – A statement of whether the subjects involved in the non-compliance are still active in the study • Name of any external sponsor(s) and funding source of the protocol

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Reporting and Assessing Compliance Concerns, Continued

Suspected non-compliance reporting process (cont.)

Below is a description of the reporting process for suspected non-compliance on the part of an investigator or research staff (continued):

Questions	Answers
How is suspected non-compliance reported? (cont.)	• Description of each finding in the complete RCO audit report with ALL of the following: – The non-compliance – The specific (with citation) federal regulation, BCM IRB procedure, or VA Handbook policy for the finding to represent non-compliance – A clear and concise description of the facts, using whatever presentation or format (paragraph, table, etc.) necessary that most appropriately describes the finding that includes the relevant information the IRB will need to: > Substantiate non-compliance > Understand the nature and severity of the non-compliance on the protection of subjects' rights and welfare, makes its determination, and suggest corrective actions, and, > Complete supporting documentation such as: copies of audit worksheets, any additional supporting documentation that may assure the IRB that subjects' rights and welfare were reasonably protected, committee approval letters, interim notices, photocopies of consent documents with irregularities, summaries of the consent dates for each subject, etc. as appendices to the report. • Description of, if any, corrective actions that have been implemented, either self-initiated by the PI's or any suggested as part of the RCO audit (research compliance education activities) to prevent or correct the same non-compliance in the future • A summary of to whom and to which offices or entities the RCO has made or will make concurrent or previous reports related to these findings of non-compliance • A statement that accompanies the report signed and dated by the PI that provides the IRB with the PI's proof of receipt and concurrence with the RCO audit findings or the PI's corrections of errors of fact with the RCO report. The IRB requires that the information in the RCO report be provided to the PI and requires his/her concurrence of the findings, in order to confirm that the finding is correct (no errors of fact); and to assure that any actions can be taken to protect subjects prior to the IRB making a finding for the PI's non-compliance as serious and/or continuing.

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Reporting and Assessing Compliance Concerns, Continued

Suspected non-compliance reporting process (cont.)

Below is a description of the reporting process for suspected non-compliance on the part of an investigator or research staff (continued):

Questions	Answers
How is suspected non-compliance reported? (cont.)	This complete RCO report with all the attachments, the PI's signed statement, and, if any, PI's corrections of errors of fact (if applicable) will be forwarded to the IRB for it to make a determination as well as suggest any additional corrective actions. ***Note*:** The IRB must review any notifications at the earliest practicable opportunity, not to exceed 30 business days after the notification. The IRB Chair may take interim action as needed to eliminate apparent immediate hazards to subjects.
What happens next?	The Director of Research Compliance and RCS determine if the allegation is a possible non-compliance issue and may refer the issue to other Committees (i.e., Scientific Integrity, Conflict of Interest) as appropriate. For self-reported concerns of non-compliance, if the allegation is considered possible non-compliance, RCS will begin the assessment procedures as indicated further in this procedure for the IRB to review and make its determination.

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Reporting and Assessing Compliance Concerns, Continued

VA research examples of non-compliance

Below is a listing of the examples of non-compliance that must be reported to the IRB within 5 business days include, but are not limited to the following:

Terms	Examples
VA research examples of non-compliance	• Initiation of human research without required: – IRB approval – Research and Development (R&D) Committee approval • Failure to obtain required: – Informed consent for one or more subjects – Documentation of informed consent – Health Insurance Portability and Accountability Act (HIPAA) authorization for one or more subjects • Other substantive informed consent or HIPAA authorization deficiencies, including HIPAA authorization deficiencies that have led to use and disclosure of protected health information (PHI) without proper legal authority • Substantive unapproved deviations from IRB-approved protocols (except to eliminate apparent immediate hazards to subjects), including substantive violations of inclusion or exclusion criteria • Failure to: – Implement any protocol or informed consent modifications, or other changes as required by the IRB – Notify the IRB of apparent unanticipated problems in human subjects research involving risks to subjects or others (UPIRTSO), including serious adverse events that are unanticipated and related or possibly related to participation in VA research • Unfounded determination of a UPIRTSO as "anticipated" or "not related" to the research • Conduct of research: – Without required credentialing, privileging, or initial training of research staff – Involving women known to be pregnant, prisoners, or children, or of international research, without required approvals from the Facility Director or Chief Research and Development Officer, as applicable • Continuation of human research beyond the specified IRB approval period • Non-compliance that substantively compromises the HRPP (e.g., violation of IRB quorum requirements; improper approval or documentation of exemptions or waivers; failure to ensure review of proposed research sufficient to identify and address privacy or data security concerns). ***Note*:** Non-compliance on the part of the IRB must be reported to the facility R&D Committee.

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Reporting and Assessing Compliance Concerns, Continued

VA research examples of non-compliance (cont.)

Below is a listing of the examples of non-compliance that must be reported to the IRB within 5 business days include, but are not limited to the following (continued):

Terms	Examples
VA research examples of non-compliance (cont.)	• Any combination of non-compliant actions that collectively present a genuine risk of substantive harm to the safety, rights, or welfare of human research subjects (including their rights to privacy and confidentiality of identifiable private information), research personnel, or others, or substantively compromise a facility's HRPP • Serious programmatic non-compliance - Examples include but are not limited to: – Conduct of IRB business by an improperly constituted committee or with less than a quorum of voting members present – Improper designation of research as exempt under 38 CFR 16.101(b) – IRB approval of a waiver of informed consent, a waiver of documentation of informed consent, or a waiver of HIPAA Privacy Rule Authorization when the respective approval criteria at 38 CFR 16.116(c) or 16.116(d), 38 CFR 16.117(c), or 45 CFR 164.512(i)(1)(i) are not met or are not documented – Programmatic failure to provide for and document Privacy Officer (PO) and Information Security Officer (ISO) review of proposed human subject research – Any programmatic non-compliance involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others • Any programmatic non-compliance that substantively compromises the effectiveness of the facility's human research protection or human research oversight programs
VA research examples of Continuing non-compliance	• Repeated failure by the: – Relevant investigator(s) to ensure timely remediation of any non-compliance, identified by or made known to the investigator(s), with requirements for the conduct of human research – Responsible official(s) to ensure timely remediation of any programmatic non-compliance, identified by or made known to the official(s), with requirements for the conduct or oversight of human research • Any non-compliance that, due to its persistence over time, results in a genuine risk of substantive harm to the safety, rights, or welfare of human research subjects, research personnel, or others, or substantively compromises a facility's HRPP • Persistence of non-compliance occurring after the implementation of a corrective action intended to effectively resolve the non-compliance

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Reporting and Assessing Compliance Concerns, Continued

VA Research Compliance Officer (RCO)

A Research Compliance Officer is an individual whose primary responsibility is auditing and reviewing research projects relative to requirements for the protection of human subjects, laboratory animal welfare, research safety, and other areas under the jurisdiction of and specified by the VA Office of Research Oversight.

The RCO may attend IRB meetings as a nonvoting consultant to the IRB, as needed and when requested by the IRB Chairperson, to present compliance matters to the IRB.

The Research Compliance Officer reports directly to the MEDVAMC Director and meet monthly with the Director and on an as needed basis. The RCO also performs the following functions:

- The RCO conducts, supervises, or verifies all audits
- Serves as a local resource for regulations, policies, memoranda, alerts, and other VA and federal requirements related to research compliance
- Serves as a consultant on the Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), Subcommittee on Research Safety (SRS), and Research and Development (R&D) Committee
- May provide education to investigators and research staff regarding regulatory and policy requirements
- Disseminates research compliance policy changes as needed to the R&D Committee, research subcommittees, and assists in the dissemination of this information to research staff
- Promptly forwards all cases of serious and/or continuing non-compliance to the necessary subcommittee(s) as appropriate
- Further, ensures prompt reporting in accordance with all applicable policies to the Office of Research Oversight (ORO)
- Ensures all required audits are completed according to the requirements and deadlines indicated in "ORO Guidance Regarding RCO Audit and Training Requirements for the (current audit year) Reporting Period" posted on the ORO Research Compliance and Technical Assistance website

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Reporting and Assessing Compliance Concerns, Continued

Investigating concerns/allegations

The process for IRB review of concerns/allegations of suspected non-compliance for an investigator or research staff is as follows:

Step	Action
1	**Initial Complaint/Concern Received** A research intermediary from Research Compliance Services (RCS) acting on behalf of the IRB, or another experienced voting IRB member, evaluates the concern/allegation to determine whether or not the concern/allegation may be reviewed through expedited procedures by the following criteria: • **Expedited Assessment Review Procedures** –An expedited procedure may be used for items that appear to be minor when the alleged compliance concern(s), if substantiated, would not constitute greater than minimal risk of harm to subjects or others. • The research intermediary or experienced IRB member may determine at any time that the above criteria for expedited review have not been met. In that case the compliance concern/allegation is forwarded for review by a subcommittee of the IRB as described below. ***Note*:** An experienced IRB member is an IRB member that has participated in at least one IRB training session and 16 IRB meetings (typical two-year service with 75% attendance). • **For VA Research**, self-reported concerns of non-compliance will proceed to Step 2 and proceed with the normal assessment process. ***Note*:** Reports of non-compliance received from the RCO, as indicated in previous sections, will proceed to Step 7 for review and determination by the IRB.

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Reporting and Assessing Compliance Concerns, Continued

Investigating concerns/allegations (cont.)

The process for IRB review of concerns/allegations of suspected non-compliance for an investigator or research staff is as follows (continued):

Step	Action
2	**Notice of Concern/Acknowledgement of Concern** A research intermediary from Research Compliance Services (RCS) acting on behalf of the IRB: • Notifies, in writing, the: – Individual who is the subject of the concern – BCM Privacy Officer if the concern involves potential unauthorized use, loss, or disclosure of individually-identifiable patient/subject information from the covered entity component of BCM – BCM Information Technology Security Officer if the concern involves potential violations of BCM information security requirements or standards – ***Note*:** If the concern is initiated by the Principal Investigator who is also the subject of concern, the RCS Research Intermediary, on behalf of the IRB, acknowledges the concern in writing. • Conducts a preliminary review of the IRB files in (BRAIN) • Determines whether or not the research is categorized as VA Research • **For VA Research**, provides notification of the concern to the VA *via* HRP@va.gov. The VA RCO may be invited to become involved in the assessment process at any point according to VA procedures, or invited to be present at subcommittee or fully convened meetings of the IRB as a nonvoting consultant to the IRB. • For Research Relying on an External IRB: Based on the reliance agreement established with the IRB of Record, the BCM HRP office will work with the IRB of Record to determine the assessment procedures. If the external IRB will lead the assessment, RCS provides notification of the concern to: – Principal Investigator – External IRB Administrator – Human Protections Administrator of any affiliate institutions associated with the research, if applicable – Department Chair, and if applicable, the Division/Section Chief • The assessment and report to the IRB will then be conducted according to the procedures described in the reliance agreement.
3	**Preliminary Report to the Subcommittee of the IRB** A research intermediary from Research Compliance Services (RCS) acting on behalf of the IRB: • Presents the preliminary review and all related documentation to the IRB or subcommittee of the IRB (Fully convened procedures), or the IRB Chair and an experienced IRB member (Expedited procedures) for review Members of the IRB subcommittee serve as primary reviewers, see Primary and Team Reviewer System for more information

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Reporting and Assessing Compliance Concerns, Continued

Investigating concerns/allegations (cont.)

The process for IRB review of concerns/allegations of suspected non-compliance for an investigator or research staff is as follows (continued):

Step	Action
4	**Decision to Assess by the IRB** • Using the information from the complaint and the intermediary's preliminary review, the subcommittee of the IRB determines: – Whether an assessment is warranted – If warranted, defines the scope of the assessment • ***Note 1*:** If significant subject safety concerns exist, the IRB Chair may temporarily suspend conduct of a study pending full IRB review. See Suspension or Termination of IRB Approval for more information regarding suspensions and required reporting of suspensions by the IRB Chair and the Institution. • ***Note 2*:** If the concern is initiated by the Principal Investigator, the decision to assess is not required by the IRB. All concerns reported by the PIs are assessed.
5	**Notice of Assessment** The research intermediary, on behalf of the IRB: • Provides notification of the IRB's decision to assess to the: – Principal Investigator – Director of Research Compliance-IRB – Human Protections Administrator of any affiliate institutions associated with the research, if applicable • Performs the assessment **For VA research:** • Any notification of assessment will be communicated to the VA *via* copy to HRP@va.gov • Any preliminary assessment findings along with the Investigator's responses will be communicated to the VA *via* copy to HRP@va.gov A report from the VA Research Compliance Officer (RCO) of non-compliance is forwarded to the IRB by the RCO to the research intermediary.
6	**Draft Assessment Report** Upon completion of the assessment, the research intermediary, on behalf of the IRB: • Communicates the preliminary findings to the Principal Investigator of the research in question • Offers the Principal Investigator an opportunity to correct any errors of fact and respond to the research intermediary within a two-week period

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Reporting and Assessing Compliance Concerns, Continued

Investigating concerns/allegations (cont.)

The process for IRB review of concerns/allegations of suspected non-compliance for an investigator or research staff is as follows (continued):

Step	Action
7	**Final Assessment Report to the Subcommittee of the IRB or Expedited Experienced Reviewers** the research intermediary, on behalf of the IRB forwards to the IRB subcommittee or expedited IRB reviewers the: • Preliminary assessment findings • Investigator's response to these findings • ***Note 1*:** Any concern of non-compliance identified through the IRB's routine monitoring procedures will begin the IRB review process at this step. • ***Note 2*:** Upon request, the subcommittee has access to all documents associated with the assessment and the entire IRB file related to the research. • **For VA Research**, RCO reports of non-compliance are continued here from Step 1. The RCO's report which contains all the details of their completed assessment, is provided to the IRB.
8	**Final Assessment Report to the IRB** **Expedited Assessment Review Procedures:** The experienced IRB member and the Chair reviews and determines whether or not the concern of non-compliance is substantiated and if so, outlines the corrective actions. Note: Determination of serious or continuing non-compliance, as well as corrective actions to address these findings, may be made only after review by the fully convened IRB. If the experienced IRB member or the Chair is concerned about or disagrees with the determination of serious or continuing non-compliance the matter is forwarded to the fully convened IRB as described above. **Fully Convened Procedures:** • The subcommittee reviews the research intermediary's findings and investigator's response and makes a formal recommendation. • Once the subcommittee makes a formal recommendation, a final assessment report is presented at a fully convened IRB meeting with quorum present • Each member of the fully convened IRB reviews a copy of the final assessment report. Upon request, the fully convened IRB has access to all documents associated with the assessment and the entire IRB file related to the research. • Assessments of the IRB may also be conducted if non-compliance with federal regulations is suspected **For VA Research**, the final assessment report is communicated to the VA *via* copy to HRP@va.gov.

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Reporting and Assessing Compliance Concerns, Continued

Investigating concerns/allegations (cont.)

The process for IRB review of allegations of suspected non-compliance for an investigator or research staff is as follows (continued):

Step	Action
8 (cont)	The IRB determines whether the allegation is substantiated or not:

If...	Then the IRB...
Substantiated	Decides: • Whether it is… – Serious – Continuing – Or both of the above • What corrective actions are required to bring the study into compliance **Expedited Assessment Review Procedures:** • If **minor non-compliance issues** are found (not greater than minimal risk to subjects and non-continuing), the expedited reviewer, with review and approval by the IRB Chair, shall determine appropriate corrective actions. • Any compliance findings will be reported to the fully convened IRB as a part of the report on all expedited actions. **Fully Convened Assessment Review Procedures:** If the assessment indicates serious and/or continuing non-compliance: • The assessment report is reviewed at the next fully convened IRB meeting. • Based on the contents of the report, the fully convened IRB may also request additional assessment of this and/or other of the investigator's research protocols.
Not substantiated	• Dismisses the allegation • Notifies the Principal Investigator that the assessment is closed • This communication may include comments or recommendations from the IRB **Assessment Review Procedures:** Once the assessment is complete, if there are **no findings of non-compliance**, the IRB may close the assessment.

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Reporting and Assessing Compliance Concerns, Continued

Investigating concerns/allegations (cont.)

The process for IRB review of allegations of suspected non-compliance for an investigator or research staff is as follows (continued):

Step	Action
9	**Determination Letter** The IRB: Notifies the Principal Investigator, in writing, of the determination of the IRB, including corrective actions and follow-up plans **For Research Relying on an External IRB:** Following the receipt of a determination from the IRB of Record, provides a copy of the determination to the PI which includes any corrective actions and follow-up plans. **For VA research:** • Corrective actions or remedial actions to correct substantiated instances of non-compliance involving a specific study or research team must be completed within a maximum of 120 days after the IRB's determination of non-compliance • If corrective actions or remedial actions to correct substantiated instances of programmatic non-compliance require substantial renovation, fiscal expenditure, hiring, legal negotiations, or other extenuating circumstances, the VA Facility Director must provide ORO with an acceptable written justification and timeline for completion. • The final determination letter from the IRB, letters to federal oversight agencies, and any future closure letters are communicated to the VA *via* copy to HRP@va.gov • Assists in the preparation of required notification letters from the Institutional Official to appropriate regulatory authorities, sponsors, and affiliate institutions, where serious and/or continuing non-compliance has been determined

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Reporting and Assessing Compliance Concerns, Continued

Actions the IRB may take

After the IRB has made a final determination, it may take any reasonable corrective action it deems appropriate. Below are examples of possible actions, but should not be construed as an all-encompassing list:

- Approval of the investigator's proposal for implementation of corrective actions – *no further action*
- Requesting additional information to determine if a change in the risk/benefit ratio has occurred*, pending final action*
- Notification and involvement from other individuals from BCM (ex: Dean, Section Chief, Department Chair)
- Restricting the use of research data for publication
- Requiring:
  - Modification to the research protocol or informed consent document
  - Additional protocols be submitted to the IRB
  - Past or current subjects to be informed of the non-compliance and be re-consented if the information relates to their willingness to continue taking part in the study
  - The withdrawal of currently enrolled subjects, if it is in their best interest
  - Remediation, mentoring, or educational measures such as:
    - Requiring the PI or research team to take additional human subjects protection training
    - Informed Consent workshops
    - Consulting with RCS or the IRB staff
  - Appointment of an informed consent monitor
  - Increased reporting by the investigator or increased monitoring of the research
- Modifying the continuing review cycle to less than 365 days
- Restricting the investigator's human research activities, including suspension, or:
  - Limiting the privilege to conduct human subjects research to be only protocols that impart no greater than minimal risk to subjects
  - Participation only in supervised research projects
- Suspension of approval or the termination of one or more of the investigator's research activities
- Refer the issue to other committees responsible for possible further review and action
- Requesting assistance from the General Counsel
- Any other action the IRB deems appropriate to ensure compliance with federal regulations, BCM policy, or to otherwise protect the human subjects participating in research under BCM's federalwide assurance

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Reporting and Assessing Compliance Concerns, Continued

Reporting of non-compliance determinations	For information on reporting non-compliance determinations by the IRB, see Chain of Reporting.
Appeals	An investigator may appeal a determination if they have information that has not been considered previously by the IRB. The request must be submitted to the Director of Research Compliance-IRB within 15 days of receipt of the determination letter.
Concerns about the adequacy of the assessment	Any concerns that the assessment may have been inadequate may be forwarded to: • Director of Research Compliance-IRB • Executive Director of Research Compliance • Institutional Official • Senior Vice President for Research, or • President of the College Additionally, OHRP, FDA, or the sponsor may be contacted.
Related standards	AAHRPP I.4, I.5, I.5.D, II.2.C, II.2.D, II.2.F, II.2.G, II.2.H, III.1.G, III.2.D

Chain of Reporting

Introduction

Date of Last Revision/Review: 09/05/25

This topic outlines the chain of reporting regarding human subject research by investigators, IRB, and the Human Subject Signatory Official.

AAHRPP reporting

The Association for the Accreditation of Human Research Protection Programs (AAHRPP) requires notice within 48 hours after the organization becomes aware of any (researchers should report to the irb@bcm.edu asap):

- Negative actions by a government oversight office related to human research protections, including, but not limited to:
  - OHRP determination letters
  - FDA warning letters
  - FDA 483 inspection report with official action indicated
  - FDA restrictions placed on IRBs or investigators
  - Corresponding compliance actions taken under non-US authorities related to human research protections
- Litigation, arbitration, or settlements initiated related in human research protections
- Press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding the organization's HRPP

It is important that AAHRPP is aware in real time of issues affecting its accredited organizations.

Requirement

This table describes the chain of reporting:

Stage	Description
1	Investigators must report to the BCM IRB and the external IRB (if applicable according to procedures) within 5 working days any of the following: • Any event that is required to be reported to the IRB. See Event Reporting Required of Principal Investigators. • Any instance of alleged non-compliance **For Research Relying on an External IRB:** The PI must also refer to the reporting procedures for the IRB of Record accordingly. **For VA research:** • Any instance of apparent serious non-compliance or apparent continuing non-compliance must be reported to the IRB. See Reporting and Assessing Compliance Concerns. • Any unauthorized use, loss, disclosure, or data breach of VA sensitive information must be reported to the VA Privacy Officer and/or VA Information Security Officer and to the IRB upon discovery.

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Chain of Reporting, Continued

Requirement (continued)

This table describes the chain of reporting (continued):

Stage	Description
2	The following reports from Stage 1 require special reporting by the IRB: • Any event determined by the IRB to meet the criteria of an unanticipated problem involving risks to subjects or others (UPIRSO). See IRB Review of Event Reports for Determination of (UPIRSO) Unanticipated Problems Involving Risks to Subjects or Others. • Any substantiated report of non-compliance • Any suspension or termination of IRB or other approval The above are communicated as follows: • The Chair of the IRB reports determinations to the: – Principal Investigator – Human Subject Signatory Official – Department Chair and if applicable, Division/Section Chief – Human Protections Administrator of the affiliate institution(s) – Legal Counsel (if applicable) – BCM Privacy Officer (if applicable) – IT Security (if applicable) • The Director of Research Compliance-IRB and/or Research Compliance Services and the Executive Director of Research Compliance assist with the above correspondence • Recipients of these determinations are offered an opportunity to appeal the decision if new information is found that the IRB has not considered. For more information on appeals, see procedure on How an IRB Determination is Provided. **For Research Relying on an External IRB:** If a UPIRSO determination is received from the IRB of Record, the BCM IRB office will then provide the notifications outlined above if they have not already been distributed. **For VA research:** • If the convened IRB or the qualified IRB member-reviewer determines that the problem or event is serious and unanticipated and related to the research, the IRB Chair or designee must report the problem or event directly to the facility Director within 5 business days after the determination. This report must be made in writing to HRP@va.gov from the IRB Chair or designee. The recipients of the HRP@va.gov are the: Medical Center Director, Research Compliance Officers, Associate Chief of Staff for Research and the Research and Development Committee (R&DC) representative.

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Chain of Reporting, Continued

Requirement (continued)

This table describes the chain of reporting (continued):

Stage	Description
2 cont.	• For reports of any unauthorized use, loss, disclosure, or data breach of VA sensitive information, the VA PO and/or ISO will promptly report the incident (within one hour of notification) to the VA- Network Security Operations Center (VA-NSOC): – After the incident has been detected and reported, the MEDVAMC Research Service Line, IRB, Principal Investigator, and staff (as applicable) will coordinate with the VA PO and/or ISO to implement all remediation procedures in accordance with VA Directive 6500 and 6500.2. – Depending on the results of the incident, recovery activities may include training employees or personnel on applicable policy and procedures to include providing notice of credit protection services as necessary. – All VA security incidents will be tracked in the Privacy Security Event Tracking System from initiation until closure.
3	IRB determinations of the following must also be reported by the Human Subject Signatory Official to recipients in Stage 4: • Any unanticipated problems in research involving risks to subjects or others • Any serious or continuing non-compliance with the human subject regulations or the determinations of the IRB • Any suspension or termination of IRB approval of research ***Note*:** The Human Subject Signatory Official is provided a written summary of all the BCM IRB's actions in the form of IRB meeting minutes after they are approved by the IRB. For external IRBs this is provided according to the reliance agreement with that IRB of Record.

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Chain of Reporting, Continued

Requirement (continued)

This table describes the chain of reporting (continued):

Stage	Description
4	The Human Subject Signatory Official reports within 15 working days items B and C to the: • OHRP • FDA (where FDA oversight of the research is applicable) • Funding source(s) • Applicable external IRB • Human Protections Administrator of the affiliate institution(s) • Other Federal agencies with regulatory oversight of the research RCS and the Director of Research Compliance assist with the above reporting. Copies of communications to federal agencies outlining the IRB's determination will be provided to the fully convened IRB. Communications received by the Institutional Official from federal agencies in response to an IRB determination will be provided to the fully convened IRB. See Stage 5 for content of the report. The Human Subject Signatory Official reports promptly item A in Stage 3 to the below entities when: a) BCM and/or its affiliated institutions are the site at which the subject experienced an adverse event determined to be an unanticipated problem or when any other type of unanticipated problem occurred or b) BCM and/or its affiliated institutions are the central monitoring entity designated to submit reports of unanticipated problems: • OHRP • FDA (where FDA oversight of the research is applicable) • Funding source(s) • Human Protections Administrator of the affiliate institution(s) • Other Federal agencies with regulatory oversight of the research RCS and the Director of Research Compliance assist with the above reporting. Communications received by the Institutional Official from federal agencies in response to an IRB determination will be provided to the IRB subcommittee which reviewed the event. See Stage 5 for content of the report.

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Chain of Reporting, Continued

Requirement (continued)

This table describes the chain of reporting (continued):

Stage	Description
5	The content of the report is as follows: • Title of the study • Name of the principal investigator • Description of the event • Findings of the IRB • Regulatory basis for these findings • Actions taken by the IRB • Any further corrective actions taken regarding the circumstances stated in the report ***References***: • DHHS regulations at 45 CFR 46.103(b)(5) • FDA regulations at 21 CFR 56.108(b)

Research relying on an external IRB

Based on the reliance agreement established with the IRB of Record, the BCM HRP office will work with the IRB of Record on any required reporting as noted in Stage 4 of the above table.

VA research

For VA research, the IRB promptly reports the following:

- Any determination of serious or continuing non-compliance in VA Research to the VA facility director (without intermediaries) within five (5) business days after the determination is made:
  – This report must be made in writing to HRP@va.gov from the IRB Chair or designee**.** The recipients of the HRP@va.gov are the: Medical Center Director, Research Compliance Officers, Associate Chief of Staff for Research and Research and Development Committee (R&DC) representative.
  – An initial report of an IRB determination that serious non-compliance or continuing non-compliance occurred is required, even where the determination is preliminary or disposition of the matter has not been resolved at the time of the report.

Continued on next page

Chain of Reporting, Continued

VA research (cont.)	For VA research, the IRB promptly reports the following (continued): • Any termination or suspension of VA research (e.g., by the IRB) to the VA facility director (without intermediaries) within five (5) business days after the determination is made to terminate or suspend the research: – This report must be made in writing to HRP@va.gov from the IRB Chair or designee. The recipients of the HRP@va.gov are the: Medical Center Director, Research Compliance Officers, Associate Chief of Staff for Research and Research and Development Committee (R&DC) representative. – The report must include a statement of the reason(s) for the IRB's action to terminate or suspend VA research. • Any unauthorized use, loss, or disclosure of individually identifiable patient information to the VA Privacy Officer • Violations of VA information security requirements to the appropriate VA Information Security Officer
Department of Defense research	For research subject to DOD regulations, the IRB will follow these same procedures for reporting to DOD as described with input from the DOD consultant reviewer for the purpose of ensuring that all DOD regulations related to reporting are followed. See U.S. Department of Defense Research.
Communication requirement	The IRB must supply copies of any reports or correspondence to or from Federal agencies to the College's Human Subject Signatory Official, Legal Counsel, and Compliance Officer.
Related standards	AAHRPP I.1.D, I.1.D, I.5.D.1.h, II.2.F, II.2.D, II.2.E, II.2.G, II.4.B, II.4.D, II.2.H

Chapter 4
Requirements of Informed Consent

Table of Contents

Overview for Requirements of Informed Consent
Section A What Makes up Informed Consent
Overview
Introduction to Informed Consent
Required Elements and Authorization
Section B Waiver, Alteration, or Exception from Informed Consent Requirements
Overview
State or Local Public Benefit Programs
Waiver or Alteration of Consent for Minimal Risk Research
Research Involving Deception
IRB Review of Planned Emergency Research – Exception from Informed Consent
Waiver of Consent Emergency Research – Guidance and Discussion
Waiver of Documentation of Consent
Informed Consent in Language Understandable to Potential Subjects
Documentation
Completion of the Documentation
Section C Posting of Clinical Trial Consent Form
Overview
Common Rule Requirements
Guidance of Posting Consent Forms

Overview for Requirements of Informed Consent

Introduction

Date of Last Revision/Review: 04/20/11

This chapter provides the requirements of informed consent when involved with research.

In this chapter

This chapter covers the following sections:

- Section A: What Makes up Informed Consent
- Section B: Waiver or Alteration of Informed Consent Requirements
- Section C: Posting of Clinical Trial Consent Form

Related standards

AAHRPP I.1.D, II.2.C, II.2.D, II.2.E, II.4.A, II.4.B, II.4.C, III.1.F

Section A
What Makes up Informed Consent

Overview

Introduction

Date of Last Revision/Review: 04/20/11

This section introduces informed consent, including a description of it, a listing of the elements involved with creating an informed consent document, and the persons authorized to sign an informed consent document.

Institution's policies

The College's policies regarding informed consent follow:

- The elements of informed consent as outlined in these regulations shall not preempt any other Federal, State, or local regulation which requires additional information to be disclosed for informed consent to be legally effective.
- Nothing in the regulations is intended to limit the authority of a physician to provide emergency care to the extent the physician is permitted to do so under applicable Federal, State, or local law. However, such emergency care may not be identified as research, except as required by FDA reporting requirements.

In this section

This section covers the following topics:

- Introduction to Informed Consent
- Required Elements and Authorization

Related standards

AAHRPP I.1.D, II.3.F, II.3.G, II.4.A, II.4.B, II.4.C, III.1.F

Introduction to Informed Consent

Introduction

Date of Last Revision/Review: 01/13/21

This topic introduces the use of informed consent in research.

Responsibility

Research investigators are responsible for obtaining and documenting informed consent in accordance with Federal regulations (45 CFR 46.116-117 and 21 CFR 50.25 and 50.27) and Institutional specific policies. If applicable, the investigator may request a waiver of documentation of consent from the IRB. See Section B: Waiver or Alteration of Informed Consent Requirements

For VA Research:

- Any person designated to obtain informed consent must receive appropriate training and be knowledgeable enough about the protocol to answer the questions of prospective subjects.
- If the PI or LSI (lead site investigator) does not personally obtain informed consent, the PI must formally and prospectively designate in the protocol the responsibility for obtaining informed consent (including when the IRB has granted a waiver of documentation of consent). The protocol does not have to designate the individual by name but can designate the position title(s).\
- Each institution engaged in the Collaborative Research must use the informed consent document required by its respective institutional policies for subjects recruited from that institution, or procedures requiring participation of the participant at that institution. The informed consent document may contain information on the project as a whole as long as the document clearly describes which procedures will be performed under VA's auspices and which will be performed under a non-VA institution's auspice.

Presumptions

Informed consent presumes two simultaneous concepts:

- Informed decision-making
- Voluntary participation

Purpose

Prospective subjects must be given sufficient information about the research and its risks and benefits in order to reach an informed decision as to whether they will voluntarily participate.

Continued on next page

Introduction to Informed Consent, Continued

Reference: Element requirements	**Eight basic informed consent elements** For an effective informed consent process, see these regulations that mandate the inclusion of the elements: • DHHS regulations at 45 CFR 46.116(a) • The Common Rule • FDA regulations at 21 CFR 50.25(a) **Six additional elements** Depending on the nature of the research, additional elements may be required. See these regulations: • 45 CFR 46.116(b) • 21 CFR 50.25(b)
Related standards	AAHRPP I.1.D, II.2.D, II.2.I, II.3.F, II.3.G, II.4.A, III.1.F

Required Elements and Authorization

Introduction

Date of Last Revision/Review: 01/28/19

This topic provides the following requirements:

- The nine basic elements
- The nine additional elements, where appropriate
- Personnel authorized to obtain informed consent

The 9 elements

This table lists the nine basic elements required for informed consent:

Element	Name	Description
1	Research statement	Informed consent information must specifically include each of the following: • A statement that the study involves research • An explanation of the purposes of the research • An explanation of the expected duration of subjects' participation • A description of what procedures will be followed • Identification of any procedures that are experimental
2	Reasonably foreseeable risks or discomforts	Informed consent information must describe any reasonably foreseeable risks or discomforts associated with the research. All risks listed or described in the research protocol must be referenced in the informed consent document.
3	Reasonably expected benefits	Informed consent information must describe any benefits to subjects or to others, which may reasonably be expected from the research. However, benefits must not be overstated as to create an undue influence on subjects.
4	Appropriate alternatives	Informed consent information must include a disclosure of any appropriate alternative procedures or courses of treatment that may be advantageous to the subject. • Enough detail must be presented so that the subject can understand and appreciate the nature of any alternatives. • It is not sufficient simply to state that "the doctor will discuss alternatives to participating." • Where applicable, informed consent must disclose to subjects when treatments identical to those offered by the research may be obtained outside the research, i.e., "off protocol."

Continued on next page

Required Elements and Authorization, Continued

The 9 elements (cont) This table lists the nine basic elements required for informed consent (continued):

Element	Name	Description
5	Extent of confidentiality	Informed consent information: • Must describe the extent to which confidentiality of records identifying the subject will be maintained (or not maintained) • Should describe any procedures that the research team will use to protect subjects' private information or records
		Explanation Research often poses the risk of loss of confidentiality to subjects who participate. Many persons who otherwise would not be privy to identifiable, private information about the subject may be involved in the research process.
		Federal protection Federal officials have the right to inspect research records, including consent forms and individual medical records, to ascertain compliance with the rules and standards of their programs. • The FDA requires that information regarding this authority be included in the consent information for all research that it regulates. • Identifiable information obtained by Federal officials during such inspections is subject to both the privacy provisions and the disclosure provisions of the Privacy Act of 1974.
		For VA research: Photographs/Video Recordings/Audio Recordings Informed consent must include information describing any photographs, video, and/or audio recordings to be taken or obtained for research purposes, how they will be used for the research, and whether they will be disclosed outside the institution conducting the research. An informed consent to take photographs, video and/or audio recordings for research cannot be waived by the IRB. ***Note*:** In order to disclose the photographs, video, and/or audio recordings outside the VA, a HIPAA authorization is needed.

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Required Elements and Authorization, Continued

The 9 elements (cont) This table lists the nine basic elements required for informed consent (continued):

Element	Name	Description
6	Compensation or treatment for injury	Informed consent information for research involving greater than minimal risk must include explanations regarding: • Whether any compensation is available if injury occurs • Whether any medical treatments are available if injury occurs and whether there is a charge for such medical treatment • A description of any such compensation or treatments or where more information about them is available. (Language has been placed in the BRAIN consent document for instances in which no plans for compensation have been made.) • Contact the IRB staff to make changes to this section to reflect plans for compensation of subjects for treatment of injury **For Department of Defense regulated research:** The DOD component may have stricter requirements than the Common Rule requirements for compensation for research-related injury and their disclosure to research participants in the informed consent process. See U.S. Department of Defense Research for more information. **For Sponsored Research:** The sponsor must treat compensation/reimbursement for any research related injury the same for all research subjects. When a sponsor agrees to pay for research related injury, this should not be contingent on whether or not a research subject's insurance or Medicare will pay. This agreement between BCM and the sponsor must be documented in the funding agreement or contract as well as in the informed consent document.

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Required Elements and Authorization, Continued

The 9 elements (cont) This table lists the nine basic elements required for informed consent (continued):

Element	Name	Description
6 (cont)	Compensation or treatment for injury	• **For VA research**, the consent process must disclose required language for research-related injury and payment for medical care related to the research: – The VA must provide necessary medical treatment to a research subject injured by participation in a research project approved by a VA Research and Development Committee and conducted under the supervision of one or more VA employees. – Except in limited circumstances, the necessary care is provided in VA medical facilities. Exceptions include: > When VA facilities are not capable of furnishing economical care, or the required care or services > Situation involves a non-veteran subject > An explanation of the VA's authority to provide medical treatment to subjects injured by participation in a VA research project > A veteran will not be required to pay for care received as a subject in a VA research project except in accordance with Title 38 United States Code (U.S.C.) 1710(f) and 1710(g). Certain veterans are required to pay co-payments for medical care and services provided by the VA. – This requirement does not apply to treatment for injuries that result from non-compliance by a research subject with study procedures. – The Department of Veterans Affairs does not normally provide any other form of compensation for injury. – All regulations pertaining to the participation of veterans as research subjects, including requirements for indemnification in cases of research-related injury, pertain to non-veteran subjects enrolled in VA-approved research.

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Required Elements and Authorization, Continued

The 9 elements (cont)

This table lists the nine basic elements required for informed consent (continued):

Element	Name	Description
7	Contact information	Informed consent information must include details, including telephone numbers, about whom to contact for three specific situations:
		Questions about the research • The principal Investigator • Other members of the research team
		Questions about subjects' rights • The IRB Office • Legal Counsel
		In the event of a research-related injury Depending upon the nature of the research: • The research team • The IRB Office • Legal Counsel

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Required Elements and Authorization, Continued

The 9 elements (cont)

This table lists the nine basic elements required for informed consent (continued):

Element	Name	Description
8	Voluntary participation statement	Informed consent information must contain clear statements of the following: • Participation in the research is voluntary. • Refusal to participate will involve "no penalty or loss of benefits to which the subject is otherwise entitled." • The subject may discontinue participation at any time "without penalty or loss of benefits to which the subject is otherwise entitled." ***Important***: It is particularly important for subjects and prospective subjects to understand and have complete confidence that declining to participate in research will not jeopardize their care. For FDA regulated research - Informed consent information must contain clear statements of the following: • When a research participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having this data removed. • An investigator may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. – Under these circumstances, this future consent discussion with the participant should distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the participant's information. – The investigator must obtain the participant's consent for this limited participation in the study on a separate consent document – The IRB or EC must approve this new consent document prior to its use • If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, an investigator may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

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Required Elements and Authorization, Continued

The 9 elements (cont) (cont)

This table lists the nine basic elements required for informed consent (continued):

Element	Name	Description
9	Identifiers	Informed consent information must contain one of the following statements if the research study involves the collection of identifiable information or identifiable biospecimens: • A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or • A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

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Required Elements and Authorization, Continued

Additional 9 elements

Where appropriate, the regulations require that one or more of the following nine additional elements be included in the informed consent information:

Element	Description
Unforeseeable risks to subjects	Some research involves particular procedures or interventions that may result in unforeseeable risks to subjects, to the embryo, or the fetus (if the subject is or may become pregnant). For research of such a nature, the informed consent information must warn subjects that there may be risks that are not known or not foreseeable.
Investigator-initiated termination of participation	There may be instances that would require investigators to terminate the participation of particular subjects. The informed consent information should specify these circumstances. ***Examples*:** Subject non-compliance with research, subject not benefiting from direct-benefit research
Additional costs	If subjects must bear any additional costs, these must be disclosed in the informed consent information. ***Examples*:** Transportation, time away from work, health costs **For Sponsored Research:** The sponsor must treat compensation/reimbursement for any research related costs (including those that would be considered part of clinical care) the same for all research subjects. When a sponsor agrees to pay for research related costs, this should not be contingent on whether or not a research subject's insurance or Medicare will pay. This agreement between BCM and the sponsor must be documented in the funding agreement or contract as well as in the informed consent document. **For VA research:** Include a statement that veteran-subject will not be required to pay for care as part of VA research (except where co-payment may apply). As appropriate, a statement regarding any payment the subject is to receive and how payment will be made.

Continued on next page

Required Elements and Authorization, Continued

Additional 9 elements (continued)

Where appropriate, the regulations require that one or more of the following nine additional elements be included in the informed consent information (continued):

Element	Description
Early withdrawal/ procedures for termination	Subjects have the right to withdraw from the research. However, some studies involve medications or procedures that would be dangerous for subjects to discontinue abruptly. • For studies of this nature, the informed consent information must provide subjects with knowledge of the consequences affecting a decision to withdraw. • If there are procedures regarding how to withdraw safely from the research, these must also be described. After withdrawal: It is not appropriate for research staff to administer any additional research-oriented questionnaires or interventions that do not affect the safety of subjects who have decided to withdraw.
Significant new findings	Subjects will be informed of any new knowledge or findings about the medication or test article and the condition under study that may affect the risks or benefits to subjects or subjects' willingness to continue in the research.
Approximate number of subjects	When the IRB determines that the information would be material to the potential subjects' decision to participate, the informed consent information should disclose the approximate number of subjects to be enrolled.
Commercial profit from biospecimens	A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.
Results uncovered during the study that may be pertinent to subject's health	A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.
Research involving biospecimens involving genome sequencing	For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

Authorized personnel

Informed consent may be obtained by the investigator or his/her designee as described in the protocol's consent procedures and approved by the IRB.

Continued on next page

Required Elements and Authorization, Continued

Qualifications

The person who may obtain informed consent must qualify as follows:

- The person who conducts the informed consent interview must be knowledgeable about the study and be able to answer questions.
- Informed consent information can be presented by any qualified person involved in conducting the study and is not limited to persons with MDs or PhDs.

For VA research:

If someone other than the investigator obtains and documents informed consent, the investigator:

- Formally delegates this responsibility in writing (e.g., by use of a delegation letter or delegation log)
- Ensures that the delegated person has received appropriate training to perform this function and is sufficiently knowledgeable about the protocol and related concerns to answer questions from prospective subjects, and about the ethical basis of the informed consent process and protocol.

Related standards

AAHRPP I.1.D, I.8.A, II.2.D, II.3.F, II.4.A, III.1.F, III.1.G

Section B
Waiver, Alteration, or Exception from Informed Consent Requirements

Overview

Introduction

Date of Last Revision/Review: 04/20/11

This section provides the circumstances when informed consent requirements and documents may be waived or altered.

In this section

This section covers the following topics:

- State or Local Public Benefit Programs
- Waiver or Alteration of Consent for Minimal Risk Research
- Research Involving Deception
- IRB Review of Planned Emergency Research – Exception from Informed Consent
- Waiver of Consent Emergency Research – Guidance and Discussion
- Waiver of Documentation of Consent
- Informed Consent in Language Understandable to Potential Subjects
- Documentation
- Completion of the Documentation

Related standards

AAHRPP I.1.D, II.2.D, II.3.F, II.3.G, II.4.C, III.1.F

State or Local Public Benefit Programs

Introduction

Date of Last Revision/Review: 04/20/11

This topic discusses the state or local public benefit programs.

Authority

The IRB can do the following for state or local public benefit programs:

- Approve a consent procedure that eliminates or alters the required elements of informed consent
- Waive the requirement to obtain informed consent altogether

Reference: Per the DHHS regulations at 45 CFR 46.116(c) and the Common Rule

Approval requirements

To approve such a waiver or alteration, the IRB must find and document that:

- The activity constitutes a research or demonstration project that is to be conducted by or subject to the approval of State or local government officials and is designed to study, evaluate, or otherwise examine:
  - Public benefit or service programs
  - 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
- The research could not practicably be carried out without the waiver or alteration.

Documentation

These findings and their justifications will be clearly documented in IRB records when the IRB exercises this waiver provision.

Related standards

AAHRPP I.1.D, II.2.D, II.3.F, II.3.G, II.4.C, III.1.F

Waiver or Alteration of Consent for Minimal Risk Research

Introduction

Date of Last Revision/Review: 03/22/24

This topic discusses waiver or alteration of consent for minimal risk to subjects in research.

Authority

The IRB can:

- Approve a consent procedure that eliminates or alters the required elements of informed consent
- Waive the requirement to obtain informed consent altogether

Reference: DHHS regulations at 45 CFR 46.116(d); FDA regulations at 21 CFR 50.22

When following U.S. Department of Education regulations and guidance, additional requirements for waiver of parental permission and child assent must be followed.

See Children in U.S. Department of Education Research.

When following U.S. Department of Defense regulations and guidance, individuals meeting the definition of experimental subject may not be enrolled in research under a waiver of consent unless a waiver is obtained from the Secretary of Defense.

See U.S. Department of Defense Research.

Approval requirement

To approve such a waiver or alteration, the IRB must find and document that:

- The research involves no more than minimal risk to the subjects.
- The waiver or alteration will not adversely affect the rights and welfare of the subjects.
- The research could not practically be carried out without the waiver or alteration.
- Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.
- That the research could not practicably be carried out without using identifiable information in an identifiable format (when applicable)
- That the research could not practicably be carried out without using identifiable biospecimens in an identifiable format (when applicable)

Documentation

These findings and their justifications are clearly documented in IRB records when the IRB exercises this waiver provision.

Related standards

AAHRPP I.1.D, II.2.D, II.3.F, II.3.G, II.4.C, III.1.F

Research Involving Deception

Introduction	Date of Last Revision/Review: 04/20/11 This topic discusses research that involves deception or withholding of information in research.
Description	Deception research involves certain research activities in which the subject is not told or is misled about the true purpose of the research. ***Examples***: Studies of group processes, contextual influences on cognition
IRB requirements	The IRB: • Needs to be satisfied that the deception is necessary and that, when appropriate, the subjects will be debriefed ***Example***: Debriefing may be inappropriate when the debriefing itself would present an unreasonable risk of harm without a countervailing benefit. • Should make sure that the proposed subject population is suitable
Waiver approval	In making the determination to approve the use of deception under a waiver of informed consent, the IRB: • Considers each criterion in turn • Documents specifically how the proposed research satisfies that criterion in the minutes of its meeting or in the IRB protocol file
IRB review	The IRB reviewing research involving incomplete disclosure or outright deception must apply both common sense and sensitivity to the review.
Applicable regulation	Deception can only be permitted where the IRB documents that waiver of the usual informed consent requirements is justified under the criteria at 45 CFR 46.116(d).
Minimal risk only	The regulations make no provision for the use of deception in research that poses greater than minima1 risks to subjects.
For more information	See Research Involving Deception or Withholding of Information in Chapter 3.
Related standards	AAHRPP I.1.D, II.2.D, II.3.F, II.3.G, II.4.C, III.1.F

IRB Review of Planned Emergency Research – Exception from Informed Consent

Introduction	Date of Last Revision/Review: 03/26/15 This topic discusses the IRB review of requests for exception from informed consent for planned emergency research.
Applicable regulation	21 CFR Part 50: Pursuant to Section 46.101(i), the Secretary, HHS, has waived the general requirements for informed consent at 45 CFR 46.116(a-b) and 46.408, to be referred to as the "Emergency Research Consent Waiver".
IRB review	The investigator seeks approval for exception from informed consent through the IRB application and review process. This request for IRB approval is subject to all aspects of IRB review outlined in Section B of this Manual Convened Full Board Review and general approval requirements set forth in Section C Criteria for Approval.
For VA research	The VA does not conduct planned emergency research (see 21 CFR 50.24) involving human subjects. Therefore, the IRB cannot approve a waiver of informed consent for planned emergency research that is subject to VA regulations.
For Department of Defense regulated research	An exception from informed consent in emergency medicine research is prohibited in U.S. Department of Defense regulated research unless a waiver is obtained from the Secretary of Defense. See U.S. Department of Defense Research.
Additional Criteria for approval of exception from informed consent in planned emergency research	*For FDA-regulated research* – The IRB Office and membership will assure that copies of the FDA regulations at 21 CFR 50.24 on planned emergency research exceptions from informed consent are thoroughly reviewed and used for all required determinations and documentation in pre-review and by the fully convened IRB. *For non-FDA-regulated research* – The IRB Office and membership will assure that copies of the DHHS Secretary's waiver from general requirements on planned emergency research exceptions from informed consent are thoroughly reviewed all required determinations and documentation in pre-review and by the fully convened IRB.

Continued on next page

IRB Review of Planned Emergency Research – Exception from Informed Consent, Continued

Reporting

The IRB provides notification of approval, disapproval, or required changes to receive approval, to the Principal Investigator according to How an IRB determination is Provided as follows:

Research subject to FDA regulations	The Principal Investigator is responsible to communicate the IRB determination with the sponsor, or when serving as sponsor/investigator, with the FDA in reference to the IND or IDE required for planned emergency research in which an exception from informed consent is sought. See Exception from Informed Consent for Planned Emergency Research.
Research not subject to FDA regulations	After approval, the IRB Chair and Director of Research Compliance-IRB, with assistance from Research Compliance Services prepare a report of its required findings and provide this report to the Principal Investigator and to the Office for Human Research Protections (OHRP).

Documentation

The IRB documents its findings and actions according to the regulations for this exception in addition to its documentation procedure at How an IRB determination is Provided and Minutes of an IRB Meeting

Related standards

AAHRPP I.1.D, II.2.D, II.3.F, II.3.G, II.4.C, III.1.F

Waiver of Consent Emergency Research – Guidance and Discussion

Introduction

Date of Last Revision/Review: 03/27/15

This topic discusses:

- The exception from informed consent for planned emergency research for research subject to FDA regulations described in 21 CFR 50.24
- Research not subject to FDA regulations by the Secretarial Waiver provision codified in 45 CFR 46.101(i), referred to as the "Emergency Research Consent Waiver".
- This topic also provides an explanation of the wording in the regulation 21 CFR 50.24 and waiver of applicability of certain informed consent requirements, October 2, 1996 (Federal Register, Vol. 61, pp. 51531-51533).

Description

The IRB must find and document each of the following.

It is clear from the regulations' wording that it is the IRB's responsibility to make decisions as to whether the criteria of the rule are met.

Studies ineligible

This waiver applies to the Basic HHS Policy for Protection of Human Research Subjects (Subpart A of 45 CFR Part 46) and to research involving children (Subpart D of 45 CFR Part 46). However, because of special regulatory limitations relating to research involving fetuses, pregnant women, and human in vitro fertilization (Subpart B of 45 CFR 46), and research involving prisoners (Subpart C of 45 CFR Part 46), this waiver is inapplicable to these categories of research.

An exception from informed consent in emergency medicine research is prohibited in U.S. Department of Defense regulated research unless a waiver is obtained from the Secretary of Defense. See U.S. Department of Defense Research.

For VA research:

The VA does not conduct planned emergency research (see 21 CFR 50.24) involving human subjects. Therefore, the IRB cannot approve a waiver of informed consent for planned emergency research that is subject to VA regulations.

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Waiver of Consent Emergency Research – Guidance and Discussion, Continued

The IRB must find and document that the following conditions are met:	Explanation
The human subjects are in a life-threatening situation,	The criteria contained in the rule do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before consent from a legally authorized representative is feasible. Life-threatening includes diseases or conditions where the likelihood of death is high unless the course of the disease or condition is interrupted. People with the conditions cited in the examples provided in the comments--e.g., long-term or permanent coma, stroke, and head injury--may survive for long periods but the likelihood of survival is not known during the therapeutic window of treatment. People with these conditions are clearly at increased risk of death due to infection, pulmonary embolism, progression of disease, etc. The rule would apply in such situations if the intervention must be given before consent is feasible in order to be successful. The informed consent waiver provision is not intended to apply to persons who are not in an emergent situation, e.g., individuals who have been in a coma for a long period of time and for whom the research intervention should await the availability of a legally authorized representative of the subject.
available treatments are unproven or unsatisfactory, and	Clinical equipoise must exist. When the relative benefits and risks of the proposed intervention, as compared to standard therapy, are unknown, or thought to be equivalent or better, there is clinical equipoise between the historic intervention and the proposed test intervention.
the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.	Although the regulations specifically references placebo controlled trials, this was done to indicate that such trials may be conducted when appropriate. Other controls, e.g. active controls and historical controls, may also be used when they are appropriate and adequate to the task of providing evidence that the drug or device will have the effect claimed. In virtually all cases, when a placebo is used, standard care, if any, would be given to all subjects, with subjects randomized to receive, in addition, the test treatment or a placebo. An exception to this would be the situation in which the test is to determine whether standard treatment is in fact useful. In that case, there must be a group that does not receive it.

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Waiver of Consent Emergency Research – Guidance and Discussion, Continued

The IRB must find and document that the following conditions are met: (continued)	Explanation
Obtaining informed consent is not feasible because: *(i) the subjects will not be able to give their informed consent as a result of their medical condition;*	Subjects do not have to be comatose, but the medical condition under study must prevent obtaining valid informed consent. The agency expects the IRB to determine, based on the specific details of the individual clinical investigation (including the window of opportunity for treatment), the procedures the investigator must follow to attempt to obtain informed consent before enrolling a subject in an investigation without such consent. IRBs also should be knowledgeable about an institution's procedures regarding the use of advance medical directives and assess whether the proposed clinical investigation is consistent with those procedures.
(ii) the intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and	The agency expects the IRB to determine, based on the specific details of the individual clinical investigation (including the window of opportunity for treatment), the procedures the investigator must follow to attempt to obtain informed consent before enrolling a subject in an investigation without such consent.
(iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.	If an IRB determines that it is not appropriate to waive the requirement for informed consent because there is a reasonable way to identify prospectively the individuals likely to become eligible for the study, then this exception would not apply. In that case, only those subjects with the condition who gave prior consent may be enrolled in the study. Those individuals who either did not make a decision or who refused participation would be excluded from participation in the study.

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Waiver of Consent Emergency Research – Guidance and Discussion, Continued

The IRB must find and document that the following conditions are met: (continued)	Explanation
(3) Participation in the research holds out the prospect of direct benefit to the subjects because: *(i) subjects are facing a life-threatening situation that necessitates intervention;* *(ii) appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and* *(iii) risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.* *(4) The research could not practicably be carried out without the waiver.*	If scientifically sound research can be practicably carried out using only consenting subjects (directly, or in most cases for the research contemplated in the rule, with legally authorized representatives), then the agency thinks it should be carried out without involving non-consenting subjects. ***Example***: By practicable, the agency means: • That recruitment of consenting subjects does not bias the science and the science is no less rigorous as a result of restricting it to consenting subjects • That the research is not unduly delayed by restricting it to consenting subjects
(5) The proposed research defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.	The agency believes that these procedures ensure that appropriate efforts are made by the investigator to obtain consent from subjects prior to enrollment. The agency expects these procedures to be documented in the protocol or by the IRB, and the efforts made by investigators to be documented in the material presented to the IRB for its continuing review.

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Waiver of Consent Emergency Research – Guidance and Discussion , Continued

The IRB must find and document that the following conditions are met: (continued)	Explanation
(6) The IRB has reviewed and approved informed consent procedures and an informed consent document These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the research	IRBs need to be aware of state and local laws. Some states have laws which prohibit entry of subjects into research without their express consent. This new rule does not preempt state/or local law. The agency has specifically included family members under this rule because the opportunity for an available family member to object to a potential subject's participation in such a clinical investigation provides an additional and an important protection to these individuals. Otherwise, if consent from a subject or the subject's legally authorized representative were not feasible, the eligible individual could be enrolled into the investigation. Thus, by permitting a family member (even one who is not a legally authorized representative) to object to an individual's inclusion in the investigation, a further protection is provided to that individual. A family member must be provided an opportunity to object to the potential subject's participation, if feasible within the therapeutic window, when obtaining informed consent from the subject is not feasible and a legally authorized representative is not available. The agency recognizes that this may not constitute legally effective informed consent if the family member is not a legally authorized representative under State law. The regulatory agencies are not establishing a hierarchy of family members although an IRB may consider the need for creating a hierarchy in reviewing individual investigations. Under this rule only one family member would need to be consulted and agree or object to the patient's participation in the research. If family members were to disagree, the researcher and family members would need to work out the disagreement.

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Waiver of Consent Emergency Research – Guidance and Discussion, Continued

The IRB must find and document that the following conditions are met: (continued)	Explanation
Additional protections of the rights and welfare of subjects will be provided, including, at least: (i) consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn	While an IRB may appropriately decide to supplement its members with consultants from the community, broader consultation with the community is needed for this type of research. The agency expects the IRB to provide an opportunity for the community from which research subjects may be drawn to understand the proposed clinical investigation and its risks and benefits and to discuss the investigation. The IRB should consider this community discussion in reviewing the investigation. Based on this community consultation, the IRB may decide, among other things, that it is appropriate to attempt to exclude certain groups from participation in the investigation, or that wider community consultation and discussion is needed. ***Example***: As described in the preamble to the proposed rule (60 FR 49086, September 21, 1995), IRBs should consider any of the following: • Having a public meeting in the community to discuss the protocol • Establishing a separate panel of members of the community from which the subjects will be drawn • Including consultants to the IRB from the community from which the subjects will be drawn • Enhancing the membership of the IRB by adding members who are not affiliated with the institution and are representative of the community • Developing other mechanisms to ensure community involvement and input into the IRB's decision-making process It is likely that multiple methods may be needed in order to provide the supplemental information that the IRB will need from the community to review this research.

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Waiver of Consent Emergency Research – Guidance and Discussion Continued

The IRB must find and document that the following conditions are met: (continued)	Explanation
(ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;	It is the IRB's responsibility to determine the information to be disclosed. This information could include but may not necessarily be limited to the information that is found in the informed consent document, the investigator's brochure, and the research protocol. The IRB should consider how best to publicly disclose, prior to commencement of the clinical investigation, sufficient information to describe the investigation's risks and benefits ***Examples***: Relevant information from the investigator's brochure, the informed consent document, and the investigational protocol Initial disclosure of information will occur during the community consultation process. Disclosure of this information to the community will inform individuals within the community about the clinical investigation and permit them to raise concerns and objections.

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Waiver of Consent Emergency Research – Guidance and Discussion, Continued

The IRB must find and document that the following conditions are met: (continued)	Explanation
(iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;	It is necessary to provide comprehensive summary data from the completed trial to the research community in order to permit other researchers to assess the results of the clinical investigation. The agency thinks that there must be a scientific need to conduct clinical investigations involving subjects who are unable to consent; if previous investigations have already provided the scientific answer, this should be shared broadly with the research community. Sufficient information may be contained in a scientific publication of the results of the completed investigation; in other instances, a publication may need to be supplemented by additional information. For FDA-regulated research – The agency has modified Sec. 50.24(a)(7)(iii) to clarify that the information to be disclosed is to include the demographic characteristics (age, gender, and race) of the research population. For a multicenter investigation, the agency anticipates that: • The sponsor or lead investigators will be responsible for analyzing the results of the overall investigation, including the demographic characteristics of the research population. • These results will be published (or reported in the lay press) within a reasonable period of time following completion of the investigation. Publication in a scientific journal or reports of the results by lay press, that would be supplemented upon request by comprehensive summary data, will enable the research community, e.g., researchers not connected to the clinical investigation, to learn of the research's results. Following publication, the IRB will be responsible for determining appropriate mechanisms for providing this information, possibly supplemented by a lay description, to the community from which research subjects were drawn. The usual rules of marketing and promotion apply to the disclosure of this information. The agency notes that it is common for the results of research to be reported in the lay press and published in peer reviewed journals.

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Waiver of Consent Emergency Research – Guidance and Discussion, Continued

The IRB must find and document that the following conditions are met: (continued)	Explanation
(iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and	A data monitoring committee will help ensure that if it becomes clear that the benefits of the investigational intervention are established, or that risks are greater than anticipated, or that the benefits do not justify the risks of the research, the investigation can be modified to minimize those risks or the clinical investigation can be halted. The data monitoring committee is established by the sponsor of the research, as an advisory body to the sponsor. An independent committee is constituted of individuals not otherwise connected with the particular clinical investigation. A variety of expertise is required for an effective data monitoring committee. Typically included are clinicians specializing in the relevant medical field(s), biostatisticians, and bioethicists. The data monitoring committee receives study data on an ongoing basis on a schedule generally defined in the investigational protocol; based on its review of the data it may recommend to the sponsor that the clinical investigation be modified or stopped. In effect, it is responsible for making sure that continuing the investigation in its current format remains appropriate, on both safety and scientific grounds. A number of reasonable models for establishment and function of these committees are described and discussed in S. Ellenberg, N. Geller, R. Simon, S. Yusuf (editors), Practical issues in data monitoring of clinical trials (Proceeding of an International Workshop*) Statistics in Medicine*, vol. 12; 1993. If a sponsor accepts a data monitoring committee's recommendation to stop the investigation or to institute a major modification of the trial, the sponsor is required to notify FDA and all participating investigators and IRBs in a written IND or IDE safety report within 10 working days after the sponsor's initial receipt of the information. ***Reference***: See Secs. 312.32, 312.56(d), and 812.150(b)(1). If an IRB, a subcommittee of the IRB, or some other preexisting institutional committee were to serve as a data monitoring committee, it would need to be constituted as a data monitoring committee when it functions in that capacity. The agency thinks that the duties and scope of activities of an IRB and a data monitoring committee are quite different and that it is important for separate entities to be established. The agency would not object, however, to an already established committee, such as an IRB, serving as a data monitoring committee as long as that committee was constituted to perform the duties of a data monitoring committee and operated as such separately and distinctly from its IRB activities.

Waiver of Consent Emergency Research – Guidance and Discussion, Continued

The IRB must find and document that the following conditions are met: (continued)	Explanation
If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.	***Note*:** For the purposes of this waiver "family member" means any one of the following legally competent persons: spouse[s]; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship. See 21 CFR 50.3(m), 21 CFR 50.24, Guidance "Emergency Research Informed Consent Requirements", OHRP, October 31, 1996.

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Waiver of Consent Emergency Research – Guidance and Discussion, Continued

The IRB must find and document that the following conditions are met: (continued)	Explanation
(b) The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a research with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.	The agency thinks that it may not always be possible to develop a meaningful informed consent document for continued participation in the research because the relevant information may vary significantly depending upon when it becomes feasible to provide the information to the subject or legally authorized representative. It is up to the IRB to determine whether it is possible or desirable, given the nature of the clinical investigation, to have an actual document that could be signed for continued participation in the investigation. The agency notes that such a document, that would be signed after entry into an investigation, would not constitute consent for what had already occurred; it could, however, serve to document that the subject consented to continued participation in the investigation. The agency notes that Secs. 312.60 and 812.140 require the clinical investigator to document data pertinent to each individual in the investigation. This documentation should include information that the subject, legally authorized representative, or family member was informed of the subject's inclusion in the clinical investigation, the details of the investigation, and other information contained in the informed consent document. Like other IRB records, records of the determinations above must be kept for a minimum of three years after the completion of the clinical investigation (21 CFR 50.24(c)). Again, like other IRB records, these are subject to inspection and copying by FDA and OHRP.

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Waiver of Consent Emergency Research – Guidance and Discussion Continued

The IRB must find and document that the following conditions are met: (continued)	Explanation
(d) (for FDA regulated research) Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under Secs. 312.30 or 812.35 of this chapter.	The submission of a separate IND or IDE ensures that FDA reviews the application before the study may proceed. FDA review of the application will enable the agency to assess whether the available treatments for the condition are unproven or unsatisfactory, whether the intervention is reasonable, whether the study design will provide the information sought, and whether other conditions of the regulations are met. The amount of information needed in the application differs, depending upon the particular intervention.

Further explanation

When …	Then …
An IND or IDE exists	• The separate application does not need to duplicate. • The sponsor does not need to resubmit information that is contained in the existing IND or IDE. • The separate application will need to: – Reference the existing IND or IDE, – Contain a protocol for the clinical investigation that includes a description of how the investigation proposes to meet the conditions of this regulation – Contain only the study-specific information required by Secs. 312.23, 812.20, and 812.25, as appropriate
• The investigation involves a product that has received marketing approval • The use is within the product's approved labeling, and without dosage or schedule change if for a drug product	The protocol may simply need to be accompanied by the product's approved labeling and a description of how the investigation proposes to meet the conditions of this regulation. No toxicology or manufacturing controls or chemistry information may need to be submitted. By submitting this information to the agency for review, the dual review by both FDA and an IRB will provide additional protections to the subjects of this research.

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Waiver of Consent Emergency Research – Guidance and Discussion, Continued

Further explanation (cont)

When …	Then …
The clinical investigation involves either • A product that has received marketing approval but involves a route of administration or dosage level or use in a subject population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the product • An investigational product for which an IND or IDE does not exist	The IND or IDE would need to include information to support the altered conditions of use, including toxicology, chemistry, and clinical information, as appropriate.

The IRB must find and document that the following conditions are met: (continued)	Explanation
(e) (for FDA regulated research) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRBs that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.	By "substantially equivalent" the agency means other clinical investigations that propose to invoke this exception from informed consent and that involve basically the same medical conditions and investigational treatments. The agency intends this requirement to refer to clinical investigations conducted by the same sponsor. It is the sponsor's responsibility to determine that a study is "substantially equivalent." • If a protocol invoking this exception is modified by the sponsor in order to respond to IRB concerns that it does not meet the criteria in Sec. 50.24(a) of the exception or because of other relevant ethical concerns, and it is a multicenter study, then the IRB's written findings are to be disclosed to other centers that either are, or may be, participating in the study. • If there is a change in a protocol in a multicenter trial, there is re-review of the protocol by all the IRBs of the institutions participating in the multicenter trial. • If the change is minor, it may be eligible for expedited review under Sec. 56.110, which permits the IRB to use an expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. • If the change is significant, it would need to be reviewed by the full committee. It is the sponsor's responsibility to determine if it has a substantially similar protocol necessitating information dissemination.

Related standards AAHRPP I.1.D, I.4.C, II.2.D, II.3.F, II.3.G, II.4.C, III.1.F

Waiver of Documentation of Consent

Introduction	Date of Last Revision/Review: 01/28/19 This topic discusses the conditions for the waiver of the documentation of consent.
Authority	The IRB can waive the requirement to obtain written documentation of informed consent. ***Reference***: Per DHHS regulations at 45 CFR 46.117(c) and the Common Rule
Approval requirement	To approve such a waiver, the IRB must find and document one of the following conditions: • The only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality. ***Solution***: Each subject is asked whether the subject wants documentation linking the subject with the research, and the subject's wishes govern. • The research presents no more than minimal risk of harm to subjects and involves procedures or activities for which written consent is not normally required outside of the research context. • If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. ***Note*:** The IRB must review a written description of the information that will be provided to subjects.
FDA-regulated research approval requirement	• The IRB may, for some or all subjects, waive the requirement that the subject, or the subject's legally authorized representative, sign a written consent form if it finds that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context; or • The IRB may, for some or all subjects, find that the requirements for an exception from informed consent for emergency research are met.
IRB possible requirement	When the documentation requirement is waived, the IRB may require the Principal Investigator to provide subjects with a written statement regarding the research.
Documentation	These findings and their justifications are clearly documented in IRB records when the IRB exercises this waiver provision.
Related standards	AAHRPP I.1.D, II.2.D, II.3.F, II.3.G, II.4.C, III.1.F

Informed Consent in Language Understandable to Potential Subjects

Introduction

Date of Last Revision/Review: 01/28/19

This topic discusses the requirements for informed consent understandable to the subject (or the subject's legally authorized representative).

Regulation requirements

- Informed consent must be obtained in language that is understandable to the subject (or the subject's legally authorized representative).
- The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.
- Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.
- Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.
- Informed consent discussions must be discussed as required to assure that the potential subject can understand the information being provided. This informed consent discussion may be hindered by language and educational barriers, as well as physical impairment.
- Informed consent discussions must include a reliable translator when the prospective subject does not understand the language of the person who is obtaining consent.
- Additional protections and assistance may be required in aiding the informed consent and research participation communication requirements.

Reference: Per Federal regulations at 45 CFR 46.116 and 21 CFR 50.20

Languages

The College provides generic short form consent documents to investigators in languages typically encountered among subject populations.

Investigators are responsible for providing documents in languages not typically encountered.

Methods

Investigators may document informed consent from non-english speakers in either of two ways:

- A full-length informed consent document written in language understandable to the subject
- A short-form consent document in the language of the subject that states the general elements of informed consent

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Informed Consent in Language Understandable to Potential Subjects, Continued

Requirements by method

This table provides the requirements for an investigator, depending on which method used to document informed consent in languages other than English:

When the Investigator uses …	Then the Investigator must …
The full-length consent form translated to the subject's language to document informed consent	• Submit appropriately translated documents to the IRB for review and approval before use • Provide the subject with: – The full-length informed consent document in the subject's language – A person designated to obtain informed consent (with a translator as necessary) who can take part in the informed consent discussion to ensure the subject's understanding • Obtain appropriate signatures - The following people sign the full-length consent document in the subject's language: – Subject (or the subject's legally authorized representative) – Person obtaining consent • Provide a copy of the signed and dated full-length consent document to the subject

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Informed Consent in Language Understandable to Potential Subjects, Continued

Requirements by method (cont)

This table provides the requirements for an investigator, depending on which method used to document informed consent in languages other than English (continued):

When the Investigator uses …	Then the Investigator must …
The short form in the subject's language to document informed consent	• Submit the appropriately translated document (short form) to the IRB for review and approval before use • Provide the subject with**:** – The full-length informed consent document in English – A person designated to obtain informed consent (with a translator as necessary) who can take part in the informed consent discussion to ensure the subject's understanding – A short form consent document – A witness to the informed consent discussion who is fluent in both English and the language of the potential subject to observe the informed consent discussion and assure that the information in the full-length English form has been presented orally to the subject – ***Note*****:** A translator may serve as witness • Obtain appropriate signatures: – The following people sign the translated short form: > Subject (or the subject's legally authorized representative) > Witness (may be the translator; cannot be the person obtaining consent) – The following people sign the full-length English form: > Person obtaining consent > Witness • Provide a copy of the signed and dated full-length consent document to the subject • Provide a copy of the signed and dated short form to the subject FDA regulations require that the informed consent document be signed and dated by the subject for FDA-regulated research. Regulations applicable to other research do not require that the consent forms be dated, but it is recommended. No subject should be asked to sign a form written in a language s/he does not understand.

Related standards AAHRPP I.1.D, II.2.D, II.3.F, II.3.G, II.4.C, III.1.F

Documentation

Introduction

Date of Last Revision/Review: 10/01/20

This topic discusses the documentation required for the informed consent of subjects in research.

Approval requirement

To approve research, the IRB must determine that informed consent of adult subjects (or the subject's legally authorized representative) and the permission of the parent(s) or guardian(s) of child subjects, will be documented in writing unless documentation can be waived under Federal regulations.

Only the IRB-approved informed consent or permission document can be used for the informed consent or permission process.

Reference: Documentation of Assent in Chapter 6 details the requirements for documentation of permission for the involvement of children in research.

Regulation

FDA's requirements for electronic records/electronic signatures, informed consent, and IRBs are set forth in 21 CFR parts 11, 50, and 56, respectively.

HHS requirements regarding the protection of human subjects are set forth in 45 CFR part 46. The information presented to the subject, processes used for obtaining informed consent, and documentation of the electronic informed consent (eIC) must meet the requirements of these and other applicable regulations.

If the study is conducted or supported by HHS and involves an FDA-regulated product, the study is subject to both 45 CFR part 46 and 21 CFR parts 50 and 56, meaning that both sets of regulations must be followed. Where the regulations differ, the regulations that offer the greater protection to human subjects should be followed. Research not subject to 21 CFR parts 50 and 56 is also not generally subject to 21 CFR part 11 (FDA regulations regarding electronic records and electronic signatures).

Federal regulations at 45 CFR 46.117 and 21 CFR 50.27 provide two methods for documenting informed consent and permission, see Methods below.

The method of documenting the assent of child subjects will be determined by the IRB in accordance with Subpart D of the DHHS and FDA regulations at 45 CFR 46.408 and 21 CFR 50.55, respectively.

Methods

The two methods provided by the regulations for documenting informed consent and parental or Legally Authorized Representative permission are:

- Through a written long form document that embodies all of the required elements of informed consent
- Through a short form document which states that the elements of informed consent have been presented orally to the subject (or the legally authorized representative, parent(s) or guardian(s) in compliance with all regulatory requirements)

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Documentation, Continued

Electronic or digital methods to obtain, document, and maintain documentation of informed consent

When obtaining and documenting informed consent from research subjects (or parental permission or permission for adults who lack decision-making capacity, using their legally authorized representatives), the consent or permission process must be obtained and documented in one of the two methods described above.

- When using a digital or electronic method to either obtain and/or document informed consent, the regulations governing the research study will determine whether or not the electronic system for obtaining and documenting informed consent must be 21 CFR 11 compliant. For research not regulated by the FDA, informed consent does not have to be obtained and documented in a manner compliant with 21 CFR 11.
- For FDA regulated research, electronic systems used to generate electronic signatures on clinical trial records, including informed consent documents, must comply with the requirements outlined in FDA regulations at 21 CFR 11 when applicable even in a public health emergency, such as a pandemic, hurricanes, or other disasters.
- Principal Investigators are responsible for ensuring that the electronic systems planned for use for obtaining, documenting, and maintaining the documentation for FDA regulated research are compliant with 21 CFR 11.
- Principal Investigators can work with the Office of Information Technology to obtain documentation that their electronic systems have been 21 CFR 11 validated.
- In all circumstances, Principal Investigators should ensure that the planned methods for obtaining, documenting, and maintaining the documentation of informed consent are IRB-approved by the IRB of Record and are consistent and compliant with the policies and procedures of the affiliated institution where the research is conducted.

***References*:**

- FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency: Guidance for Industry, Investigators, and Institutional Review Boards
- OHRP Guidance, Use of Electronic Informed Consent: Questions and Answers
- FDA Guidance, Use of Electronic Informed Consent in Clinical Investigations - Questions and Answers, Guidance for Institutional Review Boards, Investigators, and Sponsors
- FDA Guidance Part 11, Electronic Records; Electronic Signatures — Scope and Application
- FDA Guidance Use of Electronic Records and Electronic Signatures in Clinical Investigations under 21 CFR Part 11 – Questions and Answers

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Documentation, Continued

Methods for VA research	For VA research, the following applies for documenting informed consent and permission: Department of Veterans Affairs (VA) Form 10-1086 as provided in BRAIN, Research Consent Form (long form), which includes specific indemnification and notification clauses, may be used as the informed consent form for VA human subject research.
Long form documentation	The long form document must: • Be signed by the subject, or the subject's legally authorized representative, parent(s) or guardian(s), in compliance with all regulatory requirements (when a short form is not used) • Be copied and given to the person signing the form • Have the signature dated ***Reference***: FDA regulations requirement
Short form documentation	When the short form documentation is used: • There must be a witness to the oral presentation. • The IRB must approve a written summary of what is to be presented orally. • Only the short form must be signed by the subject, representative, parent(s), or guardian(s). • For FDA-regulated research the short form must be dated as well • The witness must sign both the short form and the summary. For subjects who do not speak English, the witness is conversant in both English and the language of the subject. • The person actually obtaining consent must sign the summary, and the short form. • A copy of the summary and the short form will be given to the subject, representative, the parent(s) or guardian(s).
Related standards	AAHRPP I.1.D, II.2.D, II.3.F, II.3.G, II.4.C, III.1.F

Completion of the Documentation

Introduction

Date of Last Revision/Review: 01/13/21

This topic discusses the ways to complete the documentation for consent.

Illiterate subjects

Illiterate persons may have informed consent or permission information read to them and may "make their mark" in a manner consistent with the laws of Texas (or other state in which the research is conducted) to document their understanding.

It is desirable to obtain the signature of a witness to the process and the signature of the person conducting the consent or permission interview.

Witness signature

The IRB or the institution where the research is being conducted may require the signature of a witness who has been present during the entire consent or permission interview and who can attest to the accuracy of the presentation and the apparent understanding of the subject, representative, parent, or guardian, on the informed consent or permission document.

- Such attestation is noted in writing on the document.
- The witness is present to attest to the validity of the individual's signature.

Reference: Informed Consent in Language Understandable to Potential Subjects

Decision

The individual making the participation decision may take the document home to discuss the matter with family, friends, spouses, or other professionals.

When the subject, representative, parent(s) or guardian(s) decide(s) that the subject will enter the study, he/she/they sign(s) and date(s) the informed consent or permission document.

Date stamp required

All informed consent and permission documents must have a date stamp indicating the beginning and end of the approval period during which the document may be used to obtain consent or permission. The short forms do not have to have the IRB date stamp and approval; however, they should be utilized by printing them from the attachments section in BRAIN from the approved protocol.

Copy to decision-maker required

When the informed consent or permission information has been presented, the informed consent or permission document is given to the subject, legally authorized representative, parent, or guardian for further review.

For VA research

The consent document must be signed and dated by the participant or legally authorized representative, and by the person obtaining consent.

Continued on next page

Completion of the Documentation, Continued

Retention requirement	The Investigator is responsible for storing signed informed consent and permission documents for at least three years following the completion of the research. **For VA Research** All research records, including identifiers, must be retained until disposition instructions are approved by the National Archives and Records Administration (NARA) and are published in VHA RCS 10-1. Once the disposition schedule is determined, records should be disposed in accordance with VHA RCS 10-1.
Related standard	AAHRPP II.3.F

Section C
Posting of Clinical Trial Consent Form

Overview

Introduction

Date of Last Revision/Review: 11/18/19

This chapter provides information on the requirement to post clinical trial consent forms on a publicly available federal website.

In this section

This section covers the following topics:

- Common Rule Requirements
- Guidance on Posting Consent Forms

Common Rule Requirements

Introduction

Date of Last Revision/Review: 11/18/19

This topic discusses the requirements of posting informed consents as stated by the regulations.

Reference: Per DHHS regulations at 45 CFR 46.116 (h)

Requirements

- For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal Web site that will be established as a repository for such informed consent forms.
- If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Web site (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.
- The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

Related standards

AAHRPP I.1.D, II.3.F

Guidance on Posting Consent Forms

Introduction

Date of Last Revision/Review: 07/27/23

This topic discusses available guidance on how and where to post consent forms.

Reference: Per DHHS regulations at 45 CFR 46.116 (h)

Guidance

The revised Common Rule requires that for any clinical trial conducted or supported by a Common Rule department or agency, one consent form be posted on a publicly available federal website by the awardee or the federal department or agency component conducting the trial. The consent form must have been used in enrolling participants and be posted to a designated federal website after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol in order to satisfy this new provision.

At this time, two publicly available federal websites that will satisfy the consent form posting requirement, as required by the revised Common Rule, have been identified: ClinicalTrials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021). Additional federal websites that would satisfy the revised Common Rule's clinical trial consent form posting requirement might be identified in the future. See additional guidance below for more information.

Additional Guidance

Uploading a Clinical Trial Informed Consent to Regulations.gov

Guidance on Posting Informed Consent Forms for NIH-Funded Clinical Trials

Uploading a Clinical Trial Informed Consent form to ClinicalTrials.Gov – Includes specific instructions on how to register with ClinicalTrials.gov and upload documents (including clinical trial informed consent forms). Through its website the BCM Office of Clinical Research provides guidance and registration information.

Related standards

AAHRPP I.1.D, II.3.F

Chapter 5
IRB Review of FDA-Regulated Research: Investigational Drugs, Devices, and Biologics

Table of Contents

Overview for IRB Review of FDA-Regulated Research
Section A: Introduction to Investigational Drugs, Devices, and Biologics
Overview
Regulations and Terms
How the College Manages FDA-Regulated Research
Investigational New Drugs
Reporting Responsibilities of Investigators/Sponsors
Section B: Research with Investigational Drugs, Devices, and Biologics
Overview
Description of an Investigational Device Study
How a Device Study Is Reviewed
Off-Label (Unapproved) Use of FDA-Regulated Products in Medical Practice Versus Research
PI Responsibilities for Handling Investigational Drugs in Research
PI Responsibilities for Handling Investigational Devices in Research
Human Gene Transfer (HGT) Research
Review of Research Involving HGT
Section C: Expanded Access to Investigational Drugs, Biologics, or Devices for Treatment Use
Overview
Expanded Access for Drugs and Biologics (Compassionate Use)
Expanded Access for Individual Patients, Including for Emergency Use
Expanded Access for Widespread Use (Treatment INDs)
Expanded Access for Devices
Expanded Access for Widespread Use (Treatment IDEs)
Emergency Use of a Test Article Without IRB Review
Emergency Use of a Test Article Without Informed Consent
Section D: Special Uses of Drugs, Devices, or Biologics
Overview
Humanitarian Device Exemptions
Exception from Informed Consent for Planned Emergency Research

Overview for IRB Review of FDA-Regulated Research

Introduction	Date of Last Revision/Review: 01/13/21 This chapter focuses on the special requirements for FDA-regulated research, covering investigational drugs, devices, and biologics.
Description: FDA	The Food and Drug Administration (FDA) is a component of the U.S. Department of Health and Human Services (DHHS) that is responsible for implementing and enforcing the Federal Food, Drug, and Cosmetic Act to regulate the safety and efficacy of these products for human use.
Function	The FDA regulates clinical investigations that are conducted on drugs, biologics, and devices. All such investigations must be conducted in accordance with FDA requirements for informed consent and IRB review.
Jurisdiction	Clinical trials involving an investigational drug, device, or biologic that are supported by DHHS (the National Institutes of Health) fall under the jurisdiction of both the FDA and the DHHS Office for Human Research Protections (OHRP). Such trials must comply with both the FDA and the DHHS human subject regulations, including the Common Rule.
Industry sponsored research	BCM requires all industry sponsored and funded research protocols to be submitted to a commercial IRB. See Submission Process for a list of commercial IRBs on which BCM PIs may rely as well as instructions for reliance submissions in the BCM BRAIN system.
In this chapter	This chapter covers the following sections: • Section A: Introduction to Investigational Drugs, Devices, and Biologics • Section B: Research with Investigational Drugs, Devices, and Biologics • Section C: Expanded Access to Investigational Drugs, Biologics or Devices for Treatment Use • Section D: Special Uses of Drugs, Devices, or Biologics
Related standards	AAHRPP I.1.D, I.7.A, I.7.B, I.7.C

Section A
Introduction to
Investigational Drugs, Devices, and Biologics

Overview

Introduction	Date of Last Revision/Review: 11/27/18 This section introduces the requirements to investigational drugs, devices, and biologics.
In this section	This section covers the following topics: • Regulations and Terms • How the College Manages FDA-Regulated Research • Investigational New Drugs • Reporting Responsibilities of Investigators/Sponsors
Related standards	AAHRPP I.1.D, I.7.A, I.7.B, I.7.C

Regulations and Terms

Introduction

Date of Last Revision/Review: 09/05/25

The human subject protection requirements found in FDA regulations and DHHS regulations are substantially the same as the Common Rule requirements.

FDA differences

The requirements of the FDA regulations differ from DHHS/Common Rule regulations as follows:

- Contain no Assurance requirement
- Define *human subject* and *clinical investigation* (*research*) differently
- Require specific determinations for the IRB review of device studies
- Have different conditions for exemption, exception, and waiver of IRB review and Informed Consent requirements
- Include specific requirements for reporting adverse events that are not found in the Common Rule or DHHS regulations
- Do not include specific additional protections for pregnant women, fetuses, and human neonates (Subpart B) and prisoners (Subpart C)

Terms

This table identifies terms used in this chapter:

Term	Description
IND	Investigational New Drug Application
IDE	Investigational Device Exemption
510(k) devices	• Devices that are substantially equivalent to other devices that are legally on the market • Can be marketed without clinical testing ***Reference***: See Application to submit below.
Biologics	Any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment, or cure of human diseases or injuries

Application to submit

This table provides when to submit each application:

When an investigation …	Then the investigator or sponsor submits to the FDA …
Can be conducted in support of a potential new drug application	An Investigational New Drug Application (IND)
Supports research to be conducted for a Pre-Market Approval application	An Investigational Device Exemption (IDE)
Requires approval for research on biological products	An Investigational New Drug Application (IND)

Related standards

AAHRPP I.1.D, I.7.A, I.7.B, I.7.C

How the College Manages FDA-Regulated Research

Introduction

Date of Last Revision/Review: 01/28/19

This topic provides the detail regarding how the College manages FDA-regulated research.

Primary responsibility

The investigator in a clinical trial is responsible for the conduct of the study and for leading the team of individuals coordinating the study.

Reference: Per FDA regulations

Clinical investigator responsibilities

Each clinical investigator must accept specific responsibilities that include the following:

- Ensuring conduct of the research according the investigator agreement, investigational plan (protocol), and all applicable regulations
- Protecting the rights, safety, and welfare of the research subjects
- Controlling access to and use of the test article (drug / biologic / device)

Sponsor

A *sponsor*:

- Is usually a pharmaceutical, biotech, or medical device company
- Can be an individual or group of individuals
- Can be the investigator, called the sponsor-investigator when the individual investigator is also the initiator of the clinical investigation

Sponsor responsibilities

The sponsor of a clinical investigation:

- Initiates and holds the IND or IDE for a clinical investigation
- Maintains the Biologics License, when applicable
- May or may not actually conduct the investigation

Process

This table describes the process of FDA-regulated research:

Stage	Person Responsible	Description
1	Investigator	Submits research to IRB
2	IRB	• Determines risk • Approves/disapproves research
3	Sponsor	• Initiates the IND or IDE for a clinical investigation • Obtains qualified investigators and monitors • Provides necessary information and training for investigators

Continued on next page

How the College Manages FDA-Regulated Research, Continued

Process (continued) This table describes the process of FDA-regulated research (continued):

Stage	Person Responsible	Description
4	Investigator	• Trains members of the research team • Conducts the investigation • Supervises members of the research team
5	Sponsor	• Monitors the investigation • Controls the investigational agent
6	Investigator	• Maintains and retains accurate records • Monitors and reports adverse events to the sponsor
7	Sponsor	Reports significant adverse events to FDA/investigators
8	Investigator	Forwards reports from Sponsor to the IRB

Related standards AAHRPP I.1.D, I.7.A, I.7.B, I.7.C, III.2.B, III.2.C, III.2.D

Investigational New Drugs

Introduction

Date of Last Revision/Review: 11/27/18

This topic provides a description of Investigational New Drug (IND) requirements.

Requirement

It is a requirement of the College that a decision be made regarding the applicability of IND requirements. This decision regarding the applicability of the IND requirements as well as the validity of the IND is to be made by the IRB.

Reference: Per FDA regulations

Definitions

Drug – Any substance that is used to elicit a pharmacologic or physiologic response whether it is for treatment or diagnostic purposes.

Biologic - A virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other similar product used to prevent, treat or cure disease or injury

When an IND application is not needed

An IND application is not necessary if ALL of the following seven drug criteria are met:

- The drug is lawfully marketed in the U.S.
- It is not intended to be reported to the FDA in support of a new indication for use or to support any other significant change in labeling of the drug; and
- It is not intended to support a significant change in the advertising of the product; and
- It does not involve a route of administration or dosage level, used in a subject population, or other factor that significantly increase the risks (or decreases the acceptability of the risks) associated with the use of the drug product; and
- It is conducted in compliance with the requirements for IRB review and informed consent 21 CFR, parts 56 & 50; and
- It is conducted in compliance with the requirements concerning the promotion and sale of drugs 21 CFR 312.7; and
- It does not intend to invoke 21 CFR 50.24 (Emergency Use)

Note: The Principal Investigator attests to these criteria being true. The IRB determines whether these criteria have indeed been met. The IRB reviews and approves the plan for storage, control and dispensing of the investigational drug.

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Investigational New Drugs, Continued

IRB review for an IND application	The IRB reviews to determine whether the research involves a drug or biologic (including radioactive drugs) that is not approved by the FDA and assures appropriate review by the Radioactive Drug Research Subcommittee of the BCM Institutional Biosafety Committee where applicable. The IRB reviews and requires demonstration of, and the validity of, an Investigational New Drug application with the FDA when any of the following are true for the research: • Will be conducted with a: – Drug product that is not lawfully marketed in the United States, see 21 CFR 312.2(1) – Commercially available drug, lawfully marketed in the United States, to support a new indication or support a change in advertising or labeling of the product; or • Uses a commercially available drug**,** lawfully marketed in the United States, that is: – Being administered via a new route (that significantly increases the risks) or for us in a different part of the body; or – Being given at a dosage level that might significantly increase the risk to the subject population; or – Going to be used in a new patient population that may result in a significant increase in risk(s) to the patient population
IRB review of drug plan	The IRB reviews and approves the plan for storage, control and dispensing of the investigational drug.
IRB review of investigator-initiated new drug studies	When the BCM Principal Investigator (PI) is acting as the sponsor of research involving an investigational new drug, the IRB proceeds as follows: • Reviews documentation that the proposed drug preparation is in compliance with Good Manufacturing Practices and • Requires documentation of a review of the reporting and record-keeping responsibilities as stated in 21 CFR 312 and 21 CFR 314 (for investigational drugs)
Related standard	AAHRPP I.1.D, I.7.A, I.7.B, I.7.C

Reporting Responsibilities of Investigators/Sponsors

Introduction

Date of Last Revision/Review: 09/05/25

This topic provides the responsibilities of sponsors and investigators. Investigators must be aware of sponsor responsibilities when serving in the dual role of sponsor/investigator.

Sponsor responsibilities

Sponsors are responsible for:

- Selecting qualified investigators and providing them with the information they need to conduct the investigation properly;
- Ensuring proper monitoring of the investigation;
- Ensuring that any reviewing IRB and FDA are promptly informed of significant new information about an investigation
- Ensuring that IRB review and approval are obtained
- Submitting an IDE or IND application to FDA;
- Maintaining the following accurate, complete, and current records relating to an investigation:

(1) All correspondence with another sponsor, a monitor, an investigator, an IRB, or FDA, including required reports.

(2) Records of shipment and disposition. Records of shipment shall include the name and address of the consignee, type and quantity of device or drug, date of shipment, and batch number or code mark. Records of disposition shall describe the batch number or code marks of any devices returned to the sponsor, repaired, or disposed of in other ways by the investigator or another person, and the reasons for and method of disposal.

(3) Signed investigator agreements

(4) For each investigation:

(i) The name and intended use of the device and the objectives of the investigation, or name of the drug as applicable;

(ii) A brief explanation of why the device is not a significant risk device:

(iii) The name and address of each investigator:

(iv) The name and address of each IRB that has reviewed the investigation:

(v) A statement of the extent to which the good manufacturing practice will be followed; and

(vi) Any other information required by FDA.

(5) Records concerning adverse device or drug effects (whether anticipated or unanticipated) and complaints and

(6) Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigation or a particular investigation.

Continued on next page

Reporting Responsibilities of Investigators/Sponsors, Continued

Sponsor responsibilities (cont.)

- Preparing and submitting the following complete, accurate, and timely reports:

(1) Unanticipated adverse device/drug effects. A sponsor who conducts an evaluation of an unanticipated adverse effect under shall report the results of such evaluation to FDA and to all reviewing IRBs and participating investigators within 10 working days (5 working days to the BCM IRB) after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests.

(2) Withdrawal of IRB approval. A sponsor shall notify FDA and all reviewing IRBs and participating investigators of any withdrawal of approval of an investigation or a part of an investigation by a reviewing IRB within 5 working days after receipt of the withdrawal of approval.

(3) Withdrawal of FDA approval. A sponsor shall notify all reviewing IRBs and participating investigators of any withdrawal of FDA approval of the investigation, and shall do so within 5 working days after receipt of notice of the withdrawal of approval.

(4) Current investigator list. A sponsor shall submit to FDA, at 6-month intervals, a current list of the names and addresses of all investigators participating in the investigation. The sponsor shall submit the first such list 6 months after FDA approval.

(5) Progress reports. At regular intervals, and at least yearly, a sponsor shall submit progress reports to all reviewing IRBs. In the case of a significant risk device, a sponsor shall also submit progress reports to FDA. A sponsor of a treatment IDE shall submit semi-annual progress reports to all reviewing IRBs and FDA in accordance with § 812.36(f) and annual reports in accordance with this section.

(6) Recall and device disposition. A sponsor shall notify FDA and all reviewing IRBs of any request that an investigator return, repair, or otherwise dispose of any units of a device. Such notice shall occur within 30 working days after the request is made and shall state why the request was made.

(7) Final report. In the case of a significant risk device, the sponsor shall notify FDA within 30 working days of the completion or termination of the investigation and shall submit a final report to FDA and all reviewing the IRBs and participating investigators within 6 months after completion or termination. In the case of a device that is not a significant risk device, the sponsor shall submit a final report to all reviewing IRBs within 6 months after termination or completion.

(8) Informed consent. A sponsor shall submit to FDA a copy of any report by an investigator under paragraph (a)(5) of this section of use of a device without obtaining informed consent, within 5 working days of receipt of notice of such use.

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Reporting Responsibilities of Investigators/Sponsors, Continued

Sponsor responsibilities (cont.)

(9) Significant risk device determinations. If an IRB determines that a device is a significant risk device, and the sponsor had proposed that the IRB consider the device not to be a significant risk device, the sponsor shall submit to FDA a report of the IRB's determination within 5 working days after the sponsor first learns of the IRB's determination.

(10) Protocol amendments, new investigator amendments

(11) Other. A sponsor shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

Investigator responsibilities

An investigator is responsible for:

- Ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations;
- Protecting the rights, safety, and welfare of subjects under the investigator's care;
- Ensuring the control of devices under investigation;
- Ensuring that informed consent is appropriately obtained as applicable under the federal regulations;
- Maintaining the following accurate, complete, and current records relating to the investigator's participation in an investigation:

(1) All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.

(2) Records of receipt, use or disposition of a device that relate to:

(i) The type and quantity of the device, the dates of its receipt, and the batch number or code mark.

(ii) The names of all persons who received, used, or disposed of each device.

(iii) Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.

(3) Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include:

(i) Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual shall document that informed consent was obtained prior to participation in the study.

Continued on next page

Reporting Responsibilities of Investigators/Sponsors, Continued

Investigator responsibilities (cont.)

An investigator is responsible for (continued):

(ii) All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.

(iii) A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.

(4) The protocol, with documents showing the dates of and reasons for each deviation from the protocol.

(5) Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

- Preparing and submitting the following complete, accurate, and timely reports:

(1) Unanticipated adverse device effects. An investigator shall submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

(2) Withdrawal of IRB approval. An investigator shall report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.

(3) Progress. An investigator shall submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.

(4) Deviations from the approved protocol/FDA-approved clinical investigational plan (if applicable).

(i) An investigator shall notify the sponsor and the reviewing IRB, see § 56.108(a) (3) and (4), of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred.

(ii) For non-emergent deviations from the approved protocol/FDA-approved clinical investigational plan (if applicable), prior approvals by the sponsor/sponsor-investigator and IRB are required. If these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA notification is also required.

(5) Informed consent. If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.

Continued on next page

Reporting Responsibilities of Investigators/Sponsors, Continued

Investigator responsibilities (cont.)

An investigator is responsible for (continued):

(6) Final report. An investigator shall, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor and the reviewing IRB.

(7) Other. An investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

- Ensure that the local Pharmacy Service or Research Investigational Pharmacy receives all of the following:
  (1) Documentation of IRB and other relevant approvals.
  (2) A copy of the approved protocol.
  (3) Documentation of IRB continuing review approval.
  (4) Copies of sponsor related correspondence specific to the drugs as appropriate.
  (5) Copies of all correspondence addressed to the research investigator from the FDA specific to the drugs as appropriate.
  (6) For VA regulated research: A copy of VA Form 10-9012 (if applicable)
  (7) For VA regulated research: A copy of the consent document for each participating participant with all the appropriate signatures.
- Informs the chief of pharmacy service when the study involving investigational drugs has been suspended, terminated, or closed.
- Comply with all dispensing requirements.
- Comply with all documentation requirements and make relevant records accessible to the investigational pharmacist when requested.
- **For VA regulated research:** Informs the Research and Development Committee at the VA when the study involving investigational drugs has been suspended, terminated, or closed.

***Reference*:** FDA IDE regulation 21 CFR 812.40

Reporting

The investigator reports the following to the IRB as stated elsewhere in this manual:

- Event Reporting Required of Principal Investigators
- Safety Reports see "Safety monitoring plan"
- DSMB Reports see "Risk monitoring"

Continued on next page

Reporting Responsibilities of Investigators/Sponsors, Continued

Other reporting responsibilities

Investigators and sponsor-investigators have the following additional reporting responsibilities under FDA regulations:

When …	Then …
Investigators and sponsor-investigators find any adverse effect that may reasonably be regarded as caused by or probably caused by the drug	The clinical investigator must notify the sponsor. ***Reference***: FDA IND regulations
The Sponsor learns of any adverse experience associated with the use of a drug or biologic that is both serious and unexpected	The Sponsor must notify the FDA and all participating investigators as soon as possible but no later than 15 calendar days after the sponsor determines it to be reportable. ***Reference***: FDA IND regulations, 21 CFR 312.32
The Sponsor learns of any unexpected fatal or life-threatening experience	The Sponsor should notify the FDA by telephone, facsimile, or in writing as soon as possible but no later than 7 calendar days of the sponsor's receipt of the information.
The Sponsor evaluates the event as a serious, unexpected adverse device effect	The Sponsor reports the serious, unexpected adverse device effect(s) within 15 working days of the sponsor's receipt of the information to: • The FDA • All participating investigators • The IRB

VA investigator reporting responsibilities

Additionally, VA investigators must:

- Inform the pharmacy service that IRB and the Research and Development Committee approvals have been obtained
- Provide the pharmacy with a copy of VA Form 10-9012 (if applicable)
- Provide the pharmacy with a copy of the consent document (VA Form 10-1086) for each participating participant with all the appropriate signatures.
- Inform the Chief of Pharmacy Service, and the Research and Development Committee when a study involving investigational drugs has been suspended, terminated, or closed.

Related standards

AAHRPP I.1.D, I.7.A, I.7.B, I.7.C, II.2.H, III.2.D

Section B
Research with Investigational Drugs, Devices, and Biologics

Overview

Introduction

Date of Last Revision/Review: 11/27/18

This section provides the requirements when the research involves investigational drugs, devices, and biologics.

In this section

This section covers the following topics:

- Description of an Investigational Device Study
- How a Device Study Is Reviewed
- Off-Label (Unapproved) Use of FDA-Regulated Products in Medical Practice Versus Research
- PI Responsibilities for Handling Investigational Drugs in Research
- PI Responsibilities for Handling Investigational Devices in Research
- Human Gene Transfer (HGT) Research
- Review of Research Involving HGT

Related standards

AAHRPP I.1.D, I.7.A, I.7.B, I.7.C

Description of an Investigational Device Study

Introduction

Date of Last Revision/Review: 11/27/18

This topic provides a description of an investigational device study.

Requirement

It is the requirement of the College that a decision of Significant Risk (SR) or Non-Significant Risk (NSR) for a medical device must be determined before approval of the medical device study can be considered. See "Types of studies" below.

Reference: Per FDA requirements

IRB review

The convened IRB review includes the following:

- Determining the risk: Significant Risk or Non-Significant Risk
- Approving/disapproving the device study based on the same criteria for any FDA-regulated study

Types of studies

This table describes the types of device studies:

Study Type	Description
Significant Risk (SR) Device	A SR device study: • Presents a potential for serious risk to the health, safety, or welfare of a subject • Is one of the following: – Intended as an implant – Used in supporting or sustaining human life – Of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise prevents impairment of human health. • Requires: – Full IRB review – Full Board approval for all devices with an IDE number ***Reason***: The FDA considers studies of all SR devices to present more than minimal risk.
Non-Significant Risk (NSR) Device	• A device study that does not meet the definition of a SR study • Some investigations involving Non-Significant Risk devices are considered to have approved applications for IDEs under the abbreviated requirements 21 CFR 812.2(b)

Related standards

AAHRPP I.1.D, I.7.A, I.7.B, I.7.C

How a Device Study Is Reviewed

Introduction	Date of Last Revision/Review: 11/27/18 The following process governs the review of investigational devices by the IRB.
IRB review of IDE application	The IRB reviews and requires demonstration of, and confirms the validity of, an Investigational Device Exemption application with the FDA when any of the following are true for the research: The device… • Is intended as an implant, or • Is used in supporting or sustaining human life, or, • Is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a participant, or • Otherwise presents a potential for serious risk to the health, safety, or welfare of a participant
Review materials	The IRB may review any of the following materials: • A description of the device • Reports of prior investigations conducted with the device • The proposed investigational plan • A description of subject selection criteria • Monitoring procedures • The sponsor risk assessment and the rationale used to make the sponsor's risk determination
Basis of risk status	The determination of the risk status of the device should be based on the proposed use of the device in the investigation.
SR device study regulation	If the IRB determines or concurs with the assessment of the sponsor that a device study involves a SR, then it would be governed by the IDE regulations at 21 CFR 812. ***Note*:** Some clinical investigations may be exempt from the IDE regulations and these exempted investigations are described in 21 CFR 812.2(c).
Additional information	The IRB may also request additional information if necessary from the sponsor or investigator or ask the FDA to provide a risk assessment. ***Example*:** A device study that is deemed to involve a NSR may begin immediately since it would not require the submission of an application to the FDA. These clinical investigations involving Non-Significant Risk devices are considered to have approved applications for IDEs under the abbreviated requirements 21 CFR 812.2(b).
Important	It is very important to note that the terms "non-significant risk" and "minimal risk" are defined separately and are not synonymous.

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How a Device Study Is Reviewed, Continued

510(k) devices

The review requirements for 510(k) devices are somewhat different:

When …	Then …
FDA agrees that a new device is substantially equivalent to a device already on the market	It can be marketed without clinical testing.
Clinical data are necessary to demonstrate equivalence	Any clinical studies must be conducted in compliance with the requirements of the IDE, IRB review, and informed consent regulations.
Adverse or unanticipated 510(k) device effects are found	The reporting follows the same requirements. ***Reason***: The 510(k) devices under clinical investigation fall under the IDE regulations.

Related standards

AAHRPP I.1.D, I.7.A, I.7.B, I.7.C

Off-Label (Unapproved) Use of FDA-Regulated Products in Medical Practice Versus Research

Introduction

Date of Last Revision/Review: 11/27/18

This topic discusses the differences in the off-label or unapproved use of FDA-regulated products in medical practice and research.

Good medical practice

Good medical practice and the best interests of the patient require that physicians use legally available marketed drugs, biologics, and devices according to their best knowledge and judgment.

Responsibilities

If physicians use a product for an indication not included in the approved labeling (off-label), they have these responsibilities:

- To be well informed about the product
- To base its use on firm scientific rationale and on sound medical evidence
- To maintain records of the product's use and effects

Requirements

This table describes the requirements based on the purpose of the off-label use:

When off-label use of a marketed product …	Then …
Is solely intended as the practice of medicine	Neither are required: • The IRB review • The submission of an IND or IDE
Is part of a systematic investigation designed to develop or contribute to generalizable knowledge	The IRB review is required.
Is intended to support a change in labeling	Both are required: • The IRB review • The submission of an IND or IDE

Related standards

AAHRPP I.1.D, I.7.A, I.7.B, I.7.C

PI Responsibilities for Handling Investigational Drugs in Research

Date of Last Revision/Review: 11/27/18

Scope

Applies to all personnel involved in the handling of dangerous and investigational drugs intended for administration to research subjects treated in the various clinics which are part of Baylor College of Medicine clinical operations.

***Critical Note*:** Many hospitals and clinics where research is conducted require the use of their own Investigational Drug Service for use of dangerous/investigational drugs in research.

Research at hospitals and clinics MUST adhere to their own local standards.

Definitions

The table below includes terms and their definitions relevant to these standards:

Term	Definition
Dangerous drug	A drug which is required by federal law to bear the following statement, "Caution: Federal law prohibits dispensing without prescription"
Designated agent	• A principal investigator (PI) or an employee supervised by the principal investigator • There must be documentation outlining the delegation of responsibilities to the employee by the PI • Dispensing and administration may only be delegated to employees licensed and authorized in the state of Texas to perform the task being delegated, such as a: – Licensed nurse, physician assistant, pharmacist, or other individual designated by a practitioner to communicate prescription drug orders to a pharmacist – Licensed nurse, physician assistant, or pharmacist employed in a health care facility to whom the practitioner communicates a prescription drug order – Registered nurse or physician assistant authorized by a practitioner to carry out a prescription drug order for dangerous drugs under Subchapter B, Chapter 157, Occupations Code
Dispensing	To prepare, package, compound, or label a dangerous drug in the course of professional practice for delivery under the lawful order of a practitioner to an ultimate user or the user's agent
Investigational new drug	A new drug, antibiotic drug, or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes.

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PI Responsibilities for Handling Investigational Drugs in Research, Continued

Definitions (continued)

The table below includes terms and their definitions relevant to these standards (continued):

Term	Definition
Licensed practitioner	• A person licensed by the Texas State Board of Medical Examiners, State Board of Dental Examiners, Texas State Board of Podiatric Medical Examiners, Texas Optometry Board, to prescribe and administer dangerous drugs • An advanced practice nurse or physician assistant to whom a physician has delegated the authority to carry out or sign prescription drug orders under Section 157.0511, 157.052, 157.053, 157.054, 157.0541, or 157.0542, Occupations Code

Responsibilities

The following table indicates who is responsible for what duties:

Who	Duties
Authorized personnel	• According to federal/state regulations and BCM Policy and Procedure, properly handle drugs used in clinical research in terms of: – Receiving – Storage – Preparation – Dispensing – Administration – Disposal • May be contracted to perform this responsibility for the investigator
Principal Investigator (PI)	• Control of drug(s) under investigation • This includes ensuring that the use of the drug is performed and documented according to state and federal regulations regarding: – Receipt – Storage – Preparation – Dispensing – Administration – Return – Disposal • Ensure that the subject is eligible to receive the drug under investigation and provided informed consent according to IRB-approved procedures

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PI Responsibilities for Handling Investigational Drugs in Research, Continued

Specific PI duties

The following table describes specific duties for which the Principal Investigator (PI) is responsible:

Duty	Description
Drug accountability record	• The investigator must maintain records to include the: – Product's delivery to the study site – Inventory at the site – Use by each subject – Return to the sponsor or alternative disposition of unused/returned product • These records must include **for each transaction of each product**: – Dates – Recorder's initials – Patient name/subject identification number – Quantities – Batch/serial numbers – Expiration/retest dates (if applicable) – Unique code/kit numbers (if applicable) – Maintain records that: – Document adequately that the subjects were provided the doses specified by the protocol – Reconcile all investigational product(s) received from the sponsor • In regard to the "use by each subject", maintain drug accountability records that document adequately: – Which subject(s) received the drug – When the subject(s) received the drug – Specific dosage the subject(s) received
Drug storage	• Investigational product(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirement(s) • Storage guidelines include: – Adequate size for storage – Ability to lock storage area – Separate storage area for research product from clinical care product – Usable drug is stored separately from unusable/returned drug – Appropriate temperature, humidity levels and other environmental monitoring requirements – Access is limited to authorized study staff

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PI Responsibilities for Handling Investigational Drugs in Research, Continued

Specific PI duties (continued)

The following table describes specific duties for which the Principal Investigator is responsible (continued):

Duty	Description
Drug dispensing	Under state law, only a licensed practitioner or pharmacist is authorized to compound or dispense dangerous drugs used in a research project including those drugs not yet approved by the Food and Drug Administration.
Drug labeling	• The Code of Federal Regulations specifies the following labeling requirements for an investigational new drug: – The immediate package intended for human use shall bear a label with the statement "Caution: New Drug – Limited by Federal (or United States) law to investigational use" – The label or labeling shall not: > Bear any statement that is false or misleading in any particular > Represent that the drug is safe or effective for the purposes for which it is being investigated • According to the Texas Dangerous Drug Act, investigational and dangerous drugs dispensed to or for a subject must be labeled with the: – Name and address of the practitioner who prescribed the drug, and if applicable, the name and address of the registered nurse or physician assistant – Date the drug is delivered – Name or initials and study ID of the subject – Drug/placebo: > Name (or study identifier) > Strength > Directions for use
Drug administration	• Investigational New Drugs and Dangerous Drugs shall be administered in accordance with any applicable State or Federal Regulations and in accordance with BCM policies or procedures. • Investigational drugs are to be administered in accordance with the research protocol and in accordance with any other hospital or clinic policy pertaining to the administration of medications.

Related standards AAHRPP I.1.G, I.7.A, I.7.B, III.2.B, III.2.C

PI Responsibilities for Handling Investigational Devices in Research

Date of Last Revision/Review: 11/27/18

Scope

These standards apply to all personnel involved in the handling of investigational devices intended for administration to research subjects treated in the various clinics which are part of Baylor College of Medicine clinical operations.

***Critical Note*:** Many hospitals and clinics where research is conducted require the use of their own Investigational Drug Service for use of investigational devices in research. Research at hospitals and clinics MUST adhere to their own local standards.

Responsibilities

The following table indicates who is responsible for what duties:

Who	Duties
Authorized personnel	• According to federal/state regulations and BCM Policy and Procedure, properly handle devices used in clinical research in terms of: – Receiving – Storage – Preparation – Dispensing – Administration – Disposal • May be contracted to perform this responsibility for the investigator
Principal Investigator (PI)	• Control of device(s) under investigation • This includes ensuring that the use of the device is performed and documented according to state and federal regulations regarding: – Receipt – Storage – Preparation – Dispensing – Administration – Return – Disposal • Ensure that the subject is eligible to receive the device under investigation and provided informed consent according to IRB-approved procedures

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PI Responsibilities for Handling Investigational Devices in Research, Continued

Specific PI duties

The following table describes specific duties for which the Principal Investigator (PI) is responsible:

Duty	Description
Accountability record	• The investigator must maintain records to include the: – Product's delivery to the study site – Inventory at the site – Use by each subject – Return to the sponsor or alternative disposition of unused/returned product • These records must include **for each transaction of each product**: – Dates – Recorder's initials – Patient name/subject identification number – Quantities – Batch/serial numbers or code mark – Expiration/retest dates (if applicable) – Unique code/kit numbers (if applicable) • Maintain records that: – Document adequately that the subjects were provided the device as specified by the IRB-approved protocol – Reconcile all investigational product(s) received from the sponsor • In regard to the "use by each subject", maintain accountability records that document adequately which subject(s) received the device and when
Storage	• Investigational product(s) should be stored as specified by the sponsor and in accordance with applicable regulatory requirement(s) • Storage guidelines include: – Adequate size for storage – Ability to lock storage area – Separate storage area for research product from clinical care product – Usable product is stored separately from unusable/returned product – Appropriate temperature, humidity levels and other environmental monitoring requirements – Access is limited to authorized study staff

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PI Responsibilities for Handling Investigational Devices in Research, Continued

Specific PI duties (continued)

The following table describes specific duties for which the Principal Investigator is responsible (continued):

Duty	Description
Dispensing	The PI: • Can permit use of the investigational device only with subjects under her/his supervision • Cannot supply an investigational device to any person not authorized under the IDE regulation to receive it
Labeling	• Under federal regulations an investigational device or its immediate package must bear a label with the following information: – Name and place of business of the manufacturer, packer, or distributor – Quantity of contents, if appropriate – State, "CAUTION Investigational device. Limited by Federal (or United States) law to investigational use" • The label must also describe all relevant: – Contraindications – Hazards – Adverse effects – Interfering substances or devices – Warnings – Precautions • The labeling of an investigational device must **not**: – Contain any false or misleading statements – Imply that the device is safe or effective for the purposes being investigated

Related standards AAHRPP I.7.A, I.7.B, III.2.B, III.2.C

Human Gene Transfer (HGT) Research

Date of Last Revision/Review: 07/25/19

Introduction

This topic describes the special requirements for gene transfer research.

What is HGT?

Human Gene Transfer (HGT) is an approach to the treatment of human disease based on the transfer of genetic material (DNA) into an individual. In this way, HGT attempts to treat disease in an individual patient by the administration of DNA rather than a drug. Gene transfer research involves the administration of genetic material to alter the biological properties of living cells for therapeutic use.

Methods

Gene transfer is accomplished by one of two methods:

- In vivo – in the body
- Ex vivo – outside of the body

How transferred

The transfer of genes is typically accomplished in one of two ways:

- By placing the genetic sequence inside of a vehicle known as a vector.
- By injecting the DNA directly into the cell without the use of a vector

What are vectors?

Some of the most common vectors utilized are viruses. These viruses have been specifically engineered by removing their replication capabilities and inserting the DNA sequence of interest.

Classification

Gene transfer activities in humans are:

- Investigational
- Regulated by both the FDA and the NIH Office of Science Policy (OSP)

When to use

DHHS regulations specify that no individual may be enrolled in human gene transfer research until all the following conditions have been met:

- Review and approval by the Institutional Biosafety Committee (IBC), see the IBC Manual for reference
- Approval of relevant Institutional component-designated Committee(s) has been obtained
- Component IRB approval has been obtained
- The investigator has obtained all other regulatory authorizations, such as any consents required by regulations, from the subject.
  Reference: 65 FR 196, October 10, 2000; 81 FR 15315

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Human Gene Transfer (HGT) Research, Continued

Form to submit	FDA regulations require the submission of an IND for human gene transfer research.
Mandatory compliance	Compliance with the *NIH Guidelines* and other federal regulations governing human subjects research is mandatory for all investigators at institutions that receive NIH funds for research involving recombinant or synthetic nucleic acid molecules.
Related standards	AAHRPP I.7.A, I.7.B, III.2.B, III.2.C

Review of Research Involving HGT

Date of Last Revision/Review: 07/25/19

Introduction

This topic discusses how the IRB reviews research involving human gene transfer (HGT).

Who must review HGT protocols?

The following must review HGT protocols:

- BCM Institutional Biosafety Committee (IBC)
- BCM Institutional Review Board (IRB)
- Food and Drug Administration (FDA)

Final IRB approval: Contingent upon receipt of all required documents or approvals from the IBC and FDA

***Note*:** The deliberate transfer of recombinant or synthetic nucleic acids into one human research participant, conducted under an FDA regulated individual patient expanded access IND or protocol, including for emergency use, is not research subject to the *NIH Guidelines* and thus does not need to be submitted to an IBC for review and approval.

(*NIH Guidelines*, Section III-C-1)

Administration of an investigational recombinant or synthetic nucleic acid product outside an individual patient expanded access IND requires IBC review and approval.

For an individual patient expanded access IND,see Expanded Access for Drugs and Biologics (Compassionate Use), the treating physician must have on file the following before treating the patient:

- FDA Form 3926 approved by the FDA
- IRB Chairperson concurrence

Full board review

The IRB Analyst ensures that all protocols involving gene transfer are reviewed by the full board if not qualified for expedited review.

How HGT is handled

This tables shows how an HGT protocol is handled when being submitted for approval:

When …	Then …
A new protocol is determined to be HGT research	The protocol should be assigned according to the Assignment section of the Primary/Team Reviewer System procedure. ***Assistance***: Consult with the Director of Research Compliance-IRB if you are not sure the protocol involves gene transfer.
An HGT is submitted for the initial IRB review	The HGT protocol submission should include the following: • Proof of an Investigational New Drug (IND) number (from the FDA) provided in the drug section (Section O) in BRAIN ESP1

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Review of Research Involving HGT, Continued

How HGT is handled (continued)

This tables shows how an HGT protocol is handled when being submitted for approval (continued):

When …	Then …
An HGT is submitted for the initial IRB review (cont.)	• IBC approval letter: – The IRB will accept concurrent review of HGT protocols while the principal investigator is seeking IBC approval and FDA review – However, IRB final approval is contingent on receipt of these items for review – Full committee review may be required again based on these items once submitted
An HGT protocol is scheduled to be reviewed	The IBC Analyst is contacted to see if there is any information that should be conveyed to the IRB.
An IRB member requests that a member of the IBC serve as a consultant to the IRB	• The IBC Analyst may be contacted • The IBC Analyst: – Recommends a member – Provides contact information
An emergency use protocol involving HGT is submitted	The Director of Research Compliance-IRB and Director of Research Compliance-IBC are informed immediately.
HGT protocol amendments or adverse events might increase the risk to subjects	The Director of Research Compliance-IRB is notified.

IRB continuing review

HGT protocols can be reviewed concurrently by the IBC and IRB. These protocols can be approved for continuing review with the PI's acknowledgement that:

"Subject enrollment cannot continue until a copy of the IBC continuing review approval letter/receipt of annual report has been submitted to the IRB."

Mechanism: The modification memo mechanism may be used for this process.

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Review of Research Involving HGT, Continued

How IRB administrator handles situations

The table below explains how the IRB Administrator (Director of Research Compliance-IRB) handles various situations:

When …	Then the IRB Administrator …
An emergency use protocol involving HGT has been submitted	Informs the IBC Analyst immediately to coordinate a concurrent review
An HGT protocol amendment or adverse event might increase the risk to subjects	Informs the IBC Analyst immediately ***Result***: A convened IRB meeting reviews the amendment or adverse event for determination of final disposition.
The situation involves non-compliance	Reports the following to the IBC Analyst and Research Compliance Services: • Significant problems with or violations of regulations below: – Federal – State – College • Significant research-related: – Accidents – Illnesses – Unanticipated problems For more information see procedure on, Reporting and Assessing Compliance Concerns

Related standards

AAHRPP I.7.A, I.7.B, I.7.C, II.2.C, II.2.D

Section C
Expanded Access to Investigational Drugs, Biologics, or Devices for Treatment Use

Overview

Introduction

Date of Last Revision/Review: 04/18/22

This section provides information on the FDA's regulations on expanded access use of investigational drugs, biologics and devices for treatment use.

For VA Research

Emergency expanded access protocols or activities do not require prospective R&D Committee approval or notification.

In this section

This section covers the following topics:

- Expanded Access for Drugs and Biologics (Compassionate Use)
- Expanded Access for Individual Patients, Including for Emergency Use
- Expanded Access for Widespread Use (Treatment INDs)
- Expanded Access for Devices
- Expanded Access for Widespread Use (Treatment IDEs)
- Emergency Use of a Test Article Without IRB Review
- Emergency Use of a Test Article Without Informed Consent

Related standards

AAHRPP I.1.D, I.7.A, I.7.B, I.7.C, II.4.C

Expanded Access for Drugs and Biologics (Compassionate Use)

Introduction

Date of Last Revision/Review: 04/18/22

This chapter provides information for researchers, physicians, and the Institutional Review Board (IRB) about the implementation of FDA's regulations on expanded access to investigational drugs and biologics for treatment use under an investigational new drug application (IND) (21 CFR part 312, subpart I).

Definition

Expanded access, sometimes called "compassionate use," is the use, outside of a clinical trial, of an investigational medical product (i.e., one that has not been approved by FDA). Expanded access refers to the use of an investigational drug when the primary purpose is to diagnose, monitor, or treat a patient's disease or condition rather than to obtain the kind of information about the drug that is generally derived from clinical trials.

Categories of expanded access of drugs and biologics

21 CFR Part 312 Subpart I provides general requirements, describes criteria that must be met to authorize expanded access, lists requirements for expanded access submissions, and describes safeguards that will protect patients and preserve the ability to develop meaningful data about the use of the investigational product.

Under FDA's current regulations for investigational drugs and biologics, there are three categories of expanded access:

- Expanded access for individual patients, including for emergency use (21 CFR 312.310)
- Expanded access for intermediate-size patient populations (generally smaller than those typical of a treatment IND or treatment protocol (21 CFR 312.315)
- Expanded access for widespread treatment use through a treatment IND or treatment protocol (designed for use in larger patient populations) (21 CFR 312.320)

Expanded access uses

Wherever possible, use of an investigational medical product by a patient as part of a clinical trial is preferable because clinical trials can generate data that may lead to the approval of products and, consequently, to wider availability.

However, when patient enrollment in a clinical trial is not possible (e.g., a patient is not eligible for any ongoing clinical trials, or there are no ongoing clinical trials), patients may be able to receive the product, when appropriate, through expanded access.

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Expanded Access for Drugs and Biologics (Compassionate Use), Continued

Requirements for expanded access uses

Under the Federal Food, Drug, and Cosmetic Act (FD&C Act), a patient may seek individual patient expanded access to investigational products for the diagnosis, monitoring, or treatment of a serious disease or condition if the following conditions are met:

- The patient to be treated has a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition. The potential patient benefit justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated
- Providing the investigational drug for the requested use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use
- The patient's physician must determine that the probable risk to the person from the investigational drug is not greater than the probable risk from the disease or condition
- The FDA must determine that the patient cannot obtain the investigational drug under another IND or protocol

Expanded Access for Individual Patients, Including for Emergency Use

Introduction

Date of Last Revision/Review: 04/18/22

This procedure describes the FDA submission process and IRB review for:

- Individual Patient Expanded Access IND (Single Patient IND)
- Individual Patient Expanded Access Protocol (Single Patient Protocol)
- Individual Patient Expanded Access IND for Emergency Use
- Individual Patient Expanded Access Protocol for Emergency Use

Individual Patient Expanded Access IND (also referred to as a Single Patient IND)

Access to an investigational drug (including a biologic) for use by a single patient submitted as a protocol under a new IND, usually with the treating physician as sponsor. The investigational product may or may not be under development. Unless FDA notifies the sponsor that treatment may begin earlier, there is a *30-day waiting period* before treatment with the drug may begin.

Single Patient IND - FDA Submission Process	IRB Review
To streamline the submission process for individual patient expanded access INDs, the FDA developed Form FDA 3926. The FDA generally intends to accept submission of a completed Form FDA 3926 to comply with the IND submission requirements. • For individual patient expanded access INDs, Form FDA 3926 may also be used for certain follow-up submissions to an individual patient expanded access IND, which includes the following: – Initial written IND safety report – Follow-up to a written IND safety report – Annual report – Summary of expanded access use (treatment completed) – Change in treatment plan – General correspondence or response to FDA request for information – Response to clinical hold • If a licensed physician is making the individual patient expanded access submission, he or she also must be willing to manage the use of the investigational drug or biologic and the patient's medical care, including: – Discussing with the patient the risks and benefits of the use of the product – Obtaining informed consent from the patient – As well as complying with all regulations for the expanded access use For more information regarding how a physician should apply to the FDA, see the FDA website Expanded Access (Compassionate Use).	• For individual patient expanded access use of an investigational drug, the FDA intends to consider a completed Form FDA 3926 with the box in Field 10.b. checked and the form signed by the physician to be a request for a waiver of the requirement for IRB review and approval at a convened IRB meeting. • The physician must obtain concurrence by the IRB chairperson (or designated IRB member) **before the treatment use begins**.

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Expanded Access for Individual Patients, Including for Emergency Use, Continued

Investigational product availability and costs

The medical product company must agree to provide the investigational drug for expanded access use. The FDA cannot require a company to provide an investigational drug for expanded access use to proceed.

- A company may decide to turn down a request if, for example it is not able or willing to provide access to an investigational drug outside of clinical trials intended to support marketing approval.
- In some cases, patients may have to pay for using the investigational drug and/or for medical care associated with the use of the investigational drug. In others, pharmaceutical companies may elect not to charge. See FDA Guidance Charging for Investigational Drugs Under an IND - Questions and Answers.

Reporting requirements

As with any IND, in all cases of expanded access, sponsors are responsible for submitting IND safety reports and annual reports (when the IND or protocol continues for 1 year or longer) to FDA as required under 21 CFR 312.32 and 312.33, see § 312.305(c).

For individual patient expanded access, the regulations in § 312.310(c)(2) specify that, at the conclusion of treatment, the sponsor must provide to FDA a written summary of the results of the expanded access use, including adverse effects. With respect to reporting serious and unexpected adverse reactions in IND safety reports, under 21 CFR 312.32(c), the sponsor must report an adverse event as a suspected adverse reaction only if there is evidence to suggest a causal relationship between the drug and the adverse event. **FDA Form 3926 may be used for these reports.**

See FDA Guidance Expanded Access to Investigational Drugs for Treatment Use.

Individual Patient Expanded Access Protocol (also referred to as a Single Patient Protocol)

Access to an investigational drug (including a biologic) for use by a single patient submitted as a new protocol to an existing IND by the sponsor of the existing IND.

The investigational product may or may not be under development. There is *no 30-day waiting period* before treatment with the investigational product may begin, but the protocol must be received by FDA and have **approval by an Institutional Review Board (IRB) before treatment may begin.**

Single Patient Protocol -FDA Submission Process	IRB Review
• Only the sponsor (a company or individual who holds an IND) may apply for a single patient protocol submission. • The application process is largely the same as for a single patient IND referenced above. Make sure to include a reference to the existing IND in the cover letter	• A single patient protocol must be submitted in BRAIN for review and approval. • All supporting FDA IND correspondence must be attached in Section S of the BRAIN protocol.

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Expanded Access for Individual Patients, Including for Emergency Use, Continued

Individual patient expanded access IND for emergency use

Access to an investigational drug for treatment use by a single patient in an emergency situation (i.e., a situation that requires a patient to be treated before a written submission can be made) submitted under a new IND.

For more information on emergency use of a test article, see Emergency Use of a Test Article Without IRB Review.

IND for Emergency Use - FDA Submission Process	IRB Review
• Treatment is initially requested and authorized by telephone (or other rapid means of communication) and may start immediately upon FDA authorization. • The physician or sponsor must agree to submit a written submission (IND) within 15 working days of the initial authorization.	• Treatment may begin without prior IRB approval. • IRB **must be** notified of the emergency expanded access use within 5 working days of treatment.

Individual patient expanded access protocol for emergency use

An emergency use protocol is a subset of individual patient protocols that provides expanded access to an investigational drug for treatment use by a single patient in an emergency situation (i.e., a situation that requires a patient to be treated before a written submission can be made) submitted as a protocol to an existing IND by the sponsor of the existing IND.

For more information on emergency use of a test article, see Emergency Use of a Test Article Without IRB Review.

Protocol for Emergency Use - FDA Submission Process	IRB Review
• Treatment is initially requested and authorized by telephone (or other rapid means of communication) and may start immediately upon FDA authorization • The physician or sponsor must agree to submit a written submission (IND) within 15 working days of the initial authorization.	• Treatment may begin without prior IRB approval. • IRB **must be** notified of the emergency expanded access use within 5 working days of treatment.

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Expanded Access for Individual Patients, Including for Emergency Use, Continued

Deviation from protocol if patient already enrolled in clinical trial	If a patient is already enrolled in a clinical trial (designed to further the development of or determine the safety and/or effectiveness of an investigational drug) and the patient's results are to be included in the analysis of the investigational drug, the continued treatment of that patient with the investigational drug IS NOT considered expanded access, even if the patient does not continue to meet all the study inclusion criteria or the patient's treatment deviates from the study protocol. This is commonly known as a protocol exception and would be covered under the existing IND. **IRB Review:** • A significant protocol deviation involving additional treatment with an investigational agent should be submitted as a single patient protocol amendment with documentation of sponsor approval, for prospective IRB review. • In an emergency where prospective IRB review cannot be obtained, the deviation must be reported to the IRB within 5 working days.
Related standards	AAHRPP I.7.A, I.7.B, I.7.C

Expanded Access for Widespread Use (Treatment INDs)

Introduction

Date of Last Revision/Review: 04/18/22

This topic explains treatment INDs.

Under the FD&C Act statute, a sponsor or a physician may submit a protocol intended to provide widespread access to an investigational product for multiple patients. In this scenario, FDA will permit the investigational product to be made available under a treatment IND if certain criteria are met. Learn more about treatment INDs.

Definitions

This table defines the types of INDs:

Term	Definition
Treatment IND	A mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments
Individual Patient IND	A mechanism for a physician to obtain an unapproved drug for an individual patient

IRB review requirement

It is a requirement of the College that all Treatment IND studies and Individual Patient IND studies must be reviewed and prospectively approved by the IRB.

Requirements

This table provides how the requirements are met:

When …	Then the requirements that must be satisfied are …
A Treatment IND is to be issued	Specified in these FDA regulations: • 21 CFR 312.34 • 21 CFR 312.35
An Individual Patient IND is to be issued	Specified in these FDA regulations: • 21 CFR 312.34 • 21 CFR 312.35
Treatment IND is to be issued	Are the following: • Prospective IRB review ***Waiver***: The sponsor may apply for a waiver of local IRB review under a Treatment IND. • Informed consent ***Waiver***: No waiver applies.

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Expanded Access for Widespread Use (Treatment INDs), Continued

Descriptions This table describes the use and requirements of specific Treatment INDs, Individual Patient INDs:

Term	Description
Treatment IND	During the clinical investigation of a drug, it may be appropriate to use the drug in treatment of patients not in the clinical trials. ***Requirements***: • FDA approval under a treatment protocol (21 CFR 312.35) or a treatment IND (21 CFR 312.34) • IRB review and approval • Informed consent
Individual Patient IND	From an operational standpoint, the Individual Patient IND is a Treatment IND for a single patient-subject. ***Requirements***: • Same as a standard Treatment IND • IRB review and approval • Informed consent ***Background***: The Individual Patient IND is not described in regulations but was added to the law under the FDA Modernization Act (FDAMA) in 1997.
Group C Treatment IND	Group C drugs are Phase 3 study drugs that have shown evidence of efficacy in a specific tumor type. Group C drugs are distributed by the National Cancer Institute (NCI) with a Guideline Protocol and an informed consent document. ***Requirements***: • Informed consent • IRB review ***Important***: FDA and NCI permit the use of Group C drugs without local IRB review, but the College normally requires review and approval by the IRB. Investigators who are considering use of Group C drugs should contact the IRB Chairperson for guidance.
Treatment use of orphan drugs	The term *orphan drug* refers to a product that treats a rare disease affecting fewer than 200,000 Americans. ***Requirements***: • Prospective IRB review and approval • Informed consent (21 CFR 316.40 and 312.34)

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Expanded Access for Widespread Use (Treatment INDs), Continued

Descriptions (cont) This table describes the use and requirements of specific Treatment INDs, Individual Patient INDs (continued):

Term	Description
Parallel track studies	FDA permits wider access to promising new drugs for HIV/AIDS related diseases under a separate access protocol that parallels the controlled clinical trials that are essential to establish the safety and effectiveness of new drugs. ***Requirements***: • Prospective IRB review • Informed consent

Related standards AAHRPP I.1.D, I.7.A, I.7.B, I.7.C

Expanded Access for Devices

Introduction

Date of Last Revision/Review: 04/18/22

This section covers the circumstances under which a health care provider may use an investigational device outside of a clinical study to save the life of a patient or to help a patient suffering from a serious disease or condition for which no other alternative therapy exists.

Mechanisms of expanded access to devices

If enrollment in an existing clinical trial protocol is not possible (e.g., a patient is not eligible for any ongoing clinical trials, or there are no ongoing clinical trials to address the patient's condition), patients/physicians have the potential to receive expanded access to investigational devices under one of three alternative mechanisms.

Emergency Use

- An exemption under FDA regulations at 21 CFR 56.104(c) permits the emergency use of an investigational device on a one-time basis per institution without IRB review and approval.
- This exemption allows for one emergency use of the device without prospective IRB review. See, Emergency Use of a Test Article Without IRB Review.

Compassionate Use

- Compassionate use can be for devices that are being studied in a clinical trial under an IDE for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition.
- It can also be used for devices that are not being studied in a clinical investigation (i.e., an IDE for the device does not exist). This provision is typically approved for individual patients but may be approved to treat a small group.

Treatment Use

- A device that is not approved for marketing may be under clinical investigation for a serious or immediately life-threatening disease or condition in patients for whom no comparable or satisfactory alternative device or other therapy is available.
- During the clinical trial or prior to final action on the marketing application, it may be appropriate to use the device in the treatment of patients not in the trial under the provisions of the treatment investigational device exemption (IDE) regulations. (§812.36). See, Expanded Access for Widespread Use (Treatment IDEs).

Continued on next page

Expanded Access for Devices, Continued

FDA submission process

The FDA cannot require a company to provide an investigational device for compassionate use. If a licensed physician would like to obtain an investigational device for an individual patient, the medical device company must first agree to provide the investigational device for compassionate use.

If the device manufacturer agrees to provide the device under compassionate use, there are two different processes to follow to obtain FDA approval, depending on whether or not there is an IDE for a clinical trial for that device:

- If there is an IDE for the device, the IDE sponsor (who may be the device manufacturer or a physician who has submitted the IDE to conduct the clinical study for the device) should submit an IDE supplement requesting approval for a compassionate use under section §812.35(a) in order to treat the patient. The IDE supplement should include:
  - A description of the patient's condition and the circumstances necessitating treatment
  - A discussion of why alternative therapies are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition
  - An identification of any deviations in the approved clinical protocol that may be needed in order to treat the patient
  - The patient protection measures that will be followed:
    - A draft of the informed consent document that will be used
    - Clearance from the institution as specified by their policies
    - Concurrence of the IRB chairperson
    - An independent assessment from an uninvolved physician, and
    - Authorization from the device manufacturer on the use of the device
- **If there is no IDE for the device,** the physician or manufacturer submits the above information to FDA, along with a description of the device provided by the manufacturer.

The physician should not treat the patient identified in the request until the FDA approves use of the device under the proposed circumstances.

IRB review

The IRB chairperson provides concurrence for compassionate use requests. FDA approval for the compassionate use of a device must be obtained prior to use of the device.

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Expanded Access for Devices, Continued

Requirements for all expanded access use of a device

The table below describes the conditions that apply for each expanded access use of a device:

Use	Requirements
Compassionate	• The patient has a life-threatening or serious disease or condition; and • No generally acceptable alternative treatment for the condition exists. • Prior FDA approval and IRB Chair Concurrence
Treatment	• The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition; • There is no comparable or satisfactory alternative device available to treat or diagnose the disease or condition in the intended patient population; • The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or all clinical trials have been completed; and • The sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the investigational device with due diligence. • Prior FDA approval and IRB Approval
Emergency	• The patient has a life-threatening or serious disease or condition that needs immediate treatment; • No generally acceptable alternative treatment for the condition exists; and • Because of the immediate need to use the device, there is no time to use existing procedures to obtain FDA approval for the use. See, Emergency Use of a Test Article Without IRB Review.

For more information see, FDA Guidance Expanded Access for Medical Devices.

Continued on next page

Expanded Access for Devices, Continued

Reporting requirements

The table below describes the requirements for reporting for each expanded access use of a device:

Use	Reporting Requirements
Compassionate	• Following the compassionate use of the device, a follow-up report should be submitted by whoever submitted the original compassionate use request to FDA. • This report should present summary information regarding patient outcome. • If any problems occurred as a result of device use, these should be discussed in the follow-up report and reported to the reviewing IRB as soon as possible.
Treatment	The sponsor of a treatment IDE must submit progress reports on a semi-annual basis to all reviewing IRB's and FDA until the filing of a marketing application.
Emergency	• If there is an IDE for the device, the IDE sponsor must notify the FDA of the emergency use within 5 days through submission of an IDE Report, §812.35(a)(2). • The IRB must also be notified with 5 days of use. See, Emergency Use of a Test Article Without IRB Review.

Related standards

AAHRPP I.7.A, I.7.B, I.7.C

Expanded Access for Widespread Use (Treatment IDEs)

Introduction

Date of Last Revision/Review: 04/18/22

This topic explains treatment IDEs.

Under the FD&C Act statute, a sponsor or a physician may submit a protocol intended to provide widespread access to an investigational product for multiple patients. In this scenario, FDA will permit the investigational product to be made available under a treatment IDE if certain criteria are met. Learn more about treatment IDEs.

Definition

A Treatment IDE is a comparable mechanism to a Treatment IND for providing investigational devices to patient-subjects.

IRB review requirement

It is a requirement of the College that all Treatment IDE studies must be reviewed and prospectively approved by the IRB.

Requirement guide

When a Treatment IDE is to be issued, then the requirements that must be satisfied are specified in the FDA regulations 21 CFR 812.36 as follows:

- Prospective IRB review
  ***Waiver*:** The sponsor may apply for a waiver of local IRB review under a Treatment IDE.
- Informed consent
  ***Waiver*:** No waiver applies.

Treatment IDE

Treatment use of an investigational device facilitates the availability of promising new devices to desperately ill patients as early as possible before general marketing begins. Such use permits wide access to the device dependent upon patient need.

When such use may occur:

- The patient has a serious or immediate life-threatening condition.
- There is no comparable or satisfactory alternative available.
- The device is under investigation in a controlled trial for the same use (or such trials have been completed).
- The Sponsor is pursuing marketing approval/clearance.
- The Sponsor has submitted and the FDA has approved an IDE under 21 CFR 812.36.

Requirements:

- IRB review and approval
- Informed consent

Related standards

AAHRPP I.1.D, I.7.A, I.7.B, I.7.C

Emergency Use of a Test Article Without IRB Review

Introduction

Date of Last Revision/Review: 03/04/21

This topic discusses when it is appropriate to use a test article without IRB approval in an emergency situation. See FDA Infosheet.

Exemption and limitations

An exemption under FDA regulations at 21 CFR 56.104(c) permits the emergency use of an investigational drug, device, or biologic on a one-time basis per institution without IRB review and approval. This exemption allows for one emergency use of a test article without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval.

***Note 1*:** The FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

The IRB and the treating physician will work closely together to follow FDA guidance regarding any subsequent use of the same investigational drug, device, or biologic at the institution on an emergency use basis. The IRB may work with the FDA directly as needed for guidance on specific uses. See Emergency Use of an Investigational Drug or Biologic – Information Sheet.

Note 2: Data obtained from an emergency use of a test article cannot be used in prospectively planned research that would meet the DHHS definition of research under the Federal Policy and the DHHS Subpart A Definitions.

Institutional requirements

All emergency uses of test articles conducted at the College or by its employees or agents must be compliant with the FDA regulations and must be reported to the IRB as required.

All emergency uses of test articles conducted at the College or by its employees or agents reported to the IRB will be reviewed by an individual knowledgeable of FDA regulations to determine if they complied with the FDA regulations. Additionally, the individual will determine if the emergency use did not meet the DHHS definition of research under the Federal Policy and the DHHS Subpart A Definitions.

The Director of Research Compliance-IRB, in consultation with the IRB Chair or another qualified professional designated by the Human Subject Signatory Official will make this determination.

For more information regarding the reporting, see Exempt Emergency Use of a Test Article.

Continued on next page

Emergency Use of a Test Article Without IRB Review, Continued

Required conditions for emergency use of any test article

In an emergency use situation without IRB review and approval, the investigator or treating physician should ensure and document that ALL of the following conditions are met before proceeding with the use of the test article:

- A human subject is in a life-threatening situation, and,
- No standard acceptable treatment is available, and,
- There is insufficient time to obtain IRB approval, and,
- Informed consent from the subject or legally authorized representative will be obtained prior to the emergency use unless the conditions described in requirements for informed consent.

***Note 1*:** The emergency use must be reported to the IRB within five (5) working days.

Important: Such reporting must not be construed as IRB approval for the emergency use.

For more information regarding the reporting, see Exempt Emergency Use of a Test Article.

***Note 2*:** Data obtained from an emergency use of a test article cannot be used in prospectively planned research that would meet the DHHS definition of research under the Federal Policy and the DHHS Subpart A Definitions.

For VA Research:

Any emergency use of a test article does not require R&D Committee approval but is VA research under this policy.

Prospective IRB approval is not required if an activity meets the requirements for use of the emergency exemption from IRB approval in 21 CFR 56.104(c); informed consent must be obtained from the subjects (or LARs) unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing the requirements described in 21 CFR 50.23(a).

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Emergency Use of a Test Article Without IRB Review, Continued

Emergency use of drugs

Emergency use of an investigational new drug occurs when the emergency situation does not allow time for submission of an IND.

Requirements

This table explains the requirements:

Requirement	Description
FDA	Use of the drug requires a request to FDA to authorize the use of the drug for the emergency use. If there is an emergency that requires the patient to be treated before a written submission can be made to the FDA for an IND, the FDA may authorize the emergency use to begin without a written submission. The FDA reviewing official may authorize the emergency use by telephone.
IND	Such authorizations are conditioned on the licensed physician or sponsor explaining how the emergency use will meet the requirements of 21 CFR 312.305 and 21 CFR 312.310 and must agree to submit an expanded access submission within 15 working days of FDA's authorization of the use.
IRB review and approval	The emergency use of an investigational new drug may take place without IRB review and approval, provided the use is reported to the IRB within five (5) working days. For more information regarding the reporting, see Exempt Emergency Use of a Test Article.
Informed consent	Informed consent is required unless all the following apply: • The situation is life-threatening. • The criteria at 21 CFR 50.23(a) or 50.23(b) have been met. • The IRB is notified within 5 working days. See Emergency Use of a Test Article Without Informed Consent.

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Emergency Use of a Test Article Without IRB Review, Continued

Emergency use of devices: IDE status

Emergency use of an unapproved device may occur in an emergency situation when one of these conditions exists:

- An IDE for the device does not exist.
- A physician wants to use a device in a way not approved under an existing IDE.
- A physician is not an investigator under the existing IDE.

Emergency use of devices: Patient status

The device may be used if all these conditions exist:

- The patient has a life-threatening condition that needs immediate treatment.
- There is no generally acceptable alternative treatment.
- There is insufficient time to obtain IRB approval.
- There is no time to obtain FDA approval.
- The emergency use must be reported to the IRB within five (5) working days. ***Important***: Such reporting must not be construed as IRB approval for the emergency use.

For more information regarding the reporting, see Exempt Emergency Use of a Test Article.

Patient protections for emergency uses of devices

Such uses require as many of the following patient protections as possible:

- Informed consent
- Clearance from the Institution
- Concurrence of the IRB chairperson
  Important: This concurrence does not constitute IRB approval.
- An independent assessment of an uninvolved physician
- Authorization from the IDE sponsor (if an IDE exists)

Follow-up reporting for devices

This table provides to whom to send follow-up reports for emergency use of devices:

When an IDE …	Then follow-up reports should be provided to …
Exists	The Sponsor
Does not exist	The FDA

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Emergency Use of a Test Article Without IRB Review, Continued

Clarification of the term:	For studies involving investigational drugs, "Compassionate Use" is often meant to refer to the emergency use situations discussed earlier.
Compassionate Use	"Compassionate use" sometimes refers to use of an unapproved agent obtained under an individual patient IND (also called single patient IND); see FDA Infosheet. ***Legality***: "Compassionate use" is not a term that appears in the FDA or DHHS regulations or the Common Rule. The FDA regulations do not provide for expedited IRB approval in emergency situations. Therefore, "interim," "compassionate," "temporary" or other terms for an expedited approval process are not authorized. "Compassionate use" situations should not be confused with the Humanitarian Use Device (HUD) Exemption. ***Reference***: See Humanitarian Device Exemptions.
Reference	For more information, see Exempt Emergency Use of a Test Article.
Related standards	AAHRPP I.1.D, I.7.A, I.7.B, I.7.C, II.4.C

Emergency Use of a Test Article Without Informed Consent

Introduction

Date of Last Revision/Review: 11/27/18

This topic discusses when it is appropriate to use a test article in an emergency situation without informed consent.

Exception

An exception under FDA regulations at 21 CFR 50.23 permits the emergency use of an investigational drug, device, or biologic without informed consent where the investigator and an independent physician who is not otherwise participating in the clinical investigation certify in writing all of the specific conditions listed in "Required conditions" below.

Institutional requirement

All emergency uses of test articles conducted at the College or by its employees or agents must be compliant with the FDA regulations and must be reported to the IRB as required.

All emergency uses of test articles conducted at the College or by its employees or agents reported to the IRB will be reviewed by an individual knowledgeable of FDA regulations to determine if they complied with the FDA regulations. Additionally, the individual will determine if the emergency use did not meet the DHHS definition of research under the Federal Policy and the DHHS Subpart A Definitions.

The Director of Research Compliance-IRB, in consultation with the IRB Chair or another qualified professional designated by the Human Subject Signatory Official will make this determination. For more information, regarding the reporting see Exempt Emergency Use of a Test Article.

Required conditions

Even in an emergency use situation without IRB review and approval, the investigator is required to obtain informed consent from the subject or the subject's legally authorized representative.

The only exception is if both the investigator and a physician that is not otherwise participating in the clinical investigation (the treatment and medical care of the subject with the test article) certify in writing that ALL of the following conditions have been met for the emergency use of the test article without informed consent:

- The subject is confronted by a life-threatening situation necessitating the use of the test article, and,
- Informed consent cannot be obtained because of an inability to communicate with or obtain legally effective consent from the subject, and,
- Time is not sufficient to obtain consent from the subject's legally authorized representative, and,
- No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

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Emergency Use of a Test Article Without Informed Consent, Continued

Required conditions (continued)	***Note 1*:** If in the investigator's opinion immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. ***Note 2*:** This emergency use must not meet DHHS definition of research under the Federal Policy and the DHHS Subpart A Definitions. ***Reference*:** FDA regulations at 21 CFR 50.23 The emergency use must be reported to the IRB within 5 working days. ***Important*:** Such reporting must not be construed as IRB approval for the emergency use. For more information, regarding the reporting see Exempt Emergency Use of a Test Article.
Related standards	AAHRPP I.1.D, I.7.A, I.7.B, I.7.C, II.4.C

Section D
Special Uses of Drugs, Devices, or Biologics

Overview

Introduction	Date of Last Revision/Review: 11/27/18 This section focuses on the use of drugs, devices, or biologics: • For humanitarian device exemptions, and, • The exception of informed consent for planned emergency research Most of these are FDA-regulated.
In this section	This section covers the following topics: • Humanitarian Device Exemptions • Exception from Informed Consent for Planned Emergency Research
Related standards	AAHRPP I.1.D, I.7.A, I.7.B, I.7.C, II.4.C

Humanitarian Device Exemptions

Introduction

Date of Last Revision/Review: 11/27/18

This topic provides the exemptions for research using a Humanitarian Use Device (HUD).

Definition: HUD

A *Humanitarian Use Device* (*HUD*) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year.

Background

The FDA developed this regulation to provide an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations.

Form to use

The regulation provides for the submission of a Humanitarian Device Exemption (HDE) application.

Requirements

This table describes the requirements for use of a HUD:

Requirement	Description
Clinical investigation results	A HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose.
Risk status	The application must contain sufficient information for the FDA to determine the following: • The device does not pose an unreasonable or significant risk of illness or injury. • The probable benefit to health outweighs the risk of injury or illness from its use.
Labeling	The labeling for a HUD must state the following: • The device is a humanitarian use device. • Although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated.
IRB approval	A HUD may only be used after approval of the convened (full) IRB has been obtained for use of the device at the College for the FDA-approved indication 21 CFR 814.124(a). • An approved HDE authorizes marketing of the HUD. • After granting initial approval, the IRB may use expedited procedures for conducting continuing review.
Informed consent	Informed consent of patients is not required because a HDE provides for marketing approval, so use of the HUD does not constitute research.

Related standards

AAHRPP I.1.D, I.7.A, I.7.B, I.7.C, II.2.B, II.4.C

Exception from Informed Consent for Planned Emergency Research

Introduction	Date of Last Revision/Review: 11/27/18 This topic provides the conditions for exception from informed consent for planned emergency research. This procedure applies to both FDA regulated research described in 21 CFR 50.24, as well as, for research not subject to FDA regulations that is to be conducted in emergency settings that seek to waive the requirement for informed consent by the Secretarial Waiver provision codified in 45 CFR 46.101(i), referred to as the "Emergency Research Consent Waiver".
Applicable regulation	The conduct of planned research in life-threatening emergent situations where obtaining prospective informed consent has been waived, is provided by the regulation 21 CFR 50.24.
Research plan	The research plan must be: • Approved in advance by the FDA and the IRB (for FDA regulated research) • Reported to the OHRP stating that the IRB has made all of the required findings related to the additional protections required for the research and has documented these findings (for non-FDA regulated research) • Publicly disclosed to the community in which the research will be conducted
Emergency approvals	Such studies are usually not eligible for the emergency approvals described elsewhere.
Reference	For an explanation of the wording in 21 CFR 50.24, see the topic Waiver of Consent Emergency Research – Guidance and Discussion in Chapter 4, Requirements of Informed Consent.
Related standards	AAHRPP I.1.D, I.4.C, I.7.A, I.7.B, I.7.C, II.4.C

Chapter 6
Special Research Types

Table of Contents

Overview for Special Research Types
Section A: Types of Human Subject Research
Overview
Research Types
Quality Assurance/Quality Improvement Activities as Human Subject Research
Research Activities vs. Innovative Treatments in Medical Practice
Research Activities vs. Commercial Services
Epidemiological Research
Issues in Genetic Research
Family History Research
Research Using Potentially Addictive Substances
How Research Using Large Existing Data Sets Is Reviewed
U.S. Department of Defense Research
Section B: IRB Review of Research Involving Children
Overview
Risk-Benefit Analysis and Permitted Categories
Assent of the Child
Documentation of Assent
Parental Permission
Wards
Children in U.S. Department of Education Research
Section C: IRB Review of Research Involving Adults as Vulnerable Subjects
Overview
Special Considerations for Vulnerable Subjects
Research Involving Pregnant Women, Human Fetuses, and Neonates
Research Involving Prisoners
Research Involving Potentially Addictive Substances
Research Involving Other Potentially Vulnerable Adult Subjects
Research Involving Human Fetal Tissue Transplantation and Deceased Persons

Overview for Special Research Types

Introduction

Date of Last Revision/Review: 04/20/11

In addition to the requirements and regulations provided in the first five chapters, each of these special types of research has requirements that apply to it. This chapter looks at each type and provides the guidance needed when conducting this type of research.

Example

Some special research types discussed in Section A include epidemiological research and issues in genetic research and family history research.

In this chapter

This chapter covers the following sections:

- Section A: Types of Human Subject Research
- Section B: IRB Review of Research Involving Children
- Section C: IRB Review of Research Involving Adults as Vulnerable Subjects

Related standards

AAHRPP I.1.D, II.3.A, II.4.A, II.4.B

Section A
Types of Human Subject Research

Overview

Introduction	Date of Last Revision/Review: 04/20/11 This section provides the common types of human subject research.
Authority to determine	The IRB assurance office is authorized by the College to make determinations regarding whether an activity meets regulatory definitions of human subject research.
Disclaimer	These types are examples only and not exhaustive of all human subject research.
In this section	This section covers the following topics: • Research Types • Quality Assurance/Quality Improvement Activities as Human Subject Research • Research Activities vs. Innovative Treatments in Medical Practice • Research Activities vs. Commercial Services • Epidemiological Research • Issues in Genetic Research • Family History Research • Research Using Potentially Addictive Substances • How Research Using Large Existing Data Sets Is Reviewed • U.S. Department of Defense Research
Related standards	AAHRPP I.1.D, II.3.A, II.4.A, II.4.B

Research Types

Introduction

Date of Last Revision/Review: 12/14/15

This topic provides a summary of the research types most often used with a description of each.

Types

This table summarizes the types of research:

Type	Description
Biomedical research	Involves research: • To increase scientific understanding about normal or abnormal physiology, disease states, or development; and • To evaluate the safety, effectiveness, or usefulness of a medical product, procedure, or intervention. ***Examples***: Vaccine trials, medical device research, and cancer research
Clinical research	• Involves the evaluation of biomedical or behavioral interventions related to disease processes or normal physiological functioning • Includes often but not always drugs, devices, or biological products regulated by the Food and Drug Administration (FDA)
Social and behavioral research	• Involves: – Research with a similar goal of biomedical research (to establish a body of knowledge and to evaluate interventions) but often with different content and procedures – Human subjects, focusing on individual and group behavior, mental processes, or social constructs • Usually generates data by means of: – Surveys – Interviews – Observations – Studies of existing records – Experimental designs involving exposure to some type of stimulus or environmental intervention • These types of research may require additional IRB consideration. For example, the IRB may determine that broader community consultation is required for the planning of the research protocol (as in community based participatory research design) or that the investigators should provide an opportunity for the community from which research subjects may be drawn in order to: – Comment on the research protocol design when needed (for example, when the research will focus on vulnerable populations) – Assist with the implementation of the research protocol – Assist with the dissemination of the results from the research to the community when appropriate ***Note*:** The IRB enhances this process by including the community members who are serving on the IRB.

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Research Types, Continued

Types (continued) This table summarizes the types of research (continued):

Type	Description
Epidemiology research	• Targets specific health outcomes, interventions, or disease states • Attempts to reach conclusions about cost-effectiveness, efficacy, interventions, or delivery of services to affected populations • Is conducted: – Sometimes through surveillance, monitoring, and reporting programs, such as those employed by the Centers for Disease Control and Prevention (CDC) – Sometimes through retrospective review of medical, public health, or other records • Often involves aggregate examination of data and may not always obtain individually identifiable information and thus may quality for expedited review • Has review requirements determined in all cases by the IRB, not by the individual investigator
Repository research	• Utilizes stored data or materials from individually identifiable living persons ***Examples***: Cells, tissues, fluids, body parts • Qualifies as human subject research • Requires IRB review **Data or materials stored in a bank or repository for use in future research** • The IRB should review a protocol detailing the repository's policies and procedures for obtaining, storing, and sharing its resources for: – Verifying informed consent provisions – Protecting subjects' privacy and maintaining the confidentiality of data • The IRB may then determine the parameters under which the repository may share its data or materials with or without IRB review of individual research protocols.
Pilot studies	• Involve human subjects • Are considered human subject research • Require IRB review

Related standards AAHRPP I.1.D, I.4.C, II.3.A, II.4.A, II.4.B

Quality Assurance/Quality Improvement Activities as Human Subject Research

Introduction

Date of Last Revision/Review: 04/02/14

This topic provides a discussion of the requirements for IRB review for Quality Assurance activities.

Description

Quality Assurance (QA) or Quality Improvement (QI) activities attempt to measure the effectiveness of programs or services.

IRB review and documentation

After reviewing applicable policy and guidance, investigators are responsible for assuring that all human subject research is prospectively reviewed by the BCM IRB.

QA/QI vs. Research

If the IRB reviews the activity, documentation of the determination consists of the reviewer's written concurrence in the IRB Research Review File that the activity described in the Investigator's Application does or does not satisfy the definition of human subject research. The investigator proposing the activities will receive a notification stating the determination.

45 CFR Part 46 defines research as: A systematic investigation including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

The following are examples of QA/QI activities that do not contribute to generalizable knowledge:

- Implementing a practice to improve the quality of patient care
- Collecting patient or provider data regarding the implementation of a practice for clinical, practical, or administrative purposes
- ***Note*:** The results of the activity may be published later but this does not in and of itself mean that the activity is research.

Some QA/QI activities do meet the definition of research, for example:

Introducing an untested clinical intervention for purposes which include not only improving the quality of care but also collecting information about patient outcomes for the purpose of establishing scientific evidence to determine how well the intervention achieves its intended results

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Quality Assurance/Quality Improvement Activities as Human Subject Research, Continued

QA/QI vs. Research (cont.)

The table below compares activities of research and QA/QI:

Aspects of the Activity	Research	QA/QI
Purpose	Test a formal hypothesis	Assess a process, program or system
Starting Point	A prospectively designed research hypothesis	An established set of standards
Benefits	Knowledge sought may or may not benefit subjects involved in study	Knowledge sought is intended to benefit process/program/system
Risks/burdens	May put subjects at risk	No risk, with exception of possible loss of privacy/confidentiality
Data Collection	Systematic data collection	Systematic data collection
End Point	Answer research question	Improve the program/process/system
Testing/Analysis	Determine validity of hypothesis	Compare the program/process/system to established set of standards

This table describes when the activities constitute human subject research and require IRB review:

When …	Then …
QA/QI activities are designed or intended, at least in part, to develop or contribute to generalizable knowledge	• They may constitute human subject research • The investigator should consult with the IRB to determine whether IRB review is required
QA/QI activities are designed for program evaluation purposes with no plan to develop or contribute to generalizable knowledge	• They usually do not constitute human subject research • If there is any doubt about whether they constitute human subject research, the investigator should consult the IRB and submit a protocol for review for the Determination of Human Subjects Research if necessary
The intent of the activity changes after it has begun For example, an opportunity arises to contribute previously collected data gathered in these activities to a new project producing generalizable knowledge	• The investigator should submit a protocol for IRB review • The IRB determines the conditions under which the investigator may pursue the relevant research objectives

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Quality Assurance/Quality Improvement Activities as Human Subject Research, Continued

Example A medical department within one of the College's facilities conducts a review of patient records and then contacts patients to identify cases where recommended follow-up did not occur.

When …	Then the activity …
The sole intent is to improve the rate of follow-up within the facility	Is not human subject research
The intent of the activity, at least in part, includes either: • Introducing a clinical intervention and collecting information about patient outcomes to determine how well the intervention achieved the intended results, or • Conducting the activity with the intent to draw general conclusions and then apply these findings outside the College	• May constitute human subject research • The investigator should consult with the IRB to determine whether IRB review is required

Related standards AAHRPP I.1.A, I.1.D, II.3.A, II.4.A, II.4.C

Research Activities vs. Innovative Treatments in Medical Practice

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides the requirements for IRB review when innovative treatments are used in medical practice.

Description

In the course of medical practice, sound clinical judgment sometimes leads physicians to employ innovative treatments where more common treatments appear to be ineffective or otherwise unsuitable in addressing a patient's individual needs.

IRB review

This table describes when such treatment constitutes human subject research and whether IRB review is required:

When …	Then …
Such innovative treatments employed on an occasional basis and solely for clinical purposes	• It does not normally constitute human subject research. • IRB review is not required.
The use of innovative treatments as part of a systematic investigation designed, at least in part, to develop or contribute to generalizable knowledge	• It does constitute human subject research. • Prospective IRB review is required.

Related standards

AAHRPP I.1.A, I.1.D, II.3.A, II.4.A, II.4.C

Research Activities vs. Commercial Services

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides a discussion of the use of commercial services and when they require IRB review.

Description

Facilities and laboratories within the College may occasionally provide tests or other services to non-Institutional researchers solely on a commercial basis.

Example: An appropriately qualified Institutional laboratory performs analyses of blood samples for non-Institutional investigators solely on a commercial basis.

Conditions

All of these conditions must be met for such services not to constitute human subject research at the College:

- The research is not otherwise conducted at the College.
- The research does not otherwise involve employees or agents of the College. ***Examples***: As co-investigators in planning or analysis or receiving publication credit
- The commercial services are genuinely non-collaborative, meriting neither professional recognition nor publication privileges.
- The commercial services adhere to commonly recognized professional standards for maintaining privacy and confidentiality.
- The commercial services are conducted under a valid contract.

IRB review

This table describes when IRB is required and when it is not:

When …	Then IRB review is …
Provision of such services solely on a commercial basis • Does not constitute human subject research at the College • Meet the conditions listed	Not required
Personnel of the College are involved in any way that is more than merely providing a commercial service	Required
The services do not meet all five conditions	Required

Related standards

AAHRPP I.1.A, I.1.D, II.3.A, II.4.A, II.4.C

Epidemiological Research

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides the special requirements for epidemiological research.

Description

Epidemiological research often includes:

- Making use of sensitive, individually identifiable, private information
  Examples: Usually obtained from medical or other private records
- Linking this information with additional information obtained from other public or private records
  Examples: Employment, insurance, or police records

Combinations

Epidemiological research may combine historical research with survey and interview research.

Significant problems

Epidemiological studies often present significant problems regarding both privacy and confidentiality.

IRB review

The table discusses the issues that the IRB must review:

Issue	The IRB …
Privacy	• Must satisfy itself that the research does not constitute an unwarranted invasion of the subjects' privacy • Shall seek to establish that the investigator has legitimate access to any identifiable information that is to be utilized ***Example***: If State disease registry information is to be utilized, the IRB needs to examine State law relative to the legitimate release of such information for research.
Confidentiality	• Examines mechanisms for maintaining the confidentiality of data collected • Shall seek to establish that confidentiality protections are appropriate to the nature and sensitivity of the information that has been obtained

Waiver request reasoning

Because epidemiological research typically requires large numbers of subjects, investigators almost always request that the IRB waive the usual requirements for informed consent.

Continued on next page

Epidemiological Research, Continued

Waiver approval	To approve such a waiver in epidemiological research, the IRB must find and document that these criteria for a waiver of informed consent have been met: • The research presents no more than minimal risk to subjects. • The waiver will not adversely affect the rights and welfare of the subjects. • The research could not practicably be carried out without the waiver. • Whenever appropriate, the subjects will be provided with additional pertinent information after participation. ***Reference***: 45 CFR 46.116(d)
Related standards	AAHRPP I.1.A, I.1.D, II.3.A, II.4.A, II.4.C

Issues in Genetic Research

Introduction

Date of Last Revision/Review: 04/20/11

Information obtained through genetic research may have serious repercussions for the subject or the subject's family members.

Psychosocial risks

Genetic studies that generate information about subjects' personal health risks can:

- Provoke anxiety and confusion
- Damage familial relationships
- Compromise the subjects' insurability and employment opportunities

Conclusion: For many genetic research protocols, these psychosocial risks can be significant enough to warrant careful IRB review and discussion.

IRB review

This table lists the considerations for the IRB review:

Consideration	Description
Risk level	Those genetic studies limited to the collection of family history information and blood drawing should not automatically be classified as minimal risk studies qualifying for expedited IRB review. The addition of the genetic analysis can radically alter the level of risk.
Protection of the subjects' privacy interests and confidentiality of data collected	The investigator should describe in detail how individual privacy will be protected and how the confidentiality of obtained information will be maintained.

Related standards

AAHRPP I.1.A, I.1.D, II.3.A, II.4.A, II.4.C

Family History Research

Introduction

Date of Last Revision/Review: 01/28/19

Family history research is a common technique used in bio-social and bio-behavioral research.

Description

Family history research typically, involves obtaining information from one family member (called a proband) about other family members (third parties).

Human subject/participant definition

An individual who is the object of study in a research project

Federal Policy (Common Rule)
Human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains:

- Information or biospecimens through intervention or interaction with the individual and uses, studies, or analyzes the information or biospecimens, or;
- Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens

45 CFR 46.102(e)(1)

FDA regulations
Human subject means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient 21 CFR 50.3(g) and 56.102(e).

Family member status

If the investigators obtain identifiable private information about the family members identified and described by the proband, these members may be human subjects under the regulations.

Guidance

There is not total consensus in the available guidance on this issue of family member status.

OHRP representatives have advised that third parties about whom identifiable and private information is collected in the course of research are human subjects.

Issues

The IRB must review two issues regarding gathering information about third parties:

- Family member status
- Confidentiality in determining if minimal risk is involved

Continued on next page

Family History Research, Continued

IRB review

This table lists the issues the IRB must review:

Issue	The IRB
Family member status	• Must determine if family members (third parties) are human subjects in such research • Must consider any possible risks involved • Must determine if their informed consent is required or can be waived ***References***: • Conditions specified at 45 CFR 46.116(d) • The topic Waiver or Alteration of Consent for Minimal Risk Research
Confidentiality	• Considers if informed consent from third parties can be waived ***Reference***: Section 116 • Documents the decision in the IRB records ***Result***: In most cases, waiver of consent may be appropriate.

Related standards

AAHRPP I.1.A, I.1.D, II.3.A, II.4.A, II.4.C

Research Using Potentially Addictive Substances

Introduction

Date of Last Revision/Review: 04/20/11

Research involving potentially addictive substances often involves the use of what may be termed abuse-liable substances.

Definition: Abuse-liable

Abuse-liable substances are pharmacological substances that have the potential for creating abusive dependency.

Abuse-liable substances can include both legal and illicit drugs.

IRB review

The following are among the issues that the IRB should consider when reviewing research involving potentially addictive substances:

Consideration	Description
Risk/benefit	It is critical that the IRB focus on the considerations of risk and benefit of such research.
Ethical context	The IRB must be sensitive to the ethical context of the research in that there may be moral dilemmas associated with: • The use of placebos • Addicts being presented with alcohol or drugs
Informed consent	The IRB must consider the subjects' capacity to provide continuous informed consent, ensuring that subjects are competent and are not coerced.
Subject's autonomy	For research that involves subjects that are institutionalized, the subjects' ability to exercise autonomy may be impaired.
Equitable selection	The IRB must also consider the requirements for equitable selection of subjects and protections for maintaining confidentiality ***Reason***: A population may be at risk for being discriminated against or over-selected.

Related standards

AAHRPP I.1.A, I.1.D, II.3.A, II.4.A, II.4.C

How Research Using Large Existing Data Sets Is Reviewed

Introduction

Date of Last Revision/Review: 04/20/11

Biosocial and bio-behavioral research often involves the use of large, existing data sets.

Data set review

For more information about how the use of data sets is reviewed, see the topic Confidentiality of Data Sets in Chapter 3, IRB Reviews.

Informed consent considerations

This table shows how the IRB reviews informed consent considerations:

When the investigator obtains and uses …	Then the IRB …
Large, existing data sets that do not contain identifiable private information about living individuals	• Would usually consider the study to not constitute human subject research. • They usually do not require further IRB review and informed consent would not be required.
Data that have been made anonymous ***Examples***: Codes and other identifiers are permanently removed from the data set before the data are sent to the investigator. Result: The removal is accomplished in such a manner that neither the investigator nor the source maintaining the data set can re-establish subjects' identities. The data set is maintained as a data repository under the guidelines established by the Office for Human Research Protections (OHRP).	• Would usually consider the study to not constitute human subject research. • They usually do not require further IRB review and informed consent would not be required.

Related standards

AAHRPP I.1.A, I.1.D, II.2.A, II.2.B, II.3.A, II.4.A

U.S. Department of Defense Research

Date of Last Revision/Review: 02/22/21

Introduction

This topic provides the requirements for additional protections when research is regulated by the U.S. Department of Defense (DOD).

DOD regulated research

Research that is regulated by the DOD is research that is:

- Funded in part or in full by the DOD, or
- Conducted with targeted recruitment of active-duty military personnel as research subjects, or
- Conducted within or on location at any of the DOD components

DOD Definition:

Research involving a human being as an experimental subject

An experimental subject - is a human being that is involved in an activity, for research purposes, where there is an intervention or interaction with the human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Research involving experimental subjects as defined in DODI 3216.02 is a subset of research involving human participants.

Examples of interventions or interactions include, but are not limited to:

- A physical procedure
- A drug
- A manipulation of the subject or subject's environment
- The withholding of an intervention that would have been undertaken if not for the research purpose

Prohibited research

Human participant research involving the testing of chemical or biological agents is prohibited, pursuant to Section 1520a of Title 50, United States Code (U.S.C.). Some exceptions for research for prophylactic, protective, or other peaceful purposes apply. Before any excepted testing of chemical or biological agents involving HSR can begin, explicit written approval must be obtained from the DOD Office for Human Research Protections (DOHRP).

Not human subject research

The following activities are not considered research involving human participants:

- Public or internal information collections of facts or opinions, obtained initially or in follow-up requests, from individuals (including individuals in control groups) under treatment or clinical examination in connection with research on, or prophylaxis to prevent, a clinical disorder;
- Direct treatment of that disorder; or
- The interpretation of biological analyses of body fluids, tissues, or other specimens; or the identification or classification of such specimens.

Non-exempt classified research

Non-exempt classified research must be conducted following the requirements of Instruction 3216.02.13.

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U.S. Department of Defense Research, Continued

Multi-site research	When research is conducted in multiple sites, a formal agreement between the organizations involved in the research is required in order to specify the roles and responsibilities of each party. The PI will submit this agreement document with the research protocol submission to the BCM IRB.
International research	When research is conducted in international populations the PI must have the permission to conduct the research in that country by certification or local ethics review. The PI must also ensure that all local laws, regulations, customs, and practices are followed. Please see Location of Research.
DOD component administrative review of research	The DOD Component must conduct an appropriate administrative review of the research involving human participants. The DOD Component administrative review must be conducted before the research involving human participants can begin to ensure compliance with all applicable regulations and policies, including any applicable laws and requirements and cultural sensitivities of the country when the research is conducted in a country other than the United States. • DOD institutions collaborating with non-DOD institutions may rely on a collaborating non-DOD institution's IRB if the following conditions are met: – Each institution engaged in non-exempt human participant research must have a current federal assurance of compliance. – The involvement of DOD personnel in the conduct of the research is secondary to that of the non-DOD institution. – The DOD institution, non-DOD institution, and the non-DOD institution's IRB have a written agreement defining the responsibilities and authorities of each organization in complying with all legal requirements. This agreement must be approved by the DOD component prior to the DOD institution's engagement in the research. • For DOD-supported non-exempt research involving human participants involving classified information reviewed by a non-DOD IRB, the involvement of classified information may be limited to information needed for IRB approval and oversight of the research; information needed to inform the human participants during the consent process; and information provided by human participants during the course of the research. • When an IRB at a non-DOD institution reviews DOD-supported research, the IRB must consider the scientific merit of the research, including consideration of feasibility of completion.
IRB member training	There may be specific DOD educational requirements or certification required of the IRB when reviewing DOD regulated research. The Principal Investigator is responsible for assuring that the IRB Office is notified of DOD funding or DOD regulated activity through IRB submission of the IRB Protocol Summary (New, Amendment or Continuing Review) and will provide specific information or guidance from the DOD program officials. The Director of Research Compliance-IRB will inform the IRB staff, IRB chairperson, and IRB members of these requirements when appropriate.

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U.S. Department of Defense Research, Continued

IRB/PI review with a DOD consultant reviewer	DOD program officials, through the BCM PI, will be asked to provide in the research protocol submission to the BCM IRB the contact information of a person experienced in DOD research who may serve as a consultant reviewer to the BCM IRB for the review of the research protocol.
Equitable selection of research subjects	DOD-affiliated personnel, military and civilian supervisors, officers, and others in the chain of command: • Are prohibited from influencing their subordinates to participate in research involving human participants • Must not be present at any human participant recruitment sessions or during the consent process for DOD-affiliated personnel • May participate in separate human participant research recruitment sessions • Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements. • For greater than minimal risk research involving recruitment of DOD-personnel, when occurs in a group setting, the IRB must appoint an ombudsperson. The ombudsperson: – Must not have a conflict of interest with the research or be a part of the research team – Must be present during the HSR recruitment, monitoring that the recruitment and informed consent explain that participation is voluntary and that the information provided about the research is consistent with the IRB-approved script and materials, including digitally provided materials – Should be available to address DOD-affiliated personnel's concerns about participation.

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U.S. Department of Defense Research, Continued

Secretary of Defense duties

In conducting or supporting clinical research, the Secretary of Defense ensures that:

- Women who are members of the Armed Forces are included as participants in each project of such research; and
- Members of minority groups who are members of the Armed Forces are included as participants of such research

The Secretary of Defense may waive these requirements regarding women and members of minority groups with respect to a project of clinical research if the Secretary determines that the inclusion, as participants in the project, of women and members of minority groups, respectively:

- Is inappropriate with respect to the health of the participants,
- Is inappropriate with respect to the purpose of the research, or
- Is inappropriate under such other circumstances as the Secretary of Defense may designate.

Informed consent

If the research involves DOD-affiliated personnel as participants, in addition to the basic and required consent disclosures, consent documents must include:

- If the research involves risks to their fitness for duty (e.g., health, availability to perform job, data breach), the informed consent document (ICD) must inform DOD-affiliated personnel about these risks and that they should seek command or Component guidance before participating.
- If applicable, a statement of potential risks for the revocation of clearance, credentials, or other privileged access or duty.
- A statement that the DOD or a DOD organization is funding the study.
- A statement that representatives of the DOD are authorized to review research records.
- For greater than minimal risk research, consent documents must include the disclosure that participants may, for the duration of the study, be eligible for health care services for research-related injuries at a military treatment facility, and this eligibility for health care services extends beyond participants' participation in the study to such time after the study has ended. Written materials must document how institutions will care for subjects with research-related injuries, including injuries that are the direct result of activities performed by DOD-affiliated personnel in studies that are collaborative with a non-DOD institution.
- If consent is to be obtained from the legal representative of the experimental subjects as defined in DODI 3216.02, the research must intend to benefit each participant enrolled in the study.

Exception from informed consent in emergency medicine research

An exception from informed consent in emergency medicine research is prohibited unless a waiver is obtained from the Secretary of Defense approves of the advance informed consent provision of 10 USC 980.

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U.S. Department of Defense Research, Continued

Waiver of consent

Individuals meeting the DOD definition of experimental subject may not be enrolled in research under a waiver of consent unless a waiver is obtained from the Assistant Secretary of Defense for Research and Engineering.

- The Assistant Secretary of Defense for Research and Engineering may waive the requirements for consent when all of the following are met:
  - The research is necessary to advance the development of a medical product for the Military Services.
  - The research might directly benefit the individual experimental subject.
  - The research is conducted in compliance with all other applicable laws and regulations.
- For classified research, waivers of consent are prohibited.
- If the research participant does not meet the definition of "experimental subject," the IRB is allowed to waive the consent process.

See Waiver or Alteration of Consent for Minimal Risk Research.

Vulnerable subject protections

Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C, and D, except where modified by DODI 3216.02.

- For purposes of applying Subpart B, the phrase "biomedical knowledge" is replaced with "generalizable knowledge."
- The applicability of Subpart B is limited to research involving pregnant women as participants in research that is greater than minimal risk and includes interventions or invasive procedures involving the woman or the fetus as participants.
- Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g:
  - Research or experimentation may not be conducted, in the United States or in any other country, on a nonviable living human fetus ex utero or a living human fetus ex utero for whom viability has not been ascertained unless the research or experimentation:
    - > May enhance the well-being or meet the health needs of the fetus or enhance the probability of its survival to viability; or
    - > Will pose no added risk of suffering, injury, or death to the fetus and the purpose of the research or experimentation is the development of important biomedical knowledge which cannot be obtained by other means.
  - The risk standard must be the same for fetuses which are intended to be aborted and fetuses which are intended to be carried to term.

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U.S. Department of Defense Research, Continued

Vulnerable subject protection (con't.)

Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C, and D, except where modified by DODI 3216.02 (continued).

- For human participant research that would not otherwise be approved but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, DOD organizations must demonstrate to the senior designated official that the IRB has fulfilled its duties in accordance with Subpart B. Before human participant research activities may begin, the senior designated official must receive explicit written approval from the DOD Office for Human Research Protections.

In addition to activities permissible under Subpart C, two additional categories are permissible:

- Epidemiological research is permitted under the following conditions:
  - Where the sole purpose of the research is to describe the prevalence or incidence of a disease by identifying all cases, or study potential risk factor associations for a disease.
  - The research presents no more than minimal risk.
  - The research involves no more than inconvenience to the prisoner-participants.
  - Prisoners are not a particular focus of the research.
- Human participant research involving prisoners that would otherwise meet exemption criteria may be conducted but must first be approved by an IRB.
- DOD organizations conducting research involving prisoners must demonstrate to the senior designated official that the IRB has fulfilled its duties in accordance with Subpart C.
- When a previously enrolled human participant becomes a prisoner, and the protocol has not been reviewed and approved by the IRB in accordance with Subpart C, the key researcher must promptly notify the IRB.
  - For DOD-conducted research, the human protections director must notify the component office of human research protections.
  - For DOD-supported research, the non-DOD organization must notify the DOD human research protection official and other federal agencies.
  - The DODHRPP must concur with the IRB before the participant can continue to participate while a prisoner.
- DOD organizations must demonstrate to the senior designated official that the IRB has fulfilled its duties in accordance with DHHS Subpart D, 45 CFR 46. 407 and 21 CFR 50.54.

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U.S. Department of Defense Research, Continued

Vulnerable subject protection (con't.)

Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C, and D, except where modified by DODI 3216.02 (continued).

- Research involving a detainee or a prisoner of war as a human participant is prohibited.
  - This prohibition does not apply to activities covered by investigational new drug or investigational device provisions of FDA regulations, when the purpose is for diagnosis or treatment of a medical condition in a patient.
  - Such treatment may be offered to detainees or prisoners of war with their informed consent when the medical products are subject to FDA regulations, and only when the same product may be available to DOD-affiliated personnel consistent with established medical practices.
- The IRB is aware of the definition of "prisoner of war" for the DOD component granting the addendum.
- If the research involves DOD-affiliated personnel, the key researcher must receive command or Component approval to execute the research.
- Service members and all Reserve Component and National Guard members in a federal duty status are considered to be adults. If a Service member, Reserve Component or National Guard member in federal duty status, student at a Service Academy, or trainee is under 18 years of age, the IRB must carefully consider the HSR recruitment process and the necessity of including such member as a human participant.
- Research involving large-scale genomic data from DOD-affiliated personal requires additional protections:
  - The disclosure of DOD-affiliated personnel's genomic data may pose a risk to national security; accordingly, written materials must describe administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of de-identified data or specimens.
  - All research involving large-scale genomic data collected from DOD-affiliated personnel must have a certificate of confidentiality.
  - Research involving large-scale genomic data collected from DOD-affiliated personnel is subject to DOD Component security review to ensure the adequacy of the proposed administrative, technical, and physical safeguards, including the secondary use or sharing of de-identified data or specimens.

Surveys and questionnaires

Surveys and/or questionnaires performed on DOD personnel must be submitted, reviewed, and approved by the DOD after the research protocol is reviewed and approved by the IRB. When a survey crosses DOD Components, additional review is required. The PI is responsible for submitting these to the DOD for review and approval.

If there are any changes to the surveys and/or questionnaires required by the DOD, the PI is required to submit these surveys and/or questionnaires with the changes to the IRB for review and approval prior to implementing them.

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U.S. Department of Defense Research, Continued

Compensation for research participation	When research involves U.S. military personnel, limitations on dual compensation: • Prohibit an individual from receiving pay or compensation for research during duty hours • U.S. military personnel may be compensated for research if the participant is involved in the research when not on duty • Federal employees while on duty and non-federal persons may be compensated for blood draws for research up to $50 for each blood draw • Non-federal persons may be compensated for research participation other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research
Confidentiality agreement	Data or information acquired by the DOD Component under a pledge of confidentiality for exclusively statistical purposes must be used exclusively for statistical purposes and may not be disclosed in identifiable form for any other purpose, except with the informed consent of the respondent.
Research related injury	For compensation for research-related injury and disclosure to research participants in the informed consent process, the DOD component may have stricter requirements than the Common Rule requirements. The PI will consult with DOD program officials to inform the IRB of applicable differences through the submission of the research protocol. The IRB may rely on consultant reviewer(s) to ensure that the appropriate provisions for research-related injury are included in the consent document and follow all DOD component requirements.
DOD Definition: **Minimum risk**	The definition of minimal risk based on the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests" shall not be interpreted to include the inherent risks certain categories of human participants face in their everyday lives. For example, the risks imposed in research involving human participants focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain.)

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U.S. Department of Defense Research, Continued

Data and safety monitoring

Greater than minimal risk research - A research monitor is no longer required. Researchers may remove the requirement for a research monitor from existing open studies through a modification approved by an IRB.

Not greater than minimal risk research - While not required for research studies that impart no greater than minimal risk to subjects, a research monitor may be required to be appointed as part of the PI's data and safety monitoring plan if the IRB finds that it is appropriate.

Required elements of the monitor description - The research monitor, if required, must be:

- Independent of the research team; and
- Appointed by name as part of the PI's data and safety monitoring plan submitted to the IRB

The research monitor has the authority to:

- Stop a research study in progress
- Remove individuals from the study
- Take any steps to protect the safety and well-being of research participants until the IRB can assess the problem or concern

PI duties to report

For any DOD-supported researcher, the following shall be promptly (no longer than within 30 days) reported to the DOD human research protection officer:

- When significant changes to the research protocol are approved by the IRB
- Decreased benefit or increased risk to participants in greater than minimal risk research
- Addition of vulnerable populations as participants
- Addition of DOD-affiliated personnel as participants
- The results of the IRB continuing review
- Change of reviewing IRB
- When a previously enrolled human participant becomes pregnant, or when the researcher learns that a previously enrolled human participant is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with Subpart B
- When a previously enrolled human participant becomes incarcerated, or when the researcher learns that a previously enrolled human participant is incarcerated, and the protocol was not reviewed and approved by the IRB in accordance with Subpart C
- A DOD-supported study's closure
- When BCM is notified by any federal department, agency, or national organization that any part of an HRPP is under investigation for cause involving a DOD-supported research protocol

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U.S. Department of Defense Research, Continued

Reporting serious or continuing non-compliance	The IRB will use the same procedures for reporting to DOD as described in Chain of Reporting unless program officials of DOD provide differing requirements. Substantiated allegations related to classified HSR must be reported immediately to the DODHRP. The following must be reported to the DODHRPP within five days of completion of the report: • Any unanticipated problems involving risks to participants or others for any DOD-supported research must be reported to the DOD Office for Human Research Protections. • Results of for-cause audits, reviews, or assessments • Allegations of serious or continuing non-compliance related to HSR that are substantiated by investigation and subsequent actions taken based on the findings • Any suspension or termination of DOD-supported research must be reported to the DOD Office for Human Research Protections
Archiving research records	Submitting IRB records to the DOD for archiving may be required. The program officials of the DOD will inform the PI and the IRB of any special DOD regulations or requirements for archiving IRB records at the time of initial review.
Related standard	AAHRPP I.1.A, I.1.E, I-2, I-3, I.5.D, II.2.E.1-3, II.2.G-I, II.3.A-C, II.3.E-G, II.4.A-C, II.5A, III.1.E

Section B
IRB Review of Research Involving Children

Overview

Introduction

Date of Last Revision/Review: 01/13/21

This section provides the special requirements for research involving children.

Regulations involved

DHHS regulations at 45 CFR Part 46, Subpart D and FDA Regulations at 21 CFR 50 Subpart D require special protections for research involving children.

Note: If a subject is a member of more than one vulnerable population covered by Subparts B, C, and D all the protections given in each applicable subpart would apply to that individual subject.

Definition: children

Investigators must be aware of the jurisdiction in which the research is being conducted. The DHHS and FDA definitions of children, as persons who have not attained the legal age for consent to treatments or procedures involved in research/clinical investigations, apply to the following individuals for research conducted in Texas.

Children are persons under 18 years of age who:

- Are not married;
- Have not been married; and
- Have not had the disability of minor removed by a court of law

Reference: Texas Family Code, Title 5, Subtitle A, Chapter 101.003

Contact the IRB office for assistance when research is to be conducted outside of Texas.

Important issues

There are several important issues for the IRB to consider when reviewing research involving children, particularly including:

- The risk-benefit analysis to determine permitted regulatory categories
- Assent of the child
- Permission of one or both parents, depending upon the level of risk

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IRB Review of Research Involving Children, Continued

VA research	VA research involving children as subjects cannot be approved unless: • The VA medical facility Director approves participation in the proposed research that includes children • The study: • Presents no greater than minimal risk • Meets all requirements of Subpart D of the DHHS or FDA regulations • The Medical Center Director certifies that the facility is able to respond to pediatric emergencies • If the sponsor of the research is not VA, the facility Director makes certain that the sponsor of the research has procured appropriate liability insurance • Biological specimens and data obtained from children is considered research involving children even if de-identified. If the biological specimens or data were previously collected, they must have been collected under applicable federal policies and ethical guidelines.
In this section	This section covers the following topics: • Risk-Benefit Analysis and Permitted Categories • Assent of the Child • Documentation of Assent • Parental Permission • Wards • Children in U.S. Department of Education Research
Related standards	AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Risk-Benefit Analysis and Permitted Categories

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides a summary of risk-based analysis and the categories based on the risk level.

Responsibility

The IRB has these responsibilities:

- Making the specific findings and determinations required under federal regulations when reviewing research involving children.
- Finding and documenting that the proposed research falls within one of the four categories, based in part on its risk-benefit analysis

Reference: See "Categories" below.

Documentation

IRB records or the minutes of the IRB meeting will reflect:

- The IRB's understanding and justification for the risks and benefits posed by approved research involving children
- The required findings based on category, including *protocol-specific* information justifying each IRB finding

Reference: *OHRP Compliance Activities: Common Findings and Guidance,* 07/10/2002, Item 69

Approval requirement

Each category stipulates specific criteria that must be found and documented by the IRB to have been satisfied before the proposed research can be approved.

Categories

This table lists the categories and the specific requirements for each:

Reference: 45 CFR 46 404-407

No.	Category	Requirements
1	Research not involving greater than minimal risk 45 CFR 46.404	Assent of the child if appropriate and permission of both parents unless the IRB finds that the permission of one parent is sufficient See Assent of the Child
2	Research: • Involving greater than minimal risk • Presenting the prospect of direct benefit to the individual subjects 45 CFR 46.405	• Assent of the child if appropriate and permission of both parents unless the IRB finds that the permission of one parent is sufficient • Anticipated benefit justifies the risk • Anticipated benefit is at least as favorable as that of alternative approaches See Assent of the Child

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Risk-Benefit Analysis and Permitted Categories, Continued

Categories (cont) This table lists the categories and the specific requirements for each (continued):

No.	Category	Requirements
3	Research involving greater than minimal risk: • No prospect of direct benefit to individual subjects • Likely to yield generalizable knowledge about the subject's disorder or condition	• Assent of the child and permission of both parents, when reasonably available (unless only one parent has legal responsibility for the care and custody of the child) • Only a minor increase over minimal risk • Likely to yield generalizable knowledge about the child's disorder or condition that is of vital importance for the understanding or amelioration of the disorder or condition • Experiences to the child that are reasonably commensurate with those in the child's actual or expected medical, dental, psychological, social, or educational situations resulting from the intervention or procedure
4	Research: • Not otherwise approvable • Presenting an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children	• Assent of child if appropriate and permission of both parents, when reasonably available (unless only one parent has legal responsibility for the care and custody of the child) • An IRB finding that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children • Approval from the DHHS Secretary or the FDA Commissioner after consultation with a panel of experts in pertinent disciplines and following public comment ***Example disciplines***: Science, medicine, education, ethics, law See Assent of the Child

Related standards AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Assent of the Child

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides the requirements involved with the assent of the child.

Requirement

Ultimately, the responsibility for determining assent requirements rests with the IRB, not with the research investigator.

IRB review

The IRB must determine the following concerning the assent of child-subjects:

- When children are capable of providing assent, taking into account the ages, maturity, and psychological state of the children involved
- That adequate provisions are made for soliciting the assent of the children when the children are capable of providing assent in the judgment of the IRB
- That the assent of the children is not necessary when the IRB determines:
  - The capability of the children to be so limited that they cannot reasonably be consulted
  - The research holds out the prospect of direct benefit that is only available in the context of the research
- Whether assent can be waived (see "Waiver of assent" below)
- Whether and how assent must be documented

References: HHS regulations at 45 CFR 46.408(a) and FDA regulations at 21 CFR 50.55

Waiver of assent

The IRB may waive assent when ALL of these conditions exist:

- The research involves no more than minimal risk to subjects.
- The waiver will not adversely affect subjects' rights and welfare.
- The research could not practicably be carried out without the waiver.
- Where appropriate, subjects will be provided with pertinent information after participation.
  Example: In social and behavioral research where mild deception is involved

IRB requirement

In accordance with these requirements, the IRB requires that the assent of the child-subject will be obtained unless the IRB specifically determines that one of the following exists:

- The child-subject lacks the capacity for assent.
- The research offers an important direct benefit that cannot be obtained outside the research.
- The assent requirement can be formally waived.

Documentation: Such determinations must be documented in a protocol-specific fashion in IRB meeting minutes or other IRB documents.

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Assent of the Child, Continued

Information to be provided	**Amount and complexity** Where assent is to be obtained, the amount and complexity of the information provided to the child depends upon the child's level of cognitive and emotional maturation. **Wide age range** When subjects include a wide age range, it may be necessary for the IRB to require that different information be given to different age groups.
Additional written guidance	At its discretion, the IRB may develop additional written guidance to assist investigators in proposing appropriate methods of obtaining and documenting assent for subjects of different ages or levels of maturation.
Related standards	AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Documentation of Assent

Introduction

Date of Last Revision/Review: 10/01/20

This topic provides the requirements for the documentation of assent for a child.

Two ways

When obtained, assent can be documented in one of two ways:

- The subject can sign on an age-appropriate consent form in addition to the signed permission on an adult consent form.
- A paragraph can be added to a regular adult consent form

For electronic methods, see Documentation and Completion of Documentation.

Paragraph for adult form

The following paragraph can appear on a regular adult consent form:

> If your child is the one asked to take part in this study, you are signing to give your permission. Each child may agree to take part in a study at his or her own level of understanding. When you sign this, you also note that your child understands and agrees to take part in this study according to his or her understanding.
>
> Child's name here _____

Important: The child is not required to sign a form if assent is documented using the paragraph above in an adult consent form.

Related standards

AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Parental Permission

Introduction

Date of Last Revision/Review: 10/01/20

This topic provides the requirements for parental permission when a child is involved with the research.

IRB determination

The IRB determines that adequate provisions have been made for obtaining and documenting parental permission for the participation of children in research.

Reference: In accordance with DHHS and FDA requirements

Waiver of parental permission

The IRB may waive the requirements for obtaining parental or guardian permission if it makes and documents the findings for waiver of informed consent for research not subject to FDA regulations:

- Research on public benefit programs. See State or Local Public Benefit Programs
- Minimal risk research, see Waiver or Alteration of Consent for Minimal Risk Research; or
- Research designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the parental permission requirements provided that an appropriate mechanism is in place to protect the children, and provided that the waiver is not inconsistent with federal, state, or local law.

  The choice of an appropriate substitute mechanism (for example, appointing a child advocate or an assent monitor) for protecting children participating in research would depend on the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and the child's age, maturity, status, and condition.

One parent only

Where parental permission is to be obtained, in general the permission of both parents for their child's participation should be sought, however, the IRB may find that the permission of one parent is sufficient for:

- Research not involving greater than minimal risk
- Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects

***Exceptions*:**

- When one parent is deceased, unknown, incompetent, or not reasonably available
- When only one parent has legal responsibility for the care and custody of the child

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Parental Permission, Continued

Both parents	Where permission is to be obtained, both parents must give their permission for 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; or • Not otherwise approvable (very rare, and involves DHHS determination) which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. Documentation: The person obtaining consent documents the reason for the absence of a second parent on the second signature line of the permission form.
Guardians and legally authorized representatives	In the absence of the child's parents, permission for the involvement of the child in research may be obtained from the child's legal guardian(s) or others to the extent authorized under the laws of the State of Texas (or other State in which the research takes place). This is a person who meets the DHHS/FDA definition of "guardian" at 21 CFR 50.3(s), and 45 CFR 46.402(e). See Frequently Used Terms G – Guardian
Documentation	See Documentation and Completion of Documentation.
Related standards	AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.3.G, II.4.A, II.4.B, 45 CFR 46.408(c); 45 CFR 46.408(c), 45 CFR 46.404; 45 CFR 46.405; 45 CFR 46.406.

Wards

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides the requirements for additional protections when a child who is a ward is involved with the research.

IRB determination

The IRB determines that adequate provisions have been made for obtaining and documenting appropriate permission and child advocacy (as appropriate) for the participation of children in research.

Reference: In accordance with DHHS and FDA requirements

Guardians and legally authorized representatives

In the absence of the child's parents, permission for the involvement of the child in research may be obtained from the child's legal guardian(s) or others to the extent authorized under the laws of the State of Texas (or other State in which the research takes place).

Additional protections

This table describes additional protections for wards:

When the IRB finds that the research:	Then the IRB requires:
Is more than minimal risk, AND Holds no prospect of benefit to the child	The appointment of an advocate ***Definition***: An advocate is an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization ***Reference***: 45 CFR 46.409

Related standards

AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Children in U.S. Department of Education Research

Date of Last Revision/Review: 04/20/11

Introduction

This topic provides the requirements for additional protections when children are involved in educational research that is regulated by the U.S. Department of Education.

Department of Education regulated

The following are the indicators that BCM investigators are conducting research that is subject to the Department of Education regulations:

- Research that is funded in part or in full by the Department of Education, including subcontract awards, or,
- BCM research protocol for which any portion of the research is conducted in any educational setting when that institution's employees or agents are engaged in the human subjects research

Definitions

This table provides the relevant definitions for research that is funded by the U.S. Department of Education:

Term	Definition
Research or experimentation program or project	Any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.
Children	Persons enrolled in research not above the elementary or secondary education level, who have not reached the age of majority as determined under state law. ***Note*:** The age of majority is 18 years in the State of Texas.
Educational setting	An educational setting is an institution or school that is a commonly accepted and legally compulsory place designed for the teaching of students under the supervision of instructors or teachers.
Prior consent	Prior consent means: • Prior consent of the student, if the student is an adult or emancipated minor • Prior written consent of the parent or guardian, if the student is an unemancipated minor. ***Note*:** The term "emancipated minor" does not appear in the laws of the State of Texas. See Frequently Used Terms C – Child for a description of the equivalent terminology.

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Children in U.S. Department of Education Research, Continued

Additional protocol requirements

When investigators conduct research or experimental programs or projects funded by the U.S. Department of Education in educational settings access to all the instructional materials including:

- Teacher's manuals
- Films
- Tapes
- Or other supplementary instructional materials

must be made available for inspection by the parents or guardians of the children engaged in such research.

When BCM investigators conduct DOE-regulated research, the PI must provide to the IRB an assurance that includes a process to verify that the school and the investigators will comply with all U.S. Department of Education regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:

- The right of a parent of a student to inspect, upon the request of the parent:
  – A survey created by a third party before the survey is administered or distributed by a school to a student
  – Any instrument used in the collection of personal information before the instrument is administered or distributed to a student
- Any applicable procedures for granting a request by a parent for reasonable access to:
  – Such survey within a reasonable period of time after the request is received
  – Such instrument within a reasonable period of time after the request is received
  – Instructional material received
- The administration of physical examinations or screenings that the school or agency may administer to a student
- The collection, disclosure, or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure, or use

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Children in U.S. Department of Education Research, Continued

Additional protocol requirements (continued)

- Arrangements to protect student privacy that are provided by the agency in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items):
  - Political affiliations or beliefs of the student or the student's parent
  - Mental or psychological problems of the student or the student's family
  - Sex behavior or attitudes
  - Illegal, anti-social, self-incriminating, or demeaning behavior
  - Critical appraisals of other individuals with whom respondents have close family relationships
  - Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers
  - Religious practices, affiliations, or beliefs of the student or the student's parent
  - Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program).

***Note*:** Provisions for these procedures should be described in detail by the PI in the protocol submission materials.

IRB review

The IRB reviews for and determines that adequate provisions have been made in the research protocol for providing access to all instructional materials to the parents or guardians of children engaged in this type of research. ***Reference*:** 34 CFR 98.3

For research funded by the National Institute on Disability and Rehabilitation Research (Department of Education regulated) that purposefully requires inclusion of children with disabilities or individuals with impaired decision-making capacity as research participants, the IRB must include in its review at least one person primarily concerned with the welfare of these research participants.

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Children in U.S. Department of Education Research, Continued

Waiver of parental/student consent

The IRB review will serve as the appropriate process for compliance with the Family Educational Rights and Privacy Act (FERPA) in granting exceptions to parental/student consent for DOE-regulated research.

Under FERPA, an educational agency or institution may disclose personally identifiable information from an education record of a student without consent if the disclosure is to organizations conducting studies for, or on behalf of, educational agencies or institutions to:

- Develop, validate, or administer predictive tests
- Administer student aid programs, or,
- Improve instruction

A school district or postsecondary institution that uses this exception is required to enter into a written agreement with the Principal Investigator (PI) conducting the research that specifies:

- The determination of the exception of obtaining parental/student consent
- The purpose, scope, and duration of the research study
- The specific information from the educational records of the students to be disclosed as part of the research study
- That the information from education records may only be used to meet the purposes of the study stated in the written agreement and must contain the current requirements in Department of Education regulations on redisclosure and destruction of information
- That the research study will be conducted in a manner that does not permit personal identification of parents and students by anyone other than representatives of the College with legitimate interests
- That the PI is required to destroy or return all personally identifiable information when no longer needed for the purposes of the research study
- The time period during which the PI must either destroy or return the information

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Children in U.S. Department of Education Research, Continued

Specific information from educational records	Education records of students may be released without consent for research under FERPA if all personally identifiable information has been removed including: • Student's name and other direct personal identifiers, such as the student's social security number or student number • Indirect identifiers, such as the name of the student's parent or other family members; the student's or family's address, and personal characteristics or other information that would make the student's identity easily traceable; and date and place of birth and mother's maiden name • Biometric records, including one or more measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting • Other information that, alone or in combination, is linked or linkable to a specific student that would allow a reasonable person in the school community, who does not have personal knowledge of the relevant circumstances, to identify the student with reasonable certainty
Consent of subjects who cannot give consent or whose decision-making capacity is in question	The IRB review will serve as the appropriate process for assurance of compliance with the Protection of Pupil Rights Amendment for DOE-regulated. For research projects directly funded by the U.S. Department of Education special requirements must be made for research involving the recruitment of children who cannot give consent or whose decision-making capacity is in question. No student will be required, as part of any research project, to submit without prior consent to surveys, psychiatric examination, testing, or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following: • Political affiliations or beliefs of the student or the student's parent • Mental or psychological problems of the student or the student's family • Sex behavior or attitudes • Illegal, anti-social, self-incriminating, or demeaning behavior • Critical appraisals of other individuals with whom respondents have close family relationships • Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers • Religious practices, affiliations, or beliefs of the student or student's parent • Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program
Related standard	AAHRPP II.1.E, II.3.G, II.4.B, III.2.C

Section C
IRB Review of Research Involving Adults as Vulnerable Subjects

Overview

Introduction

Date of Last Revision/Review: 11/18/19

This section focuses on the special requirements when involving adults as vulnerable subjects in research.

Requirement

An IRB must give special consideration to protecting the welfare of other particularly vulnerable subjects.

Examples: Prisoners, persons with impaired decision-making capacity, or economically or educationally disadvantaged persons

References:

- DHHS regulations at 45 CFR 46.111(b)
- FDA regulation at 21 CFR 56.111(b)
- The Common Rule

Note: If a subject is a member of more than one vulnerable population covered by Subparts B and C, all the protections given in each subpart would apply to that individual subject. (For example, a woman who is pregnant and incarcerated is afforded the protections to pregnant women and to prisoners.)

In this section

This section covers the following topics:

- Special Considerations for Vulnerable Subjects
- Research Involving Pregnant Women, Human Fetuses, and Neonates
- Research Involving Prisoners
- Research Involving Potentially Addictive Substances
- Research Involving Other Potentially Vulnerable Adult Subjects
- Research Involving Human Fetal Tissue Transplantation and Deceased Persons

Related standards

AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Special Considerations for Vulnerable Subjects

Introduction

Date of Last Revision/Review: 04/06/15

The IRB makes every effort to obtain the expertise needed to consider specific kinds of research involving vulnerable populations in a satisfactory manner.

When the IRB reviews research involving vulnerable subjects, the IRB will include among its reviewers persons who are knowledgeable about and experienced in working with these vulnerable subjects.

Requirement

The IRB pays special attention to specific elements of the research plan when reviewing research involving vulnerable subjects.

Considerations

This table lists some considerations for the IRB review:

Consideration	Description
Critical issues	Critical issues include: • Inclusion and exclusion criteria for selecting and recruiting participants • Informed consent and voluntarism • Coercion and undue influence • Confidentiality of data
Group characteristics	The IRB carefully considers group characteristics. ***Examples***: Economic, social, physical, and environmental conditions so that the research incorporates additional safeguards for vulnerable subjects
Subject selection	Investigators are not generally permitted to over-select or exclude certain groups based on perceived limitations or complexities associated with those groups. ***Example***: It is not appropriate to target prisoners as research subjects merely because they are a readily available “captive" population.
Applicable laws and science	As it determines necessary, the IRB seeks to obtain information regarding laws and science that bear on decision-making capacity of the potentially vulnerable populations to be involved in the research.

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Special Considerations for Vulnerable Subjects, Continued

Considerations (continued)

This table lists some considerations for the IRB review (continued):

Considerations	Description
Adequate procedures for assessing subjects' capacity	Just as in providing medical care, research studies that involve potentially vulnerable populations must have adequate procedures in place for assessing subjects' capacity, understanding, and informed consent or assent. When weighing the decision whether to approve or disapprove research involving vulnerable subjects, the IRB looks to see that such procedures are a part of the research plan. • The investigator must explain the proposed research to the prospective participant when feasible even when the participant's legally authorized representative gives consent • Research participants being forced or coerced to participate in a research study is strictly prohibited • When following U.S. Department of Education regulations and guidance, other requirements for the consent of persons who cannot give consent or whose decision-making capacity is in question must be followed • See Children in U.S. Department of Education Research Special additional requirements for VA Research The VA has special requirements for assessing and documenting a subject's capacity to give informed consent before a legally authorized representative may give consent on the subject's behalf as follows: • A legal determination has been made that the subject is incompetent or has an impaired decision-making capacity • The practitioner, in consultation with the chief of service, has determined after appropriate medical evaluation that the prospective research subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time • Consultation with a psychiatrist or licensed psychologist must be obtained when the determination that the prospective research subject lacks decision-making capacity is based on a diagnosis of mental illness • These findings must be documented in the subject's research file • The practitioner should explain the proposed research to the prospective participant when feasible

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Special Considerations for Vulnerable Subjects, Continued

Considerations (continued)

This table lists some considerations for the IRB review (continued):

Considerations	Description
Enhancement of understanding	In certain instances, it may be possible for researchers to enhance understanding for potentially vulnerable subjects. ***Examples***: The following may be included: • A consent monitor • A subject advocate • An interpreter for hearing-impaired subjects • A translation of informed consent forms into languages the subjects understand • Reading the consent form to subjects slowly to gauge their understanding paragraph by paragraph
Additional safeguards	The IRB may require additional safeguards to protect potentially vulnerable populations. ***Examples***: The IRB may require the following: • The investigator must submit each signed informed consent form to the IRB. • Someone from the IRB must oversee the consent process. • A waiting period must be established between initial contact and enrollment to allow time for family discussion and questions.

Related standards

AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Research Involving Pregnant Women, Human Fetuses, and Neonates

Introduction

Date of Last Revision/Review: 01/13/21

This topic covers research involving the pregnant women, human fetuses, and neonates.

***Note*:** Pregnant women even though not considered vulnerable subjects require additional protections.

Special protections

Research involving pregnant women, human fetuses, and neonates require special protections.

- The IRB is required to document specific findings to minimize the potential for risk or harm to the fetus.
- Additional attention must be given to the conditions for obtaining informed consent.
- Research involving pregnant women and fetuses should involve the least possible risk.
- Unilateral exclusion of non-pregnant women of reproductive potential from research, in order to avoid a risk will not be permitted
  Reason: Exclusion requires compelling scientific justification. Where such justification exists, it may also be appropriate to exclude men of reproductive potential.

Reference: DHHS regulations at 45 CFR Part 46, Subpart B

Continued on next page

Research Involving Pregnant Women, Human Fetuses, and Neonates, Continued

VA research

- Research involving human fetal tissue and stem cells shall be governed by the policy set by NIH for recipients of NIH research funding.
- Research involving the provision of in vitro fertilization services can be conducted by VA researchers while on official duty, or at VA facilities, or at VA-approved off-site facilities. This includes prospective and retrospective research involving provision of or the enhancement of FDA-approved methods of in vitro fertilization for studies involving consenting participants, both male and female, undergoing or who have undergone in vitro fertilization for the treatment of certain forms of human infertility. In vitro fertilization is any fertilization of human ova that occurs outside the body of a female, either through a mixture of donor human sperm and ova or by any other means.
- Prospective and retrospective studies that enroll or include pregnant participants who conceived through in vitro fertilization or other artificial reproductive technologies are permitted.
- Research in which the focus is either a fetus, either in-utero or ex-utero, cannot be conducted by VA researchers while on official VA duty, at VA facilities, or at VA-approved off-site facilities (VA 1200.05 amended 3/30/20 Section 19C, p. 37).
- Research involving the creation of a human embryo or embryos solely for research purposes or research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.208(a)(2) and Section 498B of the Public Health Service Act (42 U.S.C. 289g(b)) cannot be conducted by VA researchers, at VA facilities, or at VA approved off-site facilities.
- Research in which the focus is either fetus, human fetal tissue, in-utero, or ex-utero, cannot be conducted by VA researchers while on official duty, or at VA facilities, or at VA-approved off-site facilities (VA 1200.05 amended 3/30/20 Section 19C, p. 37).
- VA investigators cannot conduct interventions in research that include neonates while on official VA duty, at VA facilities, or at VA-approved off-site facilities. VA researchers may conduct research involving noninvasive monitoring of neonates if the research is determined by the IRB to be minimal risk. Prospective, observational, and retrospective record review studies that involve neonates or neonatal outcomes are permitted. The reviewing IRB must have the appropriate expertise to evaluate any VA research involving neonates and must comply with the requirements of 45 CFR 46.205. The VA medical facility Director must certify that the medical facility has sufficient expertise in neonatal health to conduct the proposed research.

Categories

The regulations set out specific categories, each with their own requirements and IRB determinations, for research involving pregnant women, human fetuses and neonates. The table below summarizes these requirements.

Continued on next page

Research Involving Pregnant Women, Human Fetuses, and Neonates, Continued

Summary of requirements

This table provides a summary of requirements involving pregnant women, fetuses, and neonates:

Regulatory Category	Requirements
Pregnant women or fetuses	• Where appropriate, preclinical data identifying potential risks • Direct benefit for pregnant woman or fetus or risk to fetus not greater than minimal • Any risk least possible for achieving research objectives • Consenting persons having been fully informed • Consent of pregnant woman if direct benefit to her or risk to fetus not greater than minimal • Consent of pregnant woman and father if research offers direct benefit solely to fetus. ***Exception*:** The father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, temporary incapacity, or the pregnancy resulted from rape or incest. • For pregnant children, assent and permission per Subpart D • No inducements to terminate a pregnancy • Researchers having no part in: – Decisions to terminate pregnancy – Determining viability
Neonates of uncertain viability	• Where appropriate, preclinical data identifying potential risks • Consenting persons having been fully informed • Researchers having no part in determining viability • Enhanced probability of survival with: – Risk least possible or no added risk to neonate – Important medical knowledge as a result • Informed consent of one parent or legally authorized representative
Nonviable neonates	• Where appropriate, preclinical data identifying potential risks • Consenting persons having been fully informed • Researchers have no part in determining viability • Vital functions not artificially maintained • No termination of heartbeat or respiration • No added risk to neonate • Important medical knowledge as a result • Informed consent of both parents, unless one unable • No legally authorized representatives See definition of nonviable fetus.

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Research Involving Pregnant Women, Human Fetuses, and Neonates, Continued

Summary of requirements (continued)

This table provides a summary of requirements involving pregnant women, fetuses, and neonates (continued):

Regulatory Category	Requirements
Viable neonates	Subject to DHHS Subpart D for research involving children. See definition of viable infant.
Placenta, dead fetus, fetal material	Subject to applicable Federal, State, or local law
Not otherwise approvable	• IRB findings of reasonable opportunity to advance health or welfare • Approval of HHS Secretary after expert and public consultation

Documentation

IRB determinations regarding the applicable category and protocol-specific findings relative to the specific requirements of the relevant category must be clearly documented in IRB meeting minutes or other IRB records.

Related standards

AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Research Involving Prisoners

Introduction

Date of Last Revision/Review: 03/04/15

This topic provides the special requirements for prisoners involved with research.

Reason for special protections

Special protections are required for research involving prisoners, who, due to their incarceration, may have a limited ability to make truly voluntary and uncoerced decisions about whether or not to participate as subjects in research.

Reference: DHHS regulations at 45 CFR Part 46, Subpart C

VA research

For VA research, prisoners as subjects cannot be approved unless a waiver has been granted by the Chief Research and Development Officer.

Definition: Prisoner

A *prisoner* is defined as any individual involuntarily confined or detained in a penal institution, including persons:

- Sentenced under a criminal or civil statute,
- Detained pending arraignment, trial, or sentencing,
- Detained in other facilities under statutes or commitment procedures providing such alternatives to criminal prosecution,
  ***Example*:** For drug detoxification or treatment of alcoholism
- Incarcerated in a penal institution 45 CFR 46.303(c).

Department of Defense regulated research

For Department of Defense regulated research, involving prisoners of war is prohibited.

See U.S. Department of Defense Research for more information.

IRB review

To consider research involving prisoners, the IRB must:

- Have a majority of its members not otherwise associated with the prison
- Include a prisoner or a prisoner advocate, who can adequately represent the interests of the prisoners, unless the research has already been reviewed by an IRB that included a prisoner advocate.

Continued on next page

Research Involving Prisoners, Continued

Funding-based review

This table provides the requirements as part of the IRB review based on the funding of the research:

When the research …	Then …
Is DHHS-supported	• The IRB must certify its findings and forward them to OHRP for concurrence on behalf of the Secretary of DHHS • Following receipt of the research proposal, OHRP determines which, if any, of the four categories of research permissible under HHS regulations at 45 CFR 306(a)(2) the proposed research meets • OHRP consults with appropriate experts with respect to certain research that falls under paragraphs (iii) and (iv) of 45 CFR 46.306(a)(2) • When applicable, OHRP also publishes in the Federal Register a notice of intent to approve such research • ***Note***: HHS conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its approval in writing to the institution on behalf of the Secretary under 45 CFR 46.306(a)(2)
Is not supported by DHHS	Certification to OHRP is not required.
• Is not DHHS-supported research • Falls outside the category stipulations under 45 CFR 46.306	The IRB consults with appropriate experts before approving the research.
Is being conducted with prisoners, regardless of its source of funding or support	The IRB applies the standards of Subpart C to all prisoner research.

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Research Involving Prisoners, Continued

Categories

This list summarizes the requirements for research involving prisoners:

Category	Description
A	Studies of the possible causes, effects, and processes of incarceration and criminal behavior, involving no more than minimal risk or inconvenience
B	Studies of prisons as institutional structures or of prisoners as incarcerated persons, involving no more than minimal risk or inconvenience
C	Research on particular conditions affecting prisoners as a class ***Requirement***: The Secretary of DHHS has consulted with appropriate experts and published the intent to support such research in the Federal Register.
D	Research that has reasonable probability of benefiting the prisoner subject ***Control group requirement***: When the research involves a control group that may not benefit from the research, the DHHS must approve/disapprove after consulting experts.

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Research Involving Prisoners, Continued

Required findings

This table provides the additional required findings, regardless of category:

Finding	Description
Advantages not influential	Any possible advantages to the prisoner are not of such a magnitude that the ability to weigh risks in the limited choice environment of the prison is impaired. ***Examples***: Living conditions, medical care, quality of food, amenities, and opportunity for earnings
Risks	Risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers.
Subject selection	• Procedures for selecting subjects are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. • Control subjects are selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project. ***Exception***: The investigator may, in writing to the IRB, provide justification for following some other procedures.
Language	Information is presented in language that is understandable to the subject population.
Parole status	• Each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole. • Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole.
Follow-up examination or care	Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for: • Such examination or care, taking into account the varying lengths of individual prisoner's sentence • Informing participants of this fact

Related standards

AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Research Involving Potentially Addictive Substances

Introduction

Date of Last Revision/Review: 04/20/11

This topic provides the requirements for research that involves potentially addictive substances.

Requirement

It is essential that the IRB conduct an extremely thorough and thoughtful analysis of the risks and benefits associated with any such research proposed at the College.

Risks

Research involving potentially addictive, abuse-liable substances presents particular risks for subjects. These pharmacological substances, which may include legal as well as illegal drugs, have the potential for creating abusive dependency.

IRB review

The IRB considers the following issues when reviewing research involving potentially addictive substances:

Issue	Description: The IRB …
Children as subjects	Does not approve the participation of children as subjects in research involving potentially addictive substances unless: • The use of the relevant addictive substance(s) is dictated solely by the clinical needs of the individual child-subject. • The usual standard of care for treatment of the child's disorder or condition.
Adults as subjects	Does not approve the participation of adults as subjects in research involving potentially addictive substances unless appropriate protections are provided to ensure that subjects will be: • Competent • Uncoerced • Able to exercise continuous informed consent throughout the course of the research
Selection of subjects	Considers carefully the requirements for: • Equitable recruitment and selection of subjects • Protections for maintaining privacy and confidentiality • The need for data and safety monitoring
Ethical context of the research	Is sensitive to the ethical context of the research ***Examples***: The use of placebo controls, the special vulnerabilities of current of former addicts

Related standards

AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Research Involving Other Potentially Vulnerable Adult Subjects

Introduction

Date of Last Revision/Review: 01/28/19

This topic provides the special requirements for other potentially vulnerable adult subjects, including decisionally impaired and economically disadvantaged persons.

Definition: decisionally impaired person

A *decisionally impaired person* is an individual who has a diminished capacity for judgment and reasoning due to a psychiatric, organic, developmental, or other disorder that affects cognitive or emotional functions.

Other impaired persons

Other persons who may be considered decisionally limited, with impaired decision-making capacity, are:

- Persons under the influence of or dependent on drugs or alcohol
- Those persons suffering from degenerative diseases affecting the brain
- Terminally ill patients

Other vulnerable persons

The IRB generally considers the following groups of subject to be potentially vulnerable and carefully considers the context of the research in determining appropriate protections for them if the IRB determines that it is acceptable for enrollment of these subjects:

- Members of potentially vulnerable minority groups
- Educationally disadvantaged persons
- Economically disadvantaged persons
- Homeless persons
- Institution's employees, students, and trainees

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Research Involving Other Potentially Vulnerable Adult Subjects, Continued

IRB review

The IRB considers the following issues when reviewing research involving cognitively impaired or potentially vulnerable persons:

When the research involves …	Then the IRB considers …
Cognitively impaired persons	• Additional safeguards as part of the research plan to protect subjects, the risks and benefits of the research, and the inclusion/exclusion criteria ***Examples***: • Justification for the identification of this population for inclusion into the research • Independent physician assessment regarding the appropriateness of the invitation of these subjects to participate in the research • Involvement of subject advocates • Independent monitoring • Formal capacity assessment • Waiting periods • Specifically trained interviewers and staff • The proposed plan for LAR permission and participant assent ***Note***: Assent of an adult participant unable to consent is required unless the IRB approves a waiver of assent. Mere failure to object should not, absent affirmative agreement, be construed as assent.

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Research Involving Other Potentially Vulnerable Adult Subjects, Continued

IRB review (continued)

The IRB considers the following issues when reviewing research involving cognitively impaired or potentially vulnerable persons (continued):

When the research involves …	Then the IRB considers …
VA research with decisionally-impaired subjects	Finding and documenting in the minutes or IRB records that: • Only incompetent persons or persons with impaired decision-making capacity are suitable as subjects • Competent persons are not suitable for the proposed research • The investigator has demonstrated to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects • Incompetent persons or persons with impaired decision-making capacity are not being proposed as subjects simply because they are readily available • The research does not impose a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm • Procedures have been devised to ensure that legally authorized representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision-making capacity • Legally authorized representatives will be told that their obligation is to try to determine what the prospective subject would do if competent, or if the prospective subject's wishes cannot be determined, what they think is in the incompetent person's best interest

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Research Involving Other Potentially Vulnerable Adult Subjects, Continued

IRB review (continued)

The IRB considers the following issues when reviewing research involving cognitively impaired or potentially vulnerable persons (continued):

When the research involves …	Then the IRB considers …
Other potentially vulnerable persons	The context of the research, the risks and benefits of the research, and the inclusion/exclusion criteria ***Reason***: Persons who are considered vulnerable in these categories are at risk for unique social, psychological, or medical harms. The inclusion of members of these subjects should be justified, and protections from their unique additional risks, should be considered. Research involving significant follow-up procedures or offering significant monetary compensation may unduly influence some types of subjects. ***Examples***: • Justification for the identification of this population for inclusion into the research • Independent physician assessment regarding the appropriateness of the invitation of these subjects to participate in the research • Involvement of subject advocates • Independent monitoring • Formal capacity assessment • Waiting periods • Mechanisms to protect the privacy of subjects who are at increased risk of harm due to their status ***Examples***: – Failing students – Employees undergoing disciplinary action – People seeking illiteracy training – Women making self-directing decisions in cultures which do not recognize that right – Surveys and interviews of groups targeted for hate crimes. • Specifically trained interviewers and staff

Related standards AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Research Involving Human Fetal Tissue Transplantation and Deceased Persons

Introduction	Date of Last Revision/Review: 04/20/11 This topic provides the special requirements for research involving human fetal tissue transplantation and deceased persons.
Human fetal tissue transplantation	Human fetal transplantation research supported by DHHS is governed by NIH Public Law 103-43.
Deceased persons	Research involving deceased persons is not covered by FDA or DHHS human subject regulations or the Common Rule. However, research involving decedent's personal health information may still be subject to Privacy Board review under HIPAA.
Related standards	AAHRPP I.1.D, I.1.G, II.3.A, II.3.C, II.4.A, II.4.B

Frequently Used Terms

Date of Last Revision/Review: 09/09/22

A B C D E F G H I J L M N O P R S T U V W

A

Term	Definition
Administrative hold	An administrative hold is a voluntary interruption of research enrollments and ongoing research activities by an appropriate facility official, research investigator, or sponsor and does not apply to interruptions of research related to concerns related to the safety, rights, or welfare of human research subject, research investigators, research staff, or others. An administrative hold must not be used to avoid reporting deficiencies or circumstances otherwise covered in federal regulations, VA policies, or other federal requirements governing research. An administrative hold is not the same as a suspension or termination of IRB approval.
Adverse event (AE)	An undesirable and unintended, although not necessarily unexpected, result arising during the course of a research protocol For VA Research: An adverse event (AE) is any untoward physical or psychological occurrence in a human subject participating in research. An AE can be an unfavorable and unintended event, including an abnormal laboratory finding, symptom, or disease associated with the research or the use of a medical investigational test article. An AE does not necessarily have to have a causal relationship with the research.
Adverse Event Report	Report to appropriate institutional officials about adverse events
Advertising	One mechanism or method used by researchers to recruit subjects for research studies
Agent	Any Baylor College of Medicine faculty or employee
Alternatives	Options that exist for a subject who is thinking about participating in research
Amendment	The College defines an amendment to be any change to an approved protocol regardless of how minor it is. Investigators must report to the IRB planned changes in the conduct of the study, since these may affect the protection of human subjects.
Assent	Agreement by an individual not competent to give legally valid informed consent to participate in research ***Example***: A child

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Frequently Used Terms, Continued

A (Continued)

Assurance	A formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with regulations governing the protection of human subjects in research *Assurance* is the word used in the Federal Policy (Common Rule).
Authorized Institutional Official	See Institutional Official
Autonomy	See Respect for Persons.

B

Term	Definition
Belmont Report	A statement of basic ethical principles governing research involving human subjects issued in 1978 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
Beneficence	An ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm The principle of beneficence can be expressed in two general rules: • Do not harm • Protect from harm by maximizing possible benefits and minimizing possible risks of harm
Benefit	A valued or desired outcome; an advantage

Continued on next page

Frequently Used Terms, Continued

C

Term	Definition
Certificate of Confidentiality (CoC)	A document that protects the compelled release of identifiable information about research subjects in any legal proceeding These documents are issued by the DHHS and can be requested for all research, regardless of funding source 42 USC 241 (d).
Certification	The official notification by the institution to the supporting Federal department or agency component, in accordance with the requirements of this policy, 45 CFR 46.102(a), that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.
Chair	The person who leads the activities of the IRB
Children	Investigators must be aware of the jurisdiction in which the research is being conducted. The DHHS and FDA definitions of children, as persons who have not attained the legal age for consent to treatments or procedures involved in research/clinical investigations, apply to the following individuals for research conducted in Texas. Children are persons under 18 years of age who: • Are not married; • Have not been married; and • Have not had the disability of minor removed by a court of law ***Reference***: Texas Family Code, Title 5, Subtitle A, Chapter 101.003 Contact the IRB office for assistance when research is to be conducted outside of Texas.
Clinical investigation	Any experiment that involves a test article and one or more human subjects that is subject to Food and Drug Administration (FDA) requirements for research or marketing permits 21 CFR Part 50.3(c) and 56.102(c)
Clinical trial	A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.
CoC	Certificate of Confidentiality
Coercion	The act of inducing or pressuring an individual to consent to participate in research or to stay in research
Cognitive impairment	Some disorder that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished
Common Rule	The short description of the Federal Policy for the Protection of Human Subjects in Research 56 FR 29003

Continued on next page

Frequently Used Terms, Continued

C (Continued)

Term	Definition
Compensation	Refers to payment or other benefits that will be given to subjects who volunteer to participate in research protocols
Competence	The capacity to act on one's own behalf The ability to understand information presented; to appreciate the consequences of acting or not acting on that information, and to make a choice
Confidentiality	Pertains to the treatment of information that an individual has disclosed in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure
Consent	Agreement to do something Informed consent is agreement to do something based upon a complete understanding of that task.
Continuing non-compliance	A pattern of non-compliance that has the potential to compromise human research protections. **For VA research:** Continuing non-compliance means repeated instances of non-compliance with applicable laws, regulations, policies, agreements, or determinations of a research review committee or the prolonged persistence of non-compliance occurring after its identification, awareness, or implementation of a corrective action intended to effectively resolve the non-compliance, VHA Directive1058.01.
Continuing Review	The regulatory requirement that the Institutional Review Board (IRB) review research at intervals not greater than one year The IRB may review research at more frequent intervals 45 CFR 46.109(e); 21 CFR 56.109(f).
Control	Subject(s) used for comparison who are not given a treatment under study or who do not have a given condition, background, or risk factor that is the object of the study
Coordinating Center	A centrally located group of investigators responsible for: • Receiving, checking, storing, and analyzing clinical trial data • Preparing reports to the Data and Safety Monitoring Committee • Giving out random assignments to treatment groups by telephone when patients have given informed consent to enter a clinical trial

Continued on next page

Frequently Used Terms, Continued

D

Term	Definition
Data and Safety Monitoring Board (DSMB)	A group of people who monitor a clinical trial for adverse events and other trends The Data and Safety Monitoring Board looks for any information that might warrant modification or termination of the trial or notification of subjects about new information that might affect their willingness to continue in the trial.
Dead fetus	An expelled or delivered fetus that exhibits no heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord (if still attached), 45 CFR 46.203(f). Generally, some organs, tissues, and cells (referred to collectively as fetal tissue) remain alive for varying periods of time after the total organism is dead.
Deception	Intentionally misleading with respect to a research protocol
Declaration of Helsinki	A code of ethics for clinical research approved by the World Medical Association It has been widely adopted by medical associations worldwide and has been revised numerous times.
Department or agency head	The head of any Federal department or agency, for example, the Secretary of HHS, and any other officer or employee of any Federal department or agency to whom the authority department or agency head has been delegated
Deviation	A term not defined by federal regulations but often used in clinical research. For BCM IRB purposes, deviations are defined as unintended variances from the approved protocol. The term is often used in contrast to a violation, which is usually seen as more serious than a deviation. The BCM IRB requires the investigator to determine whether the deviation requires reporting under the BCM IRB Procedures for reporting unanticipated problems involving risks to subjects or others or reporting non-compliance. Otherwise, at time of continuing review the investigator will inform the IRB of its own quality monitoring processes by which deviations were identified, and process changes to prevent unintended variances.
DHHS	U.S. Department of Health and Human Services

Continued on next page

Frequently Used Terms, Continued

D (Continued)

Term	Definition
DOD (Department of Defense) components	The Department of Defense components include, but are not limited to: • Navy • Office of Naval Research • Naval Academy • US Naval Observatory • Army • US Army Corps of Engineers • Military Academy (West Point) • Air Force • Air Force Academy • Marines • Coast Guard • Coast Guard Academy • National Guard • Missile Defense Agency • Defense Advanced Research Projects Agency (DARPA) • Pentagon Force Protection Agency • Defense Intelligence Agency • National Geospatial-Intelligence Agency • National Security Agency • National War College • Tricare Health System
Department of Energy (DOE) research	Department of Energy (DOE) research is research conducted by or for DOE institutions, supported with DOE funds, or performed by DOE employees (including the National Nuclear Security Administration) whether done domestically or in an international environment and includes classified and proprietary research. ***Reference*:** DOE P 443.1A
DSMB	Data and Safety Monitoring Board

Continued on next page

Frequently Used Terms, Continued

E

Term	Definition
Embryo	Early stages of a developing organism, broadly used to refer to stages immediately following fertilization of an egg through implantation and very early pregnancy
Exception	A term not defined by federal regulations but often used in clinical research. For BCM IRB purposes, exceptions are defined as temporary changes to the protocol (such as inclusion criteria). Investigators may seek an exception to the protocol using the same procedure as amendment requests. Otherwise, at the time of continuing review the investigator will inform the IRB of its own quality monitoring processes by which exceptions were identified, and process changes to prevent further exceptions.
Exemptions	The Federal Policy for the Protection of Human Subjects containing six exemptions; however, the College only grants one of the six exemption types found in 45 CFR 46.101(b). All other categories of exemption under the Common Rule are reviewed by the IRB using expedited procedures. Research falling under any of these exemptions is not required to undergo further IRB review, and the investigator may not be required to abide by the requirements for obtaining informed consent 45 CFR 46.101 (b). FDA regulations contain an exemption from IRB review requirements for the emergency use of a test article 21 CFR 56.104(c) and for certain taste and food quality evaluations and consumer acceptance studies 45 CFR 46.101 (b)(6) and 21 CFR 56.104(d). ***Note*:** Research activities found to be exempt from the federal regulations must also meet the College's ethical standards.

Continued on next page

Frequently Used Terms, Continued

E (Continued)

Term	Definition
Expedited review	Review of proposed research by the IRB chair, an experienced, voting IRB member designated by the Chairperson, or group of experienced voting IRB members designated by the Chairperson (serving as a subcommittee) rather than by the entire convened IRB. Federal regulations permit expedited review for: • Certain kinds of research involving no more than minimal risk and that fall within a category listed on the November 9, 1998, Federal Register 63 FR 60364 • Minor changes in previously approved research 45 CFR 46.110; 21 CFR 56.110
Experienced IRB member	Experienced IRB member is an IRB member that has participated in at least one IRB training session and 16 IRB meetings (typical two year service with 75% attendance).
Experiment	Generally, an intervention or interaction that is unproven and not yet scientifically validated
Experimental subject	An activity, for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Examples of interventions or interactions include but are not limited to: • A physical procedure • A drug • A manipulation of the subject or subject's environment • The withholding of an intervention that would have been undertaken if not for the research purpose See U.S. Department of Defense Research.

Continued on next page

Frequently Used Terms, Continued

F

Term	Definition
Family member	This term is used in regulation and guidance that describes research involving the Waiver of Consent Emergency Research – Guidance and Discussion for research subject to FDA regulations and research not subject to FDA regulations. Family member means any one of the following legally competent persons: Spouse(s); parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship. ***References*:** See 21 CFR 50.3(m), 21 CFR 50.24, Guidance "Emergency Research Informed Consent Requirements", OHRP, October 31, 1996 and 45 CFR 46 Waiver of Informed Consent Requirements in Certain Emergency Research.
FDA	Food and Drug Administration, a component of DHHS
Federal department or agency	A federal department or agency (the department or agency itself rather than its bureaus, offices or divisions) that takes appropriate administrative action to make this policy, 45 CFR 46.102(d), applicable to the research involving human subjects it conducts, supports, or otherwise regulates (e.g., the U.S. Department of Health and Human Services, the U.S. Department of Defense, or the Central Intelligence Agency)
Federal Policy	A short reference, along with the phrase *Common Rule*, for the Federal Policy for the Protection of Human Subjects in Research 56 FR 28003
Federal Register	The government's publication in which final and proposed rules or notices are published
Federalwide assurance (FWA)	An assurance of compliance that is a written document submitted by an institution (not an Institutional Review Board) that is engaged in non-exempt human subjects research conducted or supported by HHS. Through the assurance of compliance, an institution commits to HHS that it will comply with the requirements set forth in the regulations for the protection of human subjects at 45 CFR part 46. The Federalwide Assurance is the only type of assurance of compliance accepted and approved by OHRP.
Fetal Material	The placenta, amniotic fluid, fetal membranes, and the umbilical cord

Continued on next page

Frequently Used Terms, Continued

F (Continued)

Term	Definition
Fetus	The product of conception from the time of implantation until delivery. If the delivered or expelled fetus is viable, it is designated an infant, 45 CFR 46.203(c). Hereafter, the term "fetus" will refer to a living fetus unless otherwise specified. The term "fetus" generally refers to later phases of development; the term "embryo" is usually used for earlier phases of development. ***Reference***: Subpart B of 45 CFR Part 46 for specific findings that are required for research involving fetuses
FR	Federal Register
Full Board Review	Review of proposed research at a convened meeting of the IRB, at which a majority of the membership of the IRB are present, including at least one member whose primary concerns are in a nonscientific area 45 CFR 46.109; 21 CFR 56.108

Continued on next page

Frequently Used Terms, Continued

G

Term	Definition
Generalizable knowledge	Knowledge from which broader conclusions will be drawn (i.e., knowledge that may be applied to populations outside of the specific study population). A study that is designed and intended to draw conclusions, inform policy, or generate findings that can be applied to a broader population than that of the research study sample. It is intended to add to existing scientific literature from which others may infer relevance to policy, a body of scientific evidence.
Grant	Financial support provided for a research study designed and proposed by the principal investigator
Guardian	Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care when general medical care includes participation in research. For purposes of subpart D of this part, a guardian also means an individual who is authorized to consent on behalf of a child to participate in research. *Reference*: 21 CFR 50.3(s) Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. *Reference*: 45 CFR 46.402(e) CONSENT BY NON-PARENT: (a) The following persons may consent to medical, dental, psychological, and surgical treatment of a child when the person having the right to consent as otherwise provided by law cannot be contacted and that person has not given actual notice to the contrary: 1) a grandparent of the child; 2) an adult brother or sister of the child; 3) an adult aunt or uncle of the child; 4) an educational institution in which the child is enrolled that has received written authorization to consent from a person having the right to consent; 5) an adult who has actual care, control, and possession of the child and has written authorization to consent from a person having the right to consent;

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Frequently Used Terms, Continued

G (Continued)

Term	Definition
Guardian (continued)	6) a court having jurisdiction over a suit affecting the parent-child relationship of which the child is the subject; 7) an adult responsible for the actual care, control, and possession of a child under the jurisdiction of a juvenile court or committed by a juvenile court to the care of an agency of the state or county; or 8) a peace officer who has lawfully taken custody of a minor, if the peace officer has reasonable grounds to believe the minor is in need of immediate medical treatment. (b) The Texas Youth Commission may consent to the medical, dental, psychological, and surgical treatment of a child committed to it under Title 3 when the person having the right to consent has been contacted and that person has not given actual notice to the contrary. (c) This section does not apply to consent for the immunization of a child. (d) A person who consents to the medical treatment of a minor under Subsection (a)(7) or (8) is immune from liability for damages resulting from the examination or treatment of the minor, except to the extent of the person's own acts of negligence. A physician or dentist licensed to practice in this state, or a hospital or medical facility at which a minor is treated is immune from liability for damages resulting from the examination or treatment of a minor under this section, except to the extent of the person's own acts of negligence. ***Reference***: Texas Family Code Sec. 32.001

Continued on next page

Frequently Used Terms, Continued

H

Term	Definition
Helsinki Declaration	See Declaration of Helsinki
Human in Vitro Fertilization	Any fertilization involving human sperm and ova that occurs outside the human body
Human Protections Administrator	An individual who has responsibility for day-to-day operation and implementation of the College's program for protecting human subjects The Institutional title and duties of the Human Protections Administrator may vary widely from institution to institution. ***Example***: An institutional compliance officer, head IRB administrator, or some other individual might fill this role, depending upon the nature of the College. At BCM this person is the Director of Research Compliance-IRB. The Human Protections Administrator should have detailed knowledge of institutional protection mechanisms and be readily available for consultation with federal officials and institutional personnel. The IRB Chairperson should not serve as the Human Protections Administrator.
Human Subject/ Human Participant	An individual who is the object of study in a research project **Federal Policy (Common Rule)** *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains: • Information or biospecimens through intervention or interaction with the individual and uses, studies, or analyzes the information or biospecimens, or; • Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens 45 CFR 46.102(e)(1) **FDA regulations** *Human subject* means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient 21 CFR 50.3(g) and 56.102(e).
Human subjects research	Activities that meet either the DHHS or FDA definitions of both research and human subjects/participants are considered research involving human subjects and are subject to the Federal regulations and the policies and procedures of the College's human research protection program.

Continued on next page

Frequently Used Terms, Continued

I

Term	Definition
IDE	Investigational Device Exemption
Identifiable biospecimen	A biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen. ***Note*:** 45 CFR 46.102(7) shall: **(i)** Upon consultation with appropriate experts (including experts in data matching and re-identification), reexamine the meaning of ''identifiable private information,'' as defined in paragraph (e)(5) of this section, and ''identifiable biospecimen,'' as defined in paragraph (e)(6) of this section. This reexamination shall take place within 1 year and regularly thereafter (at least every 4 years). This process will be conducted by collaboration among the Federal departments and agencies implementing this policy. If appropriate and permitted by law, such Federal departments and agencies may alter the interpretation of these terms, including through the use of guidance. **(ii)** Upon consultation with appropriate experts, assess whether there are analytic technologies or techniques that should be considered by investigators to generate ''identifiable private information,'' as defined in paragraph (e)(5) of this section, or an ''identifiable biospecimen,'' as defined in paragraph (e)(6) of this section. This assessment shall take place within 1 year and regularly thereafter (at least every 4 years). This process will be conducted by collaboration among the Federal departments and agencies implementing this policy. Any such technologies or techniques will be included on a list of technologies or techniques that produce identifiable private information or identifiable biospecimens. This list will be published in the Federal Register after notice and an opportunity for public comment. The Secretary, HHS, shall maintain the list on a publicly accessible Web site.
IEC	Independent Ethics Committee
Incapacity	A person's mental status, meaning inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice
Inclusion Criteria	The criteria that establish whether a person is eligible to participate in a clinical trial
Incompetence	A legal term meaning inability to manage one's own affairs
IND	Investigational New Drug Application
Independent Ethics Committee (IEC)	The equivalent of an IRB under the International Conference on Harmonisation Guidelines for Good Clinical Practice
Informed Consent	A person's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure

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Frequently Used Terms, Continued

I (Continued)

Term	Definition
Institution	Any public or private entity, or department or agency (including federal, state, and other agencies), 45 CFR 46.102(f)
Institutional component	A legal component that operates under a different name than the College that will be covered by the College's FWA. Legal components are generally defined as parts of an institution that may be viewed as separate organizations, but remain part of the legal entity or institution. Baylor College of Medicine does not have any components identified and named on its FWA.
Institutional Conflict of Interest	Occurs in human subject research when financial interests of BCM or of an Institutional Leader acting within his or her authority on behalf of the institution, might affect or reasonably appear to affect the institutional processes for the design, conduct, reporting, review or oversight of the human subject research, or the rights and welfare of participants.
Institutional Leader	An individual with direct responsibility for research and because of his or her position at BCM, or one of our affiliates, has the capacity to reasonably affect or appear to affect the conduct, review, or oversight of current or proposed research at the institution. *Example*: The Institutional Leader may have the authority to make supervisory decisions about College or administrative unit research programs, or promotion and tenure decisions regarding research faculty. This may include: • President • Vice President • School Deans • Department Chairs • Division Chiefs • Institute or Center Directors • Chairs and Vice Chairs of the IRB, COIC & RCOIC

Continued on next page

Frequently Used Terms, Continued

I (Continued)

Term	Definition
Institutional Official	The individual at an institution who is responsible for ensuring the effective administration and implementation of the College's system for the protection of human subjects
Institutional Review Board (IRB)	A review body established by regulation to protect the welfare of human subjects recruited to participate in research. An institutional review board established in accord with and for the purposes expressed in this policy, 45 CFR 46.102(g).
Interaction	Includes communication or interpersonal contact between investigator and subject
Intervention	Includes both physical procedures by which information or biospecimens are gathered (*e.g.,* venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes
Investigational Device Exemption (IDE)	Exemptions from certain regulations found in the FDA Medical Device Amendments that allow shipment of unapproved devices for use in clinical investigations 21 CFR 812.20
Investigational New Drug Application (IND)	An application to conduct a clinical investigation involving a drug not yet determined by the Food and Drug Administration to be safe and effective for a particular use in the general population and not yet licensed for marketing 21 CFR 312.1
Investigator	**Under FDA regulations:** The individual who actually conducts a research investigation 21 CFR 50.3(d) and 56.102(h) **For Finanical Conflict of Interest Purposes:** BCM requires disclosures of outside financial interests (domestic and foreign) be submitted for anyone that appears to meet the definition of investigators. PIs must consider all personnel designing, conducting or reporting research. This includes at a minimum: • All paid or unpaid key personnel • Paid other personnel, including but not limited to: – Post-docs – Research techs – Study coordinators – Graduate students ***Reminder***: Investigators must consider financial interests held by spouse and dependent children
IRB	Institutional Review Board
IRB approval	The determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements

Continued on next page

Frequently Used Terms, Continued

J

Term	Definition
Justice	An ethical principle discussed in the Belmont Report requiring fairness in distribution of burdens and benefits; often expressed in terms of treating persons of similar circumstances or characteristics similarly

L

Term	Definition
Legally Authorized Representative (LAR)	"Legally authorized representative" means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. ***Reference***: 45 CFR 46.102(c); 21 CFR 50.3(l) Investigators must be aware of the jurisdiction in which the research is being conducted. The DHHS and FDA definition of legally authorized representative refers to the following individuals in Texas in order of priority: 1. A parent or legal guardian if the patient is a minor 2. A legal guardian if the patient has been adjudicated incompetent to manage the patient's personal affairs 3. An agent of the patient authorized under a durable power of attorney for health care 4. An attorney ad litem appointed for the patient 5. A guardian ad litem appointed for the patient 6. A personal representative or statutory beneficiary if the patient is deceased 7. An attorney retained by the patient 8. The patient's spouse 9. An adult child of the patient who has the waiver and consent of all other qualified adult children of the patient to act as the sole decision –maker 10. A majority of the patient's reasonably available adult children 11. The patient's parents 12. The individual clearly identified to act for the patient by the patient before the patient became incapacitated

Continued on next page

Frequently Used Terms, Continued

L (Continued)

Term	Definition
Legally Authorized Representative (LAR) (continued)	13. The patient's nearest living relative 14. A member of the clergy ***Reference*:** Texas Occupations Code "Medical Practice Act", Title 3, Chapter 151, Subchapter A.6 and Texas Health and Safety Code; Title 4. 313.002(10) If you plan to conduct research outside of the state of Texas, contact the Office of Research. If you need assistance locating information on how laws for the state in which you plan to conduct the research define "guardian" for purposes of this research, contact the Office of Research for more information at irb@bcm.edu. ***Reference*:** Texas Health and Safety Code; Title 4. 313.004 Special definitions for VA Research for legally authorized representatives Authorized Person - The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority (38 CFR 17.32(e), see subpart 3aaa for personal representative for the purposes of signing a HIPAA authorization): • Health care agent – for example, an individual named by the individual in a Durable Power of Attorney for Health Care, 38 CFR.17.32(a)(iii) • Legal guardian or special guardian • Next of kin in this order: a close relative of the patient 18 years of age or older, in the following priority: spouse, child, parent, sibling, grandparent, or grandchild • Close friend ***Note*:** An individual who is qualified as a LAR to provide informed consent on behalf of a prospective research subject may not always qualify as a personal representative for purposes of consent to use or disclose a human subject's PHI (i.e., signing a HIPAA authorization). Therefore, in circumstances involving authorization for use or disclosure of a human subject's PHI, the investigator must ensure the LAR meets the requirements of a personal representative (legal guardian or power of attorney) in HIPAA and the Privacy Act of 1974 prior to the LAR's signing a HIPAA authorization.

Continued on next page

Frequently Used Terms, Continued

M

Term	Definition
Member	A person who is listed on the roster of an IRB as a voting participant in IRB deliberations and actions
Minimal Risk (Federal Policy, DHHS Subpart A, and FDA)	The probability and magnitude of harm or discomfort anticipated in the research not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests 45 CFR 46.102(i), 21 CFR 50.3(k), and 56.102(j)
Minimal Risk (DHHS Subpart C - prisoners)	The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons 45 CFR 46.303(d)
Monitoring	A mechanism for keeping track of any part of the research process, including data analysis, recruitment of subjects, informed consent process, to ensure its compliance with Institutional Review Board dictates and the federal regulations

Continued on next page

Frequently Used Terms, Continued

N

Term	Definition
National Bioethics Advisory Commission (NBAC)	A President-appointed commission that issues reports and makes recommendations relating to the protection of human subjects in research
NIH	National Institutes of Health
Non-Affiliated Member	Member of an IRB who has no ties (and whose immediate family members have no ties) to the parent institution, its staff, or faculty This individual is usually from the local community 45 CFR 46.107(c) and 21 CFR 56.107(d).
Non-Scientist	Member of an IRB who does not have a scientific background but may be affiliated with the College 45 CFR 46.107(b) At least one non-scientist member must be present at convened meetings to approve research 45 CFR 46.108(b).
Nonviable Fetus	An expelled or delivered fetus which, although it is living, cannot possibly survive to the point of sustaining life independently, even with the support of available medical therapy. Although it may be presumed that an expelled or delivered fetus is nonviable at a gestational age less than 20 weeks and weight less than 500 grams (Federal Register 40, August 8, 1975: 33552), a specific determination as to viability must be made by a physician in each instance.
Normal Volunteers	Volunteer subjects in a research study who do not have the condition under study. The Office for Human Research Protections guidance defines *normal volunteers* as follows: Volunteer subjects used to study normal physiology and behavior or who do not have the condition under study in a particular protocol, used as comparisons with subjects who do have the condition. "Normal" may not mean normal in all respects. For example, patients with broken legs (if not on medication that will affect the results) may serve as normal volunteers in studies of metabolism, cognitive development, and the like. Similarly, patients with heart disease but without diabetes may be the "normals" in a study of diabetes complicated by heart disease.
Notice of Proposed Rule-Making (NPRM)	Pursuant to the Administrative Procedure Act, the government requirement to issue a notice of a proposed rule before it issues the final rule This affords the public the opportunity to comment on contemplated government action.

Continued on next page

Frequently Used Terms, Continued

N (Continued)

Term	Definition
Not research	For purposes of 45 CFR 46.102(I), the following activities are deemed not to be research: 1) Scholarly and journalistic activities (*e.g.,* oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected. (2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. –Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). –Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters). (3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes. (4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. *Written,* or *in writing,* for purposes of this part, refers to writing on a tangible medium (*e.g.,* paper) or in an electronic format.
Nuremberg Code	A code of research ethics developed during the trials of Nazi war criminals following World War II and widely recognized as a standard during the 1950s and 1960s for protecting human subjects

Continued on next page

Frequently Used Terms, Continued

O

Term	Definition
Oral Consent	Typically refers to informed consent that is obtained from a subject without use of a written informed consent document
Office for Human Research Protections (OHRP)	An office within the DHHS that was created in June of 2000 OHRP is responsible for the implementation of the DHHS regulations 45 CFR Part 46 governing the protection of human subjects in research.
Office for Protection from Research Risks (OPRR)	Until June 2000, an office within the DHHS as part of the National Institutes of Health (NIH) OPRR was responsible for the implementation of the DHHS regulations 45 CFR Part 46 governing research involving human subjects. The Office for Human Research Protections supersedes OPRR.

P

Term	Definition
Parental Permission	The agreement of one or both parents or a guardian to research involving a minor 45 CFR 46.402(c)
Phase 1,2,3,4 Clinical Trials	Different stages of testing drugs in humans, from first application in humans (Phase 1) through limited and broad clinical tests (Phase 3) to post-marketing studies (Phase 4)
Phase 1 Clinical Trials	The initial introduction of an investigational new drug into humans These studies are typically conducted with healthy volunteers; however, where the drug is intended for use in patients with a particular disease, such patients may participate as subjects, Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses (to establish a safe dose range), and, if possible, to gain early evidence of effectiveness. They are typically closely monitored. The ultimate goal of Phase 1 trials is to obtain sufficient information about the drug's pharmacokinetics and pharmacological effects to permit the design of well-controlled, sufficiently valid Phase 2 studies. Other examples of Phase 1 studies include studies of drug metabolism, structure-activity relationships, and mechanisms of actions in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. Typically, Phase 1 investigations involve anywhere from 20 to 80 subjects 21 CFR 312.21 (a).

Continued on next page

Frequently Used Terms, Continued

P (Continued)

Term	Definition
Phase 2 Clinical Trials	Controlled clinical studies conducted to evaluate the drug's effectiveness for a particular indication in patients with the disease or condition under study, and to determine the common short-term side effects and risks associated with the drug These studies are typically well-controlled, closely monitored, and conducted with a relatively small number of patients, usually involving no more than several hundred subjects 21 CFR 312.21 (d).
Phase 3 Clinical Trials	The administration of a new drug to a larger number of patients in different clinical settings to determine its safety, efficacy, and appropriate dosage They are performed after preliminary evidence of effectiveness has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide an adequate basis for physician labeling. In Phase 3 studies, the drug is used the way it would be administered when marketed. When these studies are completed and the sponsor believes that the drug is safe and effective under specific conditions, the sponsor applies to the FDA for approval to market the drug. Phase 3 trials usually involve several hundred to several thousand subjects 21 CFR 312.21(c).
Phase 4 Clinical Trials	The conduct of certain post-marketing studies by the sponsor to ascertain additional information about the drug's risks, benefits, and optimal use, sought by FDA when it gives market approval These studies could include but would not be limited to studying different doses or schedules of administration than were used in Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time 21 CFR 312.85.
PHS (Public Health Service)	A division within the DHHS PHS agencies include the National Institutes of Health, Centers for Disease Control, the Indian Health Service, and the Substance Abuse and Mental Health Services Administration.

Continued on next page

Frequently Used Terms, Continued

P (Continued)

Term	Definition
Placebo	• In biomedical research, a chemically inert substance given in the guise of medicine for its psychologically suggestive effect • Used in controlled clinical trials to determine whether improvement and side effects may reflect imagination or anticipation rather than the actual power of a drug • In social and behavioral research, a condition that mimics the experimental context but does not include the experimental manipulation under study As in biomedical research, the control condition is used to confirm that observed effects are the result of the experimental manipulation rather than the research context itself.
Pregnancy	The period of time from confirmation of implantation of a fertilized egg within the uterus until the fetus has entirely left the uterus (has been delivered). Implantation is confirmed through a presumptive sign of pregnancy, such as missed menses or a positive pregnancy test 45 CFR 46.203(b). This "confirmation" may be in error, but, for research purposes, investigators presume that a living fetus is present until evidence to the contrary is clear. Although fertilization occurs a week or more before implantation, the current inability to detect the fertilization event or the presence of a newly fertilized egg makes a definition of pregnancy based on implantation necessary.
PRIM&R (Public Responsibility in Medicine and Research)	A non-profit organization that organizes conferences, workshops, and other activities to further the protection of human subjects in research.
Principal Investigator (PI)	The person with primary responsibility for design and conduct of a research project
Prior consent	Prior consent means: • Prior consent of the student, if the student is an adult or emancipated minor • Prior written consent of the parent or guardian, if the student is an unemancipated minor
Prisoner	An individual involuntarily confined or detained in a penal institution, including persons: • Sentenced under a criminal or civil statute • Detained pending arraignment, trial, or sentencing • Detained in other facilities under statutes or commitment procedures providing such alternatives to criminal prosecution ***Example***: For drug detoxification or treatment of alcoholism • Incarcerated in a penal institution 45 CFR 46.303(c)

Continued on next page

Frequently Used Terms, Continued

P (Continued)

Prisoner Representative	A member of an IRB who has appropriate background and experience to represent the interests and concerns of an individual who is involuntarily confined to an institution 45 CFR 46.304(b)
Privacy	Privacy can be defined in terms of having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others. ***Reference*:** OHRP guidance
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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record)
Protocol	The formal design or plan of an experiment or research activity The protocol includes • A description of the research design or methodology to be employed • The eligibility requirements for prospective subjects and controls • The treatment regimen(s) • The proposed methods of analysis that will be performed on the collected data

R

Term	Definition
Random assignment	Assignment of subjects to different treatments, interventions, or conditions according to chance
Recruitment	The process of enrolling human subjects in research protocols
Reportable	The term "reportable" refers to an incident, event, or situation that must be reported under the requirements of an applicable regulatory or oversight entity.

Continued on next page

Frequently Used Terms, Continued

R (Continued)

Term	Definition
Research	**Under the Federal Policy and the DHHS Subpart A** 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 45 CFR 46.102(l). For example, some demonstration and service programs may include research activities. **Under FDA regulations** Synonymous with clinical investigation 21 CFR 56.102(c) **For the VA:** • Research is defined as: – The testing of concepts by the scientific method of formulating an hypothesis or research question – Systematically collecting and recording relevant data – Interpreting the results in terms of the hypothesis or question • The Common Rule (38 CFR 16) defines research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. • The FDA definition of research differs according to the applicable regulations. See 21 CFR 812.3(h), 21 CFR 50.3(c), 21 CFR 56.102(c), and 21 CFR 312.3(b). • VA research is research conducted by VA investigators (serving on compensated, WOC, or IPA appointments) while on VA time or on VA property. The research may be funded by VA, by other sponsors, or be unfunded. The research must be approved by the R&D Committee before it is considered VA research and before it can be initiated. All research activities approved by the R&D Committee are considered VA Research. • ***Note*:** Any emergency use of a test article does not require R&D Committee approval but is VA research under VHA Directive 1200.05.

Continued on next page

Frequently Used Terms, Continued

R (Continued)

Research Compliance Officer (RCO)	**For VA Research:** A Research Compliance Officer is an individual whose primary responsibility is auditing and reviewing research projects relative to requirements for the protection of human subjects, laboratory animal welfare, research safety, and other areas under the jurisdiction of and specified by the VA Office of Research Oversight.
Respect for Persons	A principle enunciated in the Belmont Report stating that • Individuals should be treated as autonomous agents. • Persons with diminished autonomy are entitled to protection.
Risk	The probability of harm or injury occurring as a result of participation in a research study

Continued on next page

Frequently Used Terms, Continued

S

Term	Definition
Scientist	• Any individual who has had substantive training or experience in a scientific discipline (i.e., behavioral or biomedical) or in a scientific method should be considered a scientist • May-have had experience and expertise in human subject research • Are recruited from among the College's faculty and staff as well as the community
Secretary	In the context of the federal regulations pertaining to the protection of human subjects in research, the head of a federal agency 45 CFR 46.102(a)
Serious Adverse Event (SAE)	A serious adverse event (SAE) is an adverse event (AE) in *human* research that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly, or birth defect. An AE is also considered serious when medical, surgical, behavioral, social, or other intervention is needed to prevent such an outcome.
Serious non-compliance	Violations that have or pose a greater than minimal risk of harm or discomfort to research participants or others involved in the research. **For VA research** - A failure to adhere to the laws, regulations, or policies governing *human* research that may reasonably be regarded as: • Presenting a genuine risk of substantive harm to the safety, rights, or welfare of human research subjects or others, including their rights to privacy and confidentiality of identifiable private information; VHA Directive 1058.01 • Presenting a genuine risk of substantive harm to the safety, rights, or welfare of research personnel who conduct research • Presenting a genuine risk of substantive harm to the health or welfare of animals used in research • Presenting a genuine risk of substantive reputational harm to VA; or • Substantively compromising a VA medical facility's Animal Care and Use Program (ACUP), Human Research Protection Program (HRPP), Research Safety and Security Program (RSSP), or research information security processes.

Continued on next page

Frequently Used Terms, Continued

S (Continued)

Term	Definition
Signature	A person may be unable to sign documents because of an injury, a muscular or neurological disease, or lack of writing skills. Texas Law defines "Signed" to include any symbol executed or adopted by a person with present intention to authenticate in writing. ***Reference***: Texas Government Code – Code Construction Act
Site Visit	Typically, a visit from a federal office to ensure the entity is complying with federal regulations
Sponsor	Typically refers to the entity that initiates a clinical investigation but does not actually conduct the investigation 21 CFR 50.3(e) and 56.102(j). **For drugs, 21 CFR 312.3(b)** *Sponsor* means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators. *Sponsor-Investigator* means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor. **For devices 21 CFR 821.3(n) and (o)** (n) *Sponsor* means a person who initiates, but who does not actually conduct, the investigation, that is, the investigational device is administered, dispensed, or used under the immediate direction of another individual. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators. (o) *Sponsor-investigator* means an individual who both initiates and actually conducts, alone or with others, an investigation, that is, under whose immediate direction the investigational device is administered, dispensed, or used. The term does not include any person other than an individual. The obligations of a sponsor-investigator under this part include those of an investigator and those of a sponsor.

Continued on next page

Frequently Used Terms, Continued

S (Continued)

Term	Definition
Sponsor-Investigator	An individual who both initiates and actually conducts a clinical investigation 21 CFR 50.3(f) and 56.102(k)
Subjects	Human Subject
Subpart A	The DHHS codification of the Federal Policy for the Protection of Human Subjects in Research found in Subpart A of 45 CFR Part 46
Subpart B	Additional protections for pregnant women and fetuses involved in research with references to human in vitro fertilization research in Subpart B of the DHHS regulations 45 CFR Part 46
Subpart C	Additional protections for prisoners who are involved in research in Subpart C of the DHHS regulations 45 CFR Part 46
Subpart D	Additional protections for children who are involved in research in Subpart D of the DHHS regulations 45 CFR Part 46
Subpart E	Regulations for the registration of Institutional Review Boards found in 45 CFR Part 46
Surveys	Studies designed to obtain information from human subjects through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures
Suspension	The temporary closing of a research project. The suspension may be partial in that certain activities may continue while others may stop. Or, the suspension may be complete in that no activity related to the research may proceed. The IRB (institutional authority) makes this determination.
Systematic investigation	An activity that involves a prospective research plan which incorporates data collection, either quantitative or qualitative, and data analysis to answer a research question.

T

Term	Definition
Termination	The ending of all activities related to a research project except for the continuation of follow-up activities necessary to protect subject safety
Test article	Any drug, biological product for human use, medical device for human use, human food additive, color additive, electronic product subject to FDA regulations under 42 USC 262, 263b-263N, 21 CFR 50.3(j), and 56.102(e)
Tuskegee	Often used erroneously to refer to the U.S. Public Health Service Syphilis Study in Tuskegee, Alabama

Continued on next page

Frequently Used Terms, Continued

U

Term	Definition
Unaffiliated Member	Non-affiliated member
Undue influence	A prohibition in the Common Rule that investigators not use unfair measures or influence to enroll persons in research 45 CFR 46.116
Unanticipated problems involving risks to subjects or others (UPIRSO)	Although federal regulations require prompt reporting to the IRB of any unanticipated problems involving risks to subjects or others, the phrase is not defined in either HHS or FDA regulations. In January 2007, the Office for Human Research Protections (OHRP) released new guidance to assist IRBs in fulfilling this requirement. According to the guidance document OHRP considers unanticipated problems, in general, to include any incident, experience, or outcome that meets all of the following criteria: • Unexpected (in terms of nature, severity, or frequency) given: – The research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and – The characteristics of the subject population being studied • Related or possibly related to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and • Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized In January 2009, the Food and drug Administration (FDA) released new guidance to assist IRBs in fulfilling this requirement. According to the guidance document, FDA considers, in general, an adverse event observed during the conduct of a study to be an unanticipated problem involving risk to human subjects, and requires reporting to the IRB, *only* if it were unexpected, serious, and would have implications for the conduct of the study (e.g., requiring a significant, and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or investigator's brochure). An individual adverse event occurrence *ordinarily* does not meet these criteria because, as an isolated event, its implications for the study cannot be understood.

Continued on next page

Frequently Used Terms, Continued

V

Term	Definition
Viable Infant	When referring to a delivered or expelled fetus, the term "viable infant" means likely to survive to the point of sustaining life independently, given the benefit of available medical therapy. This judgment is made by a physician. In accordance with DHHS regulations, the Secretary, HHS, may publish guidelines to assist in the determination of viability. Such guidelines were published in 1975, and specify an estimated gestational age of 20 weeks or more and a body weight of 500 grams or more as indices of fetal viability (Federal Register 40, August 8, 1975: 33552). These indices depend on the state of present technology and may be revised periodically.
Violation	A term not defined by federal regulations but often used in clinical research. For BCM IRB purposes, a violation is defined as an unintended variance from the approved protocol. The term is often used in contrast to a deviation, which is usually seen as less serious than a violation. The BCM IRB requires the investigator to determine whether the violation requires reporting under the BCM IRB Procedures for reporting unanticipated problems involving risks to subjects or others or reporting non-compliance. Otherwise, the investigator will inform the IRB of its own quality monitoring processes by which violations were identified, and process changes to prevent unintended variances.
Voluntary	Free of coercion, duress, or undue influence
Vulnerable population	A regulatory phrase referring to a group of people who have some condition or situation that makes them more susceptible to coercion or undue influence 45 CFR 46.107(a)

W

Term	Definition
Waiver of Informed Consent	An action taken by the IRB permitting the investigator to pursue research involving human subjects without obtaining informed consent 45 CFR 46.116(e)
Wards	Children who are wards of the state or any other agency, institution, or entity. ***Reference***: 45 CFR 46.409(a)