Use of the Evaluation Instrument for Accreditation

The Evaluation Instrument for Accreditation is intended for use by organizations seeking accreditation and by site visitors who evaluate organizations. To achieve accreditation, an organization must meet all the accreditation Standards and Elements. If an organization meets the Elements for a particular Standard, it meets the Standard. This Evaluation Instrument provides the information necessary to meet each Element.

AAHRPP has defined Domains of responsibility: organization, Institutional Review Board (IRB) or Ethics Committee (EC), and researchers and research staff. Within each Domain are Standards, and for each Standard there are Elements that provide more specificity for the Standard. Each Element contains four parts: Commentary, Regulatory and Guidance References, Required Written Materials, and Outcomes.

For some Elements, Common Types of Materials That May Be Used to Meet the Element are included. Listed under this heading are examples of written materials that organizations have used to meet the Element. They are not required, and organizations may use other types of written materials to meet the Element. If an Element refers to written policies and procedures it generally means that a written procedure (e.g., standard operating procedure) is required to meet the Element. In some cases, an application form or reviewer checklist can serve the same purpose as a written procedure. AAHRPP has attempted to identify those Elements.

By designating certain types of written materials that may be used to meet an Element, AAHRPP does not desire to reduce the flexibility of the accreditation or limit creativity. The listing of Common Types of Materials That May Be Used to Meet an Element is intended to be helpful by providing guidance on the types of materials that can meet an Element.

This Evaluation Instrument is designed to be used by organizations in the United States as well as organizations in other countries that are obligated to follow U.S. federal regulations and those that are not so obligated. The Evaluation Instrument separately designates regulations and guidance from various U.S. federal agencies as well as the International Committee on Harmonisation – Good Clinical Practice Guideline (ICH-GCP) (E6). This includes regulations and guidance from the Department of Health and Human Services (DHHS) and the U.S. Food and Drug Administration (FDA), as well as other departments or agencies that have additional requirements, such as the Department of Defense (DoD), the Department of Education (ED), the Department of Energy (DoE), the Department of Justice (DOJ), the Department of Veteran Affairs (VA), and the Environmental Protection Agency (EPA).

For each Element, there are essential requirements that all organizations must follow. These essential requirements meet many U.S. and international government requirements for protection of human research participants. For some Elements, additional requirements are listed for specific U.S. federal agencies and the ICH-GCP (E6) Guideline.

Each Element (or Standard without Elements) begins on a separate page. This gives the appearance that the Evaluation Instrument is longer than it actually is. Separating each Element provides discrete documents to print and consider.
The five sections of the Evaluation Instrument for Accreditation are:

1. **Commentary:** This section provides an explanation of how to interpret the Element.

2. **Regulatory and Guidance References:** Listed here are regulatory and guidance citations from the U.S. federal agencies that oversee research with human participants. These citations were updated on September 22, 2016. Also, listed here are the guidance citations from the International Committee on Harmonisation - Good Clinical Practice (E6) guideline.

Organizations that must follow a certain set of regulations (e.g., DHHS or FDA) must meet the regulatory requirements. Organizations that are not bound to follow a particular set of regulations are not required to meet them, but they should describe and provide equivalent protections, when applicable.

3. **Required Written Materials:** This section contains the requirements for written materials an organization must have to meet the Element.

AAHRPP uses the generic term “policies and procedures” to refer to all types of written materials. Policies and procedures include any written materials that the organization uses to define and communicate its practices, such as standard operating procedures, policy statements, procedure descriptions, checklists, guidelines, educational materials, job descriptions, memoranda, forms, templates, strategic plans, Web sites, charters, by-laws, mission statements, or other forms, that are used to administer the Human Research Protection Program. Policies and procedures are not limited to IRB or EC policies and procedures; other organizational procedures are likely to be relevant, such as some policies related to human resources, budgeting, pharmacy, contracting, student orientation, corporate compliance, or corporate ethics.

A policy is generally defined as a strategy, goal, or objective. It defines an expectation regarding a behavior or course of action. A procedure is a method by which a policy can be accomplished. Procedures should describe the operational steps that are followed to meet regulatory requirements. A restatement of the regulations or guidance is generally insufficient to provide the necessary specificity. Procedures should include: 1) An explanation of how key regulatory terms are interpreted, 2) The actions that are taken, 3) The title of the person, office, or entity responsible for taking the action, and 4) The timing of actions.

No single format is required for policies and procedures, and no specific wording is required to be used in policies and procedures. Organizations have used a range of models for writing policies and procedures. Procedures should provide enough detail to be understandable to individuals within the organization who use them. Procedures should reflect actual practice within the organization.

AAHRPP has provided a description of the content for many policies and procedures. U.S. regulatory requirements, such as the criteria for approval of research, elements of disclosure for the consent process, or types of disclosure for financial interests, are not listed. The organization must use the federal regulations to obtain these requirements.

4. **Common Types of Materials That May Be Used to Meet the Element:** These are examples of the types of materials organizations have provided to meet the Element. Sometimes, materials are listed under this section when there is requirement for written materials to meet the Element. AAHRPP has included this section under the Element to assist organizations in meeting the Element. Organizations that do not have the materials should not create them to meet the Element. The listing is intended only a facilitative tool.

In this section, “procedures” are not listed as an example of a written material that may be used to meet the Element. In some cases, the combination of an application form and reviewer
evaluation tool will be sufficient to meet the Element, and a written procedure in addition to the application form and reviewer evaluation tool is not needed. This must be judged uniquely for each Element and for each organization.

5. **Outcomes:** These are the practices that an organization should have in place.
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The Evaluation Instrument has been revised to be consistent with the revised Common Rule. A detailed description of the revisions to address changes to the Common Rule, including a redline version of each revised Standard and Element that highlights and tracks the changes between the previous and updated Standards and Elements can be found in the separate document, “Summary of Revisions to the Evaluation Instrument for Accreditation to Comply with the Revised Common Rule” available at http://www.aahrpp.org.


A new Standard I-9 was added that describes responsibilities when sharing oversight of research with other organizations, and the role of the relying organization and reviewing IRB or EC when review is conducted by a single IRB. The Standard addresses the 2017 NIH policy requiring single IRB review, and regulatory requirements in the revised Common Rule about single IRB review, when those go into effect.

A new Element II.2.C. was added on limited IRB review, that will apply when the revised Common Rule goes into effect.

In addition to the revisions to address requirements of the revised Common Rule, Element I.7.A. was revised to clarify that organizations must have approval from the competent authority that oversees their use of investigational drugs and devices. In the United States this is the US Food and Drug Administration, but outside the United States this is the relevant agency or department in the country in which the organization is located (examples include the SFDA in China, the Directorate of Food and Drugs Administration in India, and the Ministry of Food and Drug Safety in South Korea).

Element II.2.G. was revised in response to the US FDA’s decision to allow waivers of informed consent for minimal risk clinical investigations were obtaining consent is not practicable.


Six Tables were added to clarify requirements under the revised Common Rule and other regulations.
Commentary

This Domain describes the structural characteristics of the entity that assumes responsibility for the Human Research Protection Program (HRPP) and applies for accreditation. The organizational structure is the means by which the organization meets the range of responsibilities of the HRPP.

The organization applies its HRPP to all research regardless of funding source, type of research, or place of conduct of the research. The organization exercises these responsibilities through relationships with researchers and research staff, IRBs or ECs, sponsors, participants, and the community.

An organization has the responsibility not only to protect the rights and welfare of human research participants but also to involve research participants in the research enterprise. The involvement of research participants at every stage of the research enterprise helps everyone to achieve the ethical principle of respect for persons. In addition to enhancing the appropriate safeguards and protecting the rights and welfare of research participants, involving research participants in the research process can improve recruitment and retention of participants and also improve the overall quality of research.

The conduct of research is highly dependent upon the partnership between organizations and sponsors. A sponsor is the company, institution, individual donor, or government agency responsible for the initiation, management, or financing of a research study. Sponsors may enter into agreements with intermediaries that act as agents, such as clinical research organizations or coordinating centers. In sponsored research, both the sponsor and the organization have obligations to protect human research participants. In this Domain, the focus is on the obligations of the organization. In seeking accreditation, the organization must address human research protection requirements with all sponsors and apply its HRPP to all sponsored research.

Standard I-1: The organization has a systematic and comprehensive Human Research Protection Program that affords protections for all research participants. Individuals within the organization are knowledgeable about and follow the policies and procedures of the Human Research Protection Program.

Element I.1.A. The organization has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program.

Commentary

An organization should explain in written materials how to differentiate activities that are research involving human participants from activities that are not research involving human participants. Activities that are determined to meet the definition of research involving human participants subsequently fall under the auspices of the HRPP.

A determination of whether an activity is research involving human participants must consider the regulations, laws, codes, and guidance that the organization follows. Many organizations oversee or conduct activities that are covered by two or more sets of laws, regulations, codes, and guidance. In these cases, the organization must apply all relevant definitions of research and participant or develop a plan that guides the HRPP in determining which definitions apply in specific research instances. Written materials must describe equivalent protections for research not covered by laws, regulations, codes or guidance.

If an organization follows DHHS regulations, written materials should describe requirements in state or local
laws, tribal laws, and foreign laws, when they provide additional protections beyond those in DHHS regulations. If the organization follows neither the DHHS nor the FDA regulations, the organization should define “research” as a systematic investigation designed to produce or contribute to generalizable knowledge and “human participant” as living individuals about whom information is obtained or with whom there is interaction, or develop an equivalent definition.

The person making a decision about whether an activity represents research involving human participants should have the authority to represent the organization and have no direct involvement in the activity he or she is examining. The person making the decision should be familiar with regulations, organizational policies, and the nature of research.

Written materials should describe the communication of such decisions to the person seeking a decision.

See AAHRPP Tip Sheet 2.

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<td>• General definitions:</td>
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<td>• Research is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge, or an equivalent definition.</td>
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<td>• Define “generalizable knowledge” relevant to the organization’s research portfolio.</td>
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<td>• Human participant means a living individual about whom a researcher conducting research obtains data through intervention or interaction with the individual, or obtains identifiable private information, or an equivalent definition.</td>
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When following DHHS regulations:

• The definition encompasses activities that are “research” and involve “human subjects” as those terms are defined by DHHS regulations.

When following the revised Common Rule when it goes into effect:

• Written materials specify whether the organization:
• Applies the same policies used to comply with DHHS regulations to all research.
• Applies different requirements to research that is not covered by DHHS regulations.
• Written materials describe whether the organization will apply the revised Common Rule only to research approved after the effective date, or whether it will apply the revised Common Rule to all research approved prior to this date.
• Human participant means a living individual about whom a researcher conducting research:
  • Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens.
  • Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
• Clinical trial means 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.
• Written materials specify the following activities are not considered research:
  • 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.
  • Public health surveillance activities conducted by a public health authority, 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 the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.
    • Including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products.
    • Including 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).
• 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.
• Authorized operational activities (as determined by the relevant federal agency) in support of intelligence, homeland security, defense, or other national security missions.
• Written materials specify that secondary research involving non-identifiable newborn screening blood spots is not considered research involving human participants.

When following FDA regulations:
• Research is any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505 (i) or 520 (g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of 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 might be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used.
  • When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects.

When following VA requirements:
• Written materials indicate classified research involving human participants cannot be approved by a VA facility, IRB, or Research and Development Committee or performed at VA facilities.

When following DoD requirements:
• Non-exempt classified research must be conducted following the requirements of Instruction 3216.02 13.
• Written materials define “experimental subject” as an activity, for research purposes, where there is an intervention or interaction with a living individual 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.
When following DOE requirements:

- Requirements for human participant protections for classified research apply to all research conducted or supported by the DOE, including contracts, and including Human Terrain Mapping research.
- Requirements for human participant protections and their accompanying Contractor Requirements Documents (CRDs) apply to all research conducted at DOE institutions regardless of funding source, or by DOE employees/contractor personnel regardless of funding source or location conducted, and whether done domestically or in an international environment, and including Human Terrain Mapping research. DOE workers are considered vulnerable subjects and shall be afforded additional protections as determined by the IRB.

When following DOJ requirements:

- For research conducted within the Bureau of Prisons: Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.

### Common Types of Materials That May Be Used to Meet the Element

- Application form
- Reviewer checklist
- Template letters to researchers

### Outcomes

- The organization is able to determine and recognize when an activity is research involving human participants as defined by its policies and procedures.
- Decisions about whether an activity is research involving human participants are made promptly.
- Decisions about whether an activity is research involving human participants are made accurately.
- Researchers and others receive a decision about whether an activity is research involving human participants.
Element I.1.B. The organization delegates responsibility for the Human Research Protection Program to an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program.

Commentary
An organization should have an identified, knowledgeable leader of the HRPP who is responsible for the program and has the authority to implement the program. Although this individual may rely on others for the interpretation of laws, regulations, codes, and guidance and the day-to-day operations of the HRPP, this individual should have a basic understanding of the relevant laws, codes, regulations and guidance that govern research involving human participants, the responsibilities of an organizational official, and the responsibilities of the IRB or EC and researchers and research staff in protecting research participants. This individual should be directly involved in the allocation of resources to the HRPP. In some circumstances, more than one individual serves in this capacity.

This Element is applicable to all organizations, regardless of whether the organization has a federal assurance of compliance. If an organization has a federal assurance of compliance, the identified leader of the HRPP might or might not be the official who signs the assurance.

Regulatory and Guidance References
- DHHS: 45 CFR 46.103(c)
- VA: VHA Handbook 1200.01, 05, 06; VA Handbook 1058.01
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)

Required Written Materials

Essential requirements:
- Policies and procedures describe the responsibilities of the organizational official.
- If more than one person is designated as an organizational official, the unique responsibilities of each individual that relate to the HRPP are stated.

When following VA requirements:
- Policies and procedures describe the responsibilities of the facility director:
  - Serves as the organizational Official responsible for the facility’s research program, and the development and implementation of a human research protection program. This responsibility cannot be delegated.
- Oversees the research and development committee, the IRB, other subcommittees of the research and development committee, and all VA researchers and research staff.
- Delegates authority in writing for respective roles and responsibilities for the HRPP. This delegation of authority must provide the organizational structure and ensure leadership for oversight activities for all human subjects research conducted at or by the facility.
- Obtains permission from the central research and development officer if the facility wants to establish a new IRB or change the IRB of record, and ensuring any IRB is established according to VA requirements, and has approval from the Office of Research Oversight (ORO).
- When the facility engages another entity’s IRB, ensures responsibilities are detailed in a memorandum of understanding or authorizing agreement.
- Obtains accreditation of the facility’s HRPP by the accrediting organization specified by the VA Office of Research and Development (ORD), in accordance with a schedule determined by ORD.
- Ensures that IRB members, researchers and research staff are appropriately knowledgeable to conduct research in accordance with ethical standards and all applicable regulations.
- Develops and implements an educational plan for IRB members, staff, researchers, and research staff including initial and continuing education.
- Fulfills all educational requirements mandated by ORD and OHRP.
- Appoints one or more research compliance officers to conduct annual research consent document audits and triennial regulatory audits, and to assist in the VA facility’s assessments of regulatory compliance.
- Unless a waiver for a part-time research compliance officer is approved by the under secretary for health, each VA facility conducting research must designate at least one full-time research compliance officer.
- Reports any appointment, resignation, or change in status of the research compliance officer to Office of Research Oversight VHA Central Office, with a copy to the relevant ORO research officer, within
10 business days after the appointment, resignation, or change takes effect.

- Reports to ORO in writing within two business days after being notified of any research-related citation or determination of non-compliance by any state or federal agency; or any situation that has generated media attention or Congressional interest.
- The facility director’s written report is required regardless of whether disposition of the event has been resolved at the time of the report.
- Follow-up reports detailing any additional findings and appropriate remedial actions must be provided to the relevant ORO office at intervals and in a manner specified by that office.
- Provides a copy of any ORO compliance reports regarding the research program to the associate chief of staff for research, Research and Development Committee, any relevant research review committee(s), and the research compliance officer in a timely fashion.
- Reports the following research events to ORO Central Office, with a simultaneous copy to the appropriate ORO research officer:
  - IRB changes in number of IRBs and changes in membership rosters.
  - Substantive Memorandum of Understanding (MOU) changes must be reported to ORO Central Office within five business days.
  - Ensures that individuals working under a contract with VA cannot serve as VA investigators, but may participate in research in other ways, such as collaborators or consultants.

When following DOE requirements:

- No human participant research conducted with DOE funding at DOE institutions (Headquarters or sites/laboratories, regardless of funding source), or by DOE employees and contractor personnel (regardless of funding source or location conducted), and whether done domestically or in an international environment, including classified and proprietary research, shall be initiated without both a Federalwide Assurance and approval by the cognizant IRB in accordance with 10 CFR Part 745.103.
- For research conducted at a DOE facility, the DOE Institutional Official is responsible for:
  - Ensuring the Central DOE Review Board and the Central DOE Institutional Review Board-Classified comply with applicable requirements.
  - Formally appointing the chair, vice-chair, and other IRB members.

- Approving classified research conducted with DOE funding at its sites/laboratories and by its employees and contractors after IRB approval and prior to initiation.
- For research conducted at a DOE facility, the DOE Human Subjects Protection Program Manager is responsible for:
  - Developing procedures for the classified research program in consultation with the National Nuclear Safety Administration Human Subject Protection Program Manager.
  - Conducting biennial performance reviews of all IRBs that review classified research involving human participants to assess compliance, in consultation with the National Nuclear Security Administration human participant protection program manager.
  - Reviewing and approving local plans to correct noncompliance or mitigate adverse events and unanticipated problems involving risks to participants or others.
  - Reviewing and approving statements of work for classified Human Terrain Mapping projects submitted by DOE’s non-National Nuclear Security Administration sites or projects.
  - Making recommendations to the Secretary after concurrence from the organizational Official, on a project by project basis, regarding exemptions from the requirements for classified research.
  - Concurs on human participant provisions for classified research in interagency agreements, in consultation with the National Nuclear Security Administration, as appropriate.
  - Maintaining an unclassified list of classified projects.

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**Common Types of Materials That May Be Used to Meet the Element**

- Letter or memorandum from senior management stating the delegation
- Job description of the organizational official

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**Outcomes**

- The organizational official has overall responsibility for the HRPP.
- The organizational official is identifiable by those within the organization.
- The organizational official has sufficient standing, authority, knowledge, and independence to ensure implementation and maintenance of the program.
Element I.1.C. The organization has and follows written policies and procedures that allow the Institutional Review Board or Ethics Committee to function independently of other organizational entities in protecting research participants.

Commentary
To ensure that the IRB or EC functions independently of other organizational entities, the IRB or EC should be granted specific authorities to approve, require modifications to secure approval, disapprove research, to suspend or terminate IRB or EC approval of research, and to observe, or have a third party observe, the consent process or the research. The highest appropriate organizational person or entity should grant and recognize these authorities. Statements in the IRB or EC policies and procedures alone granting the IRB or EC such authorities are insufficient.

The organization should have policies and procedures that respond to attempts to influence the IRB’s or EC’s independence or others responsible for the oversight of research.

See AAHRPP Tip Sheet 12.

Regulatory and Guidance References
- DHHS: 45 CFR 46.109(a), 45 CFR 46.109(e), 45 CFR 46.112, 45 CFR 46.113
- FDA: 21 CFR 56.109(a), 21 CFR 56.109(e), 21 CFR 56.112, 21 CFR 56.113

Required Written Materials

Essential requirements:
- Policies and procedures grant the IRB or EC the authority:
  - To approve, require modifications to secure approval, and disapprove all research activities overseen and conducted by the organization.
  - To suspend or terminate IRB or EC approval of research not being conducted in accordance with the IRB’s requirements or that had been associated with unexpected serious harm to participants.
  - To observe, or have a third party observe, the consent process and the conduct of the research.
- Policies and procedures describe the steps the organization takes to ensure that research involving human participants does not commence until the research has received all approvals required by the organization.
- Policies and procedures do not allow the organization to approve research that has not been approved by the IRB or EC.
- Policies and procedures describe to whom IRB or EC members and staff report undue influence.
- Policies and procedures describe the organization’s response to attempts to unduly influence the IRB or EC.

When following VA requirements:
- Policies and procedures indicate:
  - The facility director is responsible for ensuring that the IRB functions independently.
  - In addition to the IRB, the privacy officer, information security officer, and research and development committee must provide their final approval before research can be initiated.
  - The facility director, research and development committee, and ORD can disapprove research.
  - If research is disapproved by the IRB, or the IRB requires modifications, the disapproval or need for modifications cannot be overruled by any other authority.

Outcomes
- The organization does not allow officials of the organization to approve research that has not been approved by the IRB or EC.
- Individuals responsible for the oversight of research know how to report undue influence.
- The organization responds to attempts to unduly influence the individuals responsible for the oversight of research.
- Individuals responsible for the oversight of research do not experience undue influence from the organizational official or others.
- The IRB or EC functions independently.
Element I.1.D. The organization has and follows written policies and procedures setting forth the ethical standards and practices of the Human Research Protection Program. Relevant policies and procedures are made available to sponsors, researchers, research Staff, research participants, and the Institutional Review Board or Ethics Committee, as appropriate.

Commentary
The protection of research participants is the responsibility of many individuals involved with the HRPP, including IRB or EC members, chairs, and staff; researchers and research staff; and the organizational official. The organization should define the roles and responsibilities of individuals responsible for the conduct or oversight of human research. Individuals should understand their roles and responsibilities. This Element includes both the responsibility to follow laws, regulations, codes, and guidance and the requirement to understand and apply ethical principles governing research.

An organization should communicate its expectations of those involved in research. The level of communication required depends on the degree of involvement and role within the HRPP. For example, the policies and procedures most relevant to researchers and research staff are different from those relevant to the IRB or EC staff. An organization should make copies available of policies and procedures, or provide guidelines, abstracts, or summaries that communicate the relevant points.

Organizations must apply DHHS regulations to covered research. However, organizations can apply different but equivalent policies to research not covered by DHHS regulations.

An organization should define all of the components (internal and external) that are involved with human research protection and ensure that those components communicate among themselves and function as an integrated program of protection.

Independent IRBs or ECs should consider not only components within their organization but also the components of organizations for which they serve as the IRB of record.

Required Written Materials

Essential requirements:

- Policies and procedures describe the ethical principles that the organization follows to govern the conduct of research involving human participants.
- Policies and procedures describe the ethical obligations and expectations of:
  - Researchers and research staff, including students involved in the conduct of research.
  - IRB or EC members and chairs.
  - IRB or EC staff.
  - The organizational official.
  - Employees.
  - Students.
- Policies and procedures describe the mechanism for communicating or making available the policies and procedures of the HRPP to all individuals.
- Policies and procedures describe the mechanism for communicating changes in the policies and procedures to all individuals.
- Policies and procedures include a description of all components that are involved with human research protection, including:
  - The roles and responsibilities for each component.
  - The relationships among the components.
  - A description of the ways the components of the organization communicate and work together to protect participants.

Regulatory and Guidance References

- VA: 38 CFR 16.103(b)(4), 38 CFR 16.103(b)(5), VHA Handbook 1200.05, 7,8
- DOJ: 28 CFR 512
- ICH-GCP: 2.1, 2.3, 2.6, 2.13, 3.3.6, 4.5.1

See AAHRPP Tip Sheet 11.
For research conducted within the Bureau of Prisons, the organization, IRB or EC, and researchers and research staff must follow the requirements of 28 CFR 512, including:
• The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing.
• The research design must be compatible with both the operation of prison facilities and protection of human participants. The researcher must observe the rules of the institution or office in which the research is conducted.
• Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the requirements of 28 CFR 512.
• All research proposals will be reviewed by the Bureau Research Review Board.

When following EPA regulations:
• Policies and procedures include that for research conducted or supported by the EPA:
  • EPA prohibits research involving the intentional exposure of pregnant women, nursing women, or children to any substance.
  • EPA requires application of 40 CFR 26 Subparts C and D to provide additional protections to pregnant women and children as participants in observational research, i.e., research that does not involve intentional exposure to any substance.
  • EPA requires submission of IRB determinations and approval to the EPA human subjects research review official for final review and approval before the research can begin.
• Policies and procedures include that for research not conducted or supported by any federal agency that has regulations for protecting human research participants and for which the intention of the research is submission to the EPA, the EPA regulations protecting human research participants apply, including:
  • EPA extends the provisions of the 40 CFR 26 to human research involving the intentional exposure of non-pregnant, non-nursing adults to substances.
  • EPA prohibits the intentional exposure of pregnant women, nursing women, or children to any substance.

When following the ICH-GCP (E6) guideline:
• Policies and procedures include a statement that clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice and the applicable regulatory requirements.

Common Types of Materials That May Be Used to Meet the Element
• HRPP plan
• IRB or EC policies and procedures
• Researcher handbook

Outcomes
• The organization follows ethical standards and practices.
• Individuals in the organization follow ethical standards and practices.
• The organization makes available to individuals involved or likely to be involved in research policies and procedures governing research with human participants.
• Individuals are kept up to date with new information and policies and procedures.
• Individuals are able to access policies and procedures.
Element I.1.E. The organization has an education program that contributes to the improvement of the qualifications and expertise of individuals responsible for protecting the rights and welfare of research participants.

**Commentary**

The protection of research participants is the responsibility of many individuals in an HRPP, including IRB or EC members, chairs, and staff; researchers and research staff; and the organizational official. To protect research participants these individuals need to understand and be able to apply several areas of knowledge, including ethical principles, professional standards, organizational policies and procedures, and laws, regulations, codes, and guidance.

The depth of knowledge and skill required depends on each individual’s specific task and role. For example, IRB or EC chairs or reviewers designated to use the expedited procedure for review should have more knowledge and skill than a new IRB or EC member. Researchers need different skills depending on the nature of their research or the expertise of their support staff.

An organization should have a process to ensure that individuals involved with human research protection have appropriate knowledge and skills. Such a process can include formal training and evaluation of previous training and experience. The size and breadth of the education program should be customized to meet the needs of the organization.

An organization should periodically evaluate the knowledge and skills of individuals involved in the HRPP.

**Regulatory and Guidance References**

- VA: VHA Handbook 1200.05, 29
- DoD: Instruction 3216.02 5 paragraph 1.f.; 3216.02 6 paragraph 5.a-d. SECNAVINST 3900.39D para. 6a(2), Minimum Education Requirements for DoD Personnel Involved in Human Research Protection Guidance (August 16, 2012)

**Required Written Materials**

**Essential requirements:**

- The organization maintains a list of educational activities designed to contribute to the improvement of the qualifications and expertise of individuals responsible for protecting the rights and welfare of research participants.

- Policies and procedures include initial education requirements, including timeframes, for researchers and research staff; IRB or EC staff, IRB or EC chairs, and members; and others.

- Policies and procedures indicate how education requirements are monitored.

- Policies and procedures describe continuing education requirements and time frames.

- Policies and procedures describe what actions the IRB or EC or the organization takes if education requirements are not fulfilled.

**When following VA requirements:**

- Policies and procedures indicate:
  - All individuals who are subject to VA regulations are required to:
    - Complete training in the ethical principles on which human research is to be conducted before they may participate in human participants research in accordance with requirements specified by ORD; the local site can require additional training.

**When following DoD requirements:**

- Policies and procedures require initial and continuing research ethics education for all personnel who conduct, review, approve, oversee, support, or manage human participants research.

- There might be specific DoD educational requirements or certification required by different DoD components.

- The DoD component may evaluate the education policies to ensure the personnel are qualified to perform the research, based on the complexity and risk of the research.

- Policies and procedures indicate how the IRB or EC staff, chair, and members; and researchers and research staff become aware of the specific requirements contained in DoD regulations and requirements and educated about these requirements when appropriate.

**Common Types of Materials That May Be Used to Meet the Element**

- Lists of educational activities
- Education plans
- Education records
Outcomes

• The organization has an education program to ensure that individuals involved in the HRPP have appropriate knowledge and skills.
Element I.1.F. The organization has and follows written policies and procedures for reviewing the scientific or scholarly validity of a proposed research study. Such procedures are coordinated with the ethics review process.

Commentary
This Element requires an organization to have a level of scientific or scholarly review sufficient to fulfill two criteria for approval of research used by the IRB or EC:
- Risks to participants are minimized by using procedures consistent with sound research design and that do not unnecessarily expose participants to risk.
- Risks to participants are reasonable in relation to anticipated benefits, if any, to participants and the importance of the knowledge that may reasonably be expected to result.

An organization may use various mechanisms to evaluate scientific or scholarly validity of proposed research. The IRB or EC may draw on its own knowledge and disciplinary expertise, or the IRB or EC may draw on the knowledge and disciplinary expertise of others, such as review by a funding agency, an organizational scientific review committee, or department chairs. The organization may also use a combination of these mechanisms. In all cases, the conduct of the scientific or scholarly review requires the reviewers to have the expertise to understand the background, aims, and methods of the research to address the two criteria of approval listed above and to draw on the discipline’s standards for conducting research.

The results of the review should be communicated to the IRB or EC as part of the process for review and approval. The IRB or EC cannot delegate its responsibility to judge whether the criteria for approval are met.

This Element does not require a merit review that compares the value of the research to other research studies or a peer review designed to maximize scientific quality, except when following DoD requirements. Therefore, this Element does not require the level of disciplinary expertise required for review of relative merit or peer review, except when following DoD requirements.

See AAHRPP Tip Sheet 11.

Regulatory and Guidance References
- DHHS: 45 CFR 46.111(a)(1)(i), 46 CFR 46.111(a)(2)
- DoD: Instruction 3216.02 6 paragraphs 3.a.(2), 4.b.(2)
- DOJ: 28 CFR 512.11(a)(2)
- ICH-GCP: 2.4, 2.5, 2.13

Required Written Materials

Essential requirements:
- Policies and procedures describe the organization’s evaluation of proposed research for scientific or scholarly validity.
- Policies and procedures indicate the individuals or entities that are responsible for scientific review.
- Scholarly or scientific review of proposed research addresses the following issues:
  - Does the research use procedures consistent with sound research design?
  - Is the research design sound enough to yield the expected knowledge?
  - If scientific review is conducted by an entity other than the IRB or EC, policies and procedures describe how the review is documented and communicated to the IRB or EC.

When following DoD requirements:
- When an IRB or EC at a non-DoD institution reviews DoD-supported research, the IRB or EC must consider the scientific merit of the research.
- The IRB or EC may rely on outside experts to provide an evaluation of the scientific merit.

When following DOJ requirements:
- Policies and procedures include that for research conducted within the Bureau of Prisons, the project must have an adequate research design and contribute to the advancement of knowledge about corrections.

When following the ICH-GCP (E6) guideline:
- Policies and procedures include the evaluation of the available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial.
- The scientific review process provides the IRB or EC the information it needs to determine whether the criteria for approval of research are met.
- The scientific review process evaluates:
  - The soundness of the research design.
  - The ability of the research to answer the proposed questions.
Common Types of Materials That May Be Used to Meet the Element

- Reviewer checklist
- Written evaluations

Outcomes

- Individuals who conduct scientific or scholarly review include members who have relevant expertise and draw upon the standards to conduct research applicable to the scientific or scholarly discipline.

- The scientific review process provides the IRB or EC the information it needs to determine whether the criteria for approval of research are met.
- The scientific review process evaluates:
  - The soundness of the research design.
  - The ability of the research to answer the proposed questions.
Element I.1.G. The organization has and follows written policies and procedures that identify applicable laws in the localities where it conducts human research, takes them into account in the review and conduct of research, and resolves differences between federal or national law and local laws.

Commentary
Sometimes, there are laws other than federal or national, such as state, provincial, or local, which govern the conduct of research involving human participants. Policies and procedures should include the definitions and applicability of these laws or define a process to determine definitions and applicability, in the jurisdiction in which the organization resides, as well as in the locations where research is conducted. This would normally include obtaining legal counsel. An organization may have its own legal counsel or rely on external legal counsel. Policies and procedures should describe the application of laws so that the laws are understandable to IRB or EC members, IRB or EC staff, and researchers and research staff, rather than simply restate the law.

Independent IRBs or ECs should have a process to determine the particular international, national, and local laws that influence IRB or EC determinations within the specific locality where the research is conducted. When research is conducted that involves children or adults who have impaired decision-making capacity, policies and procedures should define which individuals meet the legal definitions of “legally authorized representative”, “child”, and “guardian”.

In some jurisdictions, there are other laws that provide additional protections for participants of research and are applicable to IRB or EC decisions to approve research. Such laws include privacy, genetic testing, genetic information, and reporting of child, elder, or spousal abuse.

This Element applies to research conducted in the resident country; transnational research is covered in Standard I-3.

Regulatory and Guidance References
- DHHS: 45 CFR 46.101(e)-(f), 45 CFR 46.102(c), 45 CFR 46.402(d)-(e)
- FDA: 21 CFR 50.3(l), 21 CFR 50.3(o), 21 CFR 50.3(s), 21 CFR 56.103(c)
- VA: 38 CFR 16.101(e)-(f), 38 CFR 16.102(c), 38 CFR 17.32(e), 38 CFR 17.32(g), VHA Directive 2001-028, VHA Handbook 1200.05, 7,8,45,48,49

Required Written Materials

Essential requirements:
- Policies and procedures describe the application of laws relevant to research involving humans as participants, when the research is conducted:
  - In the jurisdiction where the organization resides.
  - Outside the jurisdiction where the organization resides.
- Policies and procedures describe the process to resolve conflicts between federal or national law and other applicable laws.

When following DHHS and FDA regulations:
- If the organization oversees research that involves adults unable to provide legally effective consent, policies and procedures describe the organization’s decision about or process to determine who is a “legally authorized representative” as defined by DHHS and FDA regulations.
- If the organization oversees research that involves children as participants, policies and procedures describe the organization’s decision about or process to determine who is a “child” as defined by DHHS and FDA.
- If the organization oversees research that involves children who are wards as participants, policies and procedures describe the organization’s decision about or process to determine who is a “guardian” as defined by DHHS and FDA regulations.

Outcomes
- The organization has access to legal counsel for assistance in applying laws to research involving human participants.
- Research complies with applicable laws relevant to research involving human participants.
- Conflicts among applicable laws are resolved.
Standard I-2: The organization ensures that the Human Research Protection Program has resources sufficient to protect the rights and welfare of research participants for the research activities that the organization conducts or oversees.

Commentary
Resources include all needs of an HRPP, such as staff, consultants, IRBs or ECs, meeting space, equipment, finances, information technology systems, and space to store records securely, permit private conversations, accommodate computer and office equipment, and hold meetings.

There are no standards or formulas for sufficient resources; the determination is made based on outcome. If an organization meets all other Elements, resources will be judged sufficient. If an organization does not meet an Element, insufficient resources will be considered as a possible reason.

An organization may rely on the services, such as the IRB or EC, contracting office, or conflict of interest committee, of another organization to supplement its resources. (See Standard I.9)

Regulatory and Guidance References

- DHHS: 45 CFR 46.103(b)(2), 45 CFR 46.103(d), 45 CFR 46.114, OHRP Guidance on Knowledge of Local Research Context
- FDA: 21 CFR 56.114, FDA Information Sheets: Non-Local IRB Review
- VA: 38 CFR 16.103(b)(2), VHA Handbook 1200.05, 6.7,8
- ICH-GCP: 4.2.3

Required Written Materials

Essential requirements:

- The organization maintains adequate resources for support of the operations of the HRPP, including but not limited to resources such as space and personnel, in order to meet the accreditation standards.
- Policies and procedures describe the plan to evaluate resources needed for the HRPP.
- If the organization relies on the services or components of another organization, policies and procedures describe the steps followed (e.g., criteria, evaluation, or monitoring) to evaluate whether the service or component meets the relevant accreditation standards.

When following VA requirements:

- Policies and procedures indicate the facility director is responsible for ensuring provision of adequate resources to support the operations of the HRPP so that those operations are in compliance with all VA and other federal requirements that govern human participants research protection.

- The VA facility has an established or designated IRB by:
  - Establishing its own IRB.
  - Securing the services of an OHRP-registered IRB established by another VA facility, VA central IRB, or affiliated medical or dental school, or an IRB of another federal agency. In policies and procedures:
    - The provision of services by another IRB, including the VA Central IRB, is established through a memorandum of understanding or other written agreement that outlines the responsibilities of the VA and the academic affiliate.
    - When relying on another IRB, the memorandum of understanding requires the other IRB to comply with VA requirements when reviewing VA research.
    - A VA facility’s own internal IRB cannot serve as an IRB of record for any non-VA entity except a DoD facility or a VA nonprofit research and educational foundation.
    - If using the VA Central IRB, the facility director delegates authority to one or more individuals from the local VA facility to:
      - Provide comments or suggestions to VA Central IRB, in response to VA Central IRB’s initial review considerations.
      - Respond to VA Central IRB’s approval of the study on behalf of the VA facility as to whether the VA facility chooses to participate or declines to participate in the study.
      - Serve as liaison between the VA facility and both the local site researcher and VA Central IRB.

When following DoD requirements:

- The DoD Component must conduct an appropriate administrative review of the research involving human subjects. The DoD Component administrative review must be conducted before the research involving human subjects can begin, to ensure compliance with all applicable regulations and policies, including any applicable laws and requirements and cultural sensitivities of a foreign country when the research is conducted in a foreign country.
• 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.

Outcomes
• The organization has allocated the financial and personnel resources and space necessary to carry out the operations of the HRPP in order to meet the accreditation standards.
• The organization periodically reviews the resources allocated to the HRPP and adjusts resources as needed.
• The organization periodically evaluates key functions of the HRPP, such as the number of IRBs or ECs, the conflict of interest committee, the quality improvement program, the educational activities, sponsored programs, and pharmacy services, and makes adjustments so that key functions of the HRPP are accomplished in a thorough and timely manner.
• When the organization relies on the services of another organization, the organization ensures that the services meet the relevant accreditation standards.
Standard I-3: The organization’s transnational research activities are consistent with the ethical principles set forth in its Human Research Protection Program and meet equivalent levels of participant protection as research conducted in the organization’s principal location while complying with local laws and taking into account cultural context.

Commentary
Researchers often conduct studies in other countries as well as in their own country. IRBs or ECs that review such research must be knowledgeable about the laws, regulations, codes, and guidance that govern such research in addition to the cultural context in which the research will be conducted.

Both researchers and the IRB or EC have the responsibility to ensure the research performed in other countries meets equivalent levels of protection that would be required in the organization’s principal location, taking into account local laws and cultural context.

When research is sponsored by a U.S. federal agency, the regulations of that agency apply. Providing equivalent protections is unacceptable in lieu of providing the required federal protections.

Regulatory and Guidance References
- DHHS: 71 Fed Reg 10511 (July 7, 2006)
- DoD: Instruction 3216.02 6 para. 3.a.(4); SECNAVINST 3900.39D, para. 6i
- VA: VHA Handbook 1200.05, 4, 5, 56

Required Written Materials
Essential requirements:
- The organization has policies and procedures for reviewing transnational research including:
  - Ensuring appropriate expertise and knowledge of the country either through IRB membership or consultants.
  - Confirming the qualifications of the researchers and research staff for conducting research in that country.
  - Initial review, continuing review, and review of modifications.
  - Knowledge of local laws.
  - Post-approval monitoring.
  - Handling of complaints, non-compliance, and unanticipated problems involving risk to participants or others.

- Consent process and other language issues.
- Communication and coordination with local IRBs or ECs when appropriate.
- All policies and procedures that are applied to research conducted domestically should be applied to research conducted in other countries, as appropriate.

When following VA requirements:
- Policies and procedures indicate:
  - The facility director must ensure all international research is approved explicitly in a document signed by the facility director, except for Cooperative Studies Program activities which must be approved by the CRADO.
  - All international sites must hold an international federalwide assurance, and the research must be approved by the IRB or Ethics Committee of the participating sites listed on the international federalwide assurance.
  - International research includes VA-approved research conducted at international sites not within the United States, its territories, or Commonwealths; and includes research where human tissues are sent outside the United States.
  - The researcher must conduct the research in accordance with VA requirements and all other applicable federal requirements for protecting human participants, tissue banking, use of databases, federal criminal laws, and the standards of ethical conduct for employees of the executive branch.

When following DoD requirements:
- Policies and procedures include additional safeguards for research conducted with international populations:
  - The organization or researcher has permission to conduct research in that country by certification or local ethics review.
• The researcher follows all local laws, regulations, customs, and practices.

Common Types of Materials That May Be Used to Meet the Element

• Applications
• Checklists
• Copies or summaries of local laws

Outcomes

• Researchers provide the same or equivalent protections to human participants in research conducted in other countries.

• When conducting transnational research, researchers are aware of local laws and cultural context in all locations where the research is conducted and comply with local laws and adhere to cultural norms.

• When reviewing transnational research, IRBs or ECs ensure that equivalent protections are provided to research participants enrolled in research in other countries.

• IRBs or ECs make determinations and decisions based on laws and knowledge of the country in which the research will be conducted.
Standard I-4: The organization responds to the concerns of research participants.

Element I.4.A. The organization has and follows written policies and procedures that establish a safe, confidential, and reliable channel for current, prospective, or past research participants or their designated representatives that permits them to discuss problems, concerns, and questions; obtain information; or offer input with an informed individual who is unaffiliated with the specific research protocol or plan.

Commentary
Organizations should provide information to current, former, and prospective research participants about whom to contact for concerns, questions, or complaints about the research; obtain information; or offer input. Organizations should also have a mechanism to solicit concerns, questions, or input from prospective participants. The organization should have policies and procedures that describe the steps followed by the organization to respond to contacts from participants or others.

Regulatory and Guidance References
- DHHS: 45 CFR 46.116(a)(6)-(7)
- VA: VHA Handbook 1200.05, 5

Required Written Materials

**Essential requirements:**

- Contact information for an individual or office that is unaffiliated with a specific research study is available to current, former, and prospective research participants to:
  - Discuss problems, concerns, and questions.
  - Obtain information.
  - Offer input.
- Policies and procedures describe the steps followed when the organization responds contacts from participants or others.

Common Types of Materials That May Be Used to Meet the Element

- Web site
- Pamphlet or brochure
- Consent template

Outcomes

- The organization provides information to current, former, and prospective participants or others about whom to contact in the organization to discuss problems, concerns, and questions; obtain information; and offer input.
- The organization responds to contacts from participants or others.
Element I.4.B. The organization conducts activities designed to enhance understanding of human research by participants, prospective participants, or their communities, when appropriate. These activities are evaluated on a regular basis for improvement.

Commentary
To enhance the public’s understanding of research, organizations should perform outreach activities. The scope of the outreach activities should be proportional to the size and complexity of the research program. There is no requirement that a single activity will result in measurable changes in community understanding.

Regulatory and Guidance References
• None

Required Written Materials

Essential requirements:
• Policies and procedures describe the plan and methods for enhancing the understanding of participants, prospective participants, and communities.
• Policies and procedures describe the periodic evaluation of outreach activities.

Common Types of Materials That May Be Used to Meet the Element
• Pamphlet or brochure
• Web site
• Research Day
• Mini-medical school
• Speaker bureau
• Evaluation reports
• Quality improvement plans

Outcomes
• The organization provides information designed to enhance the understanding of research involving participants and their community.
• IRB or EC members and researchers can describe the characteristics and culture of the communities in which they oversee or conduct research, respectively.
• The organization makes improvements to its outreach activities as needed, based upon a periodic assessment.
Element I.4.C. The organization promotes the involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results.

Commentary
In some instances, the design and implementation of research can be enhanced when individuals from the community in which the research will be conducted are involved in the design, conduct, and analysis of data from the research. This can occur for an individual study or group of studies. This Element is not applicable, or appropriate, for all research studies. An organization can facilitate the involvement of community members by supporting community or patient advocacy boards, supporting researchers who wish to conduct community-based participatory research or other types of research that involve community members, or supporting the IRB or EC in developing the expertise to review community-based participatory research.

Regulatory and Guidance References
• None

Required Written Materials

Essential requirements:
• Policies and procedures describe the additional considerations for reviewing research that involves community members in the research process, including the design and implementation of research and the dissemination of results.

Common Types of Materials That May Be Used to Meet the Element
• Research studies using a community-based participatory research design
• Use of community advisory boards
• Use of participant advocates
• Partnerships with community-based organizations

Outcomes
• When appropriate, the organization supports mechanisms that allow researchers to involve community members in the research process, including the design and implementation of research and the dissemination of results.
• When appropriate, researchers involve community members in the design, conduct, and analysis of data.
• When appropriate, researchers inform community members about the results of the research study and utilize community members to help disseminate results.
Standard I-5: The organization measures and improves, when necessary, compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The organization also measures and improves, when necessary, the quality, effectiveness, and efficiency of the Human Research Protection Program.

Element I.5.A. The organization conducts audits or surveys or uses other methods to assess compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The organization makes improvements to increase compliance, when necessary.

Commentary
An organization’s quality improvement program should include measures of compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The organization’s quality improvement program should include an evaluation of the HRPP to determine whether it is effective in achieving compliance.

The organization should collect objective data through audits, surveys, or other methods and use the data to make improvements and monitor compliance on an ongoing basis.

The number of audits or surveys, or the breadth of the audits or surveys, conducted should be determined by the organization and sufficiently robust to provide data that inform the quality improvement program.

Regulatory and Guidance References
- VA: VHA Handbook 1058.01, VHA Handbook 1200.05, 14, 29
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)

Required Written Materials

Essential requirements:
- The organization has a quality improvement plan that periodically assesses compliance of the HRPP.
  - The plan states the goal of the quality improvement plan with respect to achieving and maintaining compliance.
  - The plan defines at least one objective to achieve or maintain compliance.
  - The plan defines at least one measure of compliance.
- The plan describes the methods to assess compliance and make improvements.

When following VA requirements:
- Policies and procedures indicate:
  - The facility director is responsible for ensuring appropriate auditing of local human participants research studies to assess compliance with all applicable local, VA, and other federal requirements including, but not limited to, Office of Research Oversight requirements.
  - A research compliance officer is an individual whose primary responsibility is auditing and reviewing research projects relative to requirements for the protection of human participants, and who:
    - Conducts annual consent document audits.
    - Conducts triennial regulatory audits on all research protocols.
  - The VA facility’s lead research compliance officer must report directly to the facility director. The activities of the research compliance officer may not be determined or managed by the Research Service, research investigators, or any other research personnel.
  - The IRB may observe, or have a third party observe research activities, including the informed consent process.
    - Procedures must include, but are not limited to:
      - Criteria that might prompt increasing the frequency of audits beyond the minimal required frequency.
      - The timeframe for reporting audit findings to the IRB.
      - Types of corrective actions the IRB can require based on the audit findings.
• Who should implement and review the corrective actions.
• How to evaluate the results of any corrective actions.
• The IRB can accept audits conducted by the research compliance officer to fulfill auditing requirements.
• The IRB may require more frequent audits by the research compliance officer or by other means. The IRB also may require the research compliance officer to conduct more focused audits of one or more aspects of the study. The requirement to increase the frequency of audits or to audit specific aspects of the study might be based on considerations including, but not limited to:
  • Involvement of vulnerable populations.
  • Level of risk.
  • Phase I or Phase II studies.
  • Involvement of FDA approved drugs for which there has been a new safety warning issued, or change in the labeling that indicates increased risks.
• Issues of noncompliance.
• Data confidentiality or security concerns.
• When following DOE requirements:
  • The organization must periodically conduct self-assessments to ensure compliance with the HRPP procedures and other requirements.

<table>
<thead>
<tr>
<th>Common Types of Materials That May Be Used to Meet the Element</th>
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<tr>
<td>Compliance plans</td>
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<td>Audits, surveys, or data collection tools</td>
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<td>Surveys</td>
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<td>Evaluation reports</td>
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<th>Outcomes</th>
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<td>The organization monitors compliance based on objective data and makes improvements, when necessary.</td>
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</table>
Element I.5.B. The organization conducts audits or surveys or uses other methods to assess the quality, efficiency, and effectiveness of the Human Research Protection Program. The organization identifies strengths and weaknesses of the Human Research Protection Program and makes improvements, when necessary, to increase the quality, efficiency, and effectiveness of the program.

Commentary
An organization’s quality improvement program should include measures of quality, efficiency, and effectiveness to evaluate the performance of the HRPP. The organization should use results from the quality improvement program to design and implement improvements.

The organization should collect objective data through audits, surveys, or other methods and use the data to make improvements and monitor quality, efficiency, and effectiveness on an ongoing basis.

Regulatory and Guidance References
- None

Required Written Materials

*Essential requirements:*
- The organization has a quality improvement plan that periodically assesses the quality, efficiency, and effectiveness of the HRPP.
- The plan states the goals of the quality improvement plan with respect to achieving targeted levels of quality, efficiency, and effectiveness of the HRPP.
- The plan defines at least one objective of quality, efficiency, or effectiveness.
- The plan defines at least one measure of quality, efficiency, or effectiveness.
- The plan describes the methods to assess quality, efficiency, and effectiveness and make improvements.

Common Types of Materials That May Be Used to Meet the Element
- Quality improvement plan
- Audits, surveys, or other data collection tools
- Evaluation reports

Outcomes
- The organization:
  - Identifies targets for quality, efficiency, and effectiveness of the HRPP.
  - Plans improvements based on measures of quality, efficiency, and effectiveness.
  - Implements planned improvements.
  - Monitors and measures the effectiveness of improvements.
Element I.5.C. The organization has and follows written policies and procedures so that Researchers and research staff may bring forward to the organization concerns or suggestions regarding the Human Research Protection Program, including the ethics review process.

**Commentary**
The HRPP should have open communications with researchers and research staff under its oversight and be responsive to questions, concerns, and suggestions. Policies and procedures should describe the ways researchers and research staff may communicate with representatives of the HRPP.

**Regulatory and Guidance References**
- None

**Required Written Materials**

*Essential requirements:*
- Policies and procedures describe the process for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the HRPP.

**Outcomes**
- Researchers and research staff know how to obtain answers to questions regarding the HRPP.
- Researchers and research staff know how to express concerns or convey suggestions about the HRPP.
- Researchers and research staff find the organization responsive to their questions, concerns, and suggestions.
Element I.5.D. The organization has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. The organization works with the Institutional Review Board or Ethics Committee, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate.

Commentary
Non-compliance refers to not following laws or regulations that govern research involving human participants, the organization’s policies and procedures, or the requirements or determinations of the IRB or EC. Non-compliance can be relatively minor or serious. Non-compliance can also be a one-time event or a continuing problem. Policies and procedures should consider a range of corrective actions that are applicable to the spectrum of non-compliance. Corrective actions should be appropriate to the nature and degree of the non-compliance. Some laws or regulations specify reporting requirements to regulatory agencies, sponsors, or other entities that should be incorporated into the organization’s policies and procedures. See AAHRPP Tip Sheet 14. See AAHRPP Tip Sheet 21.

Regulatory and Guidance References
- DHHS: 45 CFR 46.103(b)(5)(i), 45 CFR 46.116(b)(5), OHRP Guidance on Reporting Incidents to OHRP
- FDA: 21 CFR 50.25(b)(5), 21 CFR 56.108(b)(2)
- DoD: Instruction 3216.02 6 para.4.b.(4), SECNAVINST 3900.39D, para. 8d(2) and 6k
- ICH-GCP: 5.20

Required Written Materials

Essential requirements:
- Policies and procedures define:
  - Non-compliance.
  - Serious non-compliance.
  - Continuing non-compliance.
- Policies and procedures include non-compliance of researchers, staff, other employees, and of the IRB or EC.
- Policies and procedures describe the various mechanisms for informing the organization or IRB or EC of non-compliance:
  - Reporting requirements for researchers, staff, and employees.
  - Consideration of complaints and protocol deviations.
  - Results of audits.
- Policies and procedures describe:
  - The organization’s process to decide whether each allegation of non-compliance has a basis in fact.
  - The organization’s process to decide whether each incident of non-compliance is serious or continuing.
- Policies and procedures describe the organization’s process to manage non-compliance that is neither serious nor continuing.
- Policies and procedures describe the process for management of serious or continuing non-compliance by the convened IRB or EC, including:
  - If a primary reviewer system is used, documents distributed to primary reviewers.
  - Documents distributed to all IRB or EC members.
  - The range of possible actions considered by the IRB or EC:
    - Required actions:
      - Suspension of IRB approval the research.
      - Termination of IRB approval the research.
      - Notification of current participants when such information might relate to participants’ willingness to continue to take part in the research.
    - Optional actions:
      - Modification of the protocol.
      - Modification of the information disclosed during the consent process.
      - Providing additional information to past participants.
• Requiring current participants to re-consent to participation.
• Modification of the continuing review schedule.
• Monitoring of the research.
• Monitoring of the consent process.
• Referral to other organizational entities.

• Policies and procedures describe the reporting of serious or continuing non-compliance, including:
  • A requirement for the report to be distributed to:
    • Specific organizational officials.
    • Other agencies when the research is overseen by those agencies.
  • The maximum time allowed between the recognition of a reportable event and fulfilling reporting requirements.

When following DHHS regulations:
• Policies and procedures describe the reporting of serious or continuing non-compliance to OHRP.

When following FDA regulations:
• Policies and procedures describe the reporting of serious or continuing non-compliance to FDA.

When following VA requirements:
• Policies and procedures include the following definitions, procedures, and timeframes:
  • Serious non-compliance is a failure to follow requirements for conducting human research that may reasonably be regarded as:
    • Presenting a genuine risk of substantive harm to the safety, rights, or welfare of human research participants, research staff, or others, including the rights to privacy and confidentiality of identifiable private information.
    • Substantively compromising a VA facility’s HRPP.
  • Continuing non-compliance is a persistent failure to adhere to the laws, regulations, or policies governing human research.
  • The determination that non-compliance is “serious” or “continuing” rests with the IRB.
  • Apparent serious or continuing non-compliance:
    • Within five business days of becoming aware of any apparent or possible serious or continuing non-compliance, members of the VA research community are required to ensure that the apparent non-compliance has been reported in writing to the IRB.
    • Research compliance officer reports of apparent serious or continuing non-compliance.
  • Within five business days of identifying apparent serious or continuing non-compliance based on a consent document audit, regulatory audit, or other systematic audit of VA research, the research compliance officer must provide a written report of the apparent non-compliance directly (without intermediaries) to:
    • Facility director.
    • Associate chief of staff for research.
    • The Research and Development Committee.
    • The IRB.
    • Other relevant research review committees.
  • Within five business days of receiving such notification, the facility director must report the apparent serious or continuing non-compliance to:
    • The appropriate Office of Research Oversight research officer.
    • Veterans Integrated Service Network (VISN) director.
    • Office of Research Development.
  • An initial report of apparent serious or continuing non-compliance based on a research compliance officer consent document audit, research compliance officer regulatory audit, or other systematic research compliance officer audit is required regardless of whether disposition of the matter has been resolved at the time of the report.

• IRB review of apparent serious or continuing non-compliance.
  • The IRB must review a report of apparent serious or continuing non-compliance at the earliest practicable opportunity, not to exceed 30 days after notification. The IRB chair may take interim action to eliminate apparent immediate hazards to participants.
  • Should the IRB determine that the reported incident constitutes serious non-compliance or continuing non-compliance, within five business days after the determination the IRB chair, or designee must provide a written report of the determination directly to:
    • Facility director.
    • Associate chief of staff for research.
    • Research and Development Committee.
    • The RCO, if the apparent serious or continuing non-compliance was identified by an RCO audit, regardless of outcome.
    • Other relevant research review committee.
  • Unless the non-compliance has already been reported, within five business days after
receiving such notification, the facility director must report the determination to:

- The appropriate Office of Research Oversight research officer.
- The VISN director.
- Office of Research Development.

- 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.
- The IRB must reach a determination that serious or continuing non-compliance did (or did not) occur within 30-45 days after receiving a report of apparent non-compliance.
- Remedial actions involving a specific study or research team must be completed within 90-120 days after the IRB’s determination.
- Remedial actions involving programmatic non-compliance must be completed within 120-180 days after the IRB’s determination, unless remediation requires substantial renovation, fiscal expenditure, hiring, or legal negotiations.
- Members of the VA research community must report possible serious or continuing non-compliance with VA or other federal requirements related to human research or with IRB requirements or determinations to the associate chief of staff for research and development and the IRB within five business days after becoming aware of it.
- Policies and procedures describe the reporting of serious or continuing non-compliance to:
  - The Office of Research and Development, if VA-funded.
  - The Regional Office of Research Oversight.
  - The VA Privacy Office, when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information.
  - The VHA Information Security Officer when the report involves violations of VA information security requirements.
  - A research compliance officer identifying serious or continuing noncompliance, during an informed consent or regulatory audit, must report the noncompliance to the facility director, the associate chief of staff for research and development, the Research and Development Committee, and the IRB as soon as possible but no later than five business days after becoming aware of the noncompliance.
  - IRBs of academic affiliates that are the IRB of record for VA facilities must follow the VA requirements.

When following DoD requirements:
- Any determinations of serious or continuing non-compliance of DoD-supported research must be promptly (within 30 days) reported to the DoD human research protection officer.

Outcomes
- Researchers and research staff report allegations of non-compliance to the IRB or EC.
- Non-compliance is identified and managed.
- The IRB or EC or organizational official reports serious or continuing non-compliance as required.
Standard I-6: The organization has and follows written policies and procedures to ensure that research is conducted so that financial conflicts of interest are identified, managed, and minimized or eliminated.

Element I.6.A. The organization has and follows written policies and procedures to identify, manage, and minimize or eliminate financial conflicts of interest of the organization that could influence the conduct of the research or the integrity of the Human Research Protection Program.

Commentary
An organization that conducts or reviews research involving human participants has an obligation to protect the rights and welfare of participants, ensure the integrity of the research, and ensure the credibility of the HRPP. An organization or key organizational leaders sometimes have financial interests that conflict with the organization’s obligation to protect participants, preserve the integrity of the research, or maintain the credibility of the HRPP. For example, an organization or key organizational leader might have a proprietary or ownership interest in research that is being reviewed or conducted by the organization. The fact that a financial interest exists does not necessarily indicate that an organization will act contrary to the best interests of research participants. Policies and procedures should describe the process the organization uses to identify, evaluate, manage, and minimize or eliminate such interests.

Regulatory and Guidance References
- VA: VHA Standards of Ethical Conduct for Employees of the Executive Branch

Required Written Materials

Essential requirements:
- Policies and procedures provide a definition of organizational financial conflict of interest that includes:
  - Licensing, technology transfer, patents.
  - Investments of the organization.
  - Gifts to the organization when the donor has an interest in the research.
  - Financial interests of senior administrators.
  - Other financial interests.

- Policies and procedures describe the process to identify or disclose financial conflicts of interest of the organization:
  - A policy addressing financial conflict of interest pertaining to technology transfer and patents is not required if this matter is addressed in other policies and procedures.
  - A separate policy addressing the identification and management of financial conflicts of interest of senior administrative officials is not required, if this is covered in the organization’s financial conflict of interest policy for individuals.

- Policies and procedures describe the committee or individual(s) and process that the organization uses to evaluate and manage organizational financial conflict of interest.

- Policies and procedure include examples of management strategies.

Common Types of Materials That May Be Used to Meet the Element
- Financial disclosure form
- Organizational policy and procedure on individual conflict of interest that cover senior administrative officials
- Organizational policy and procedure on technology transfer and patents

Outcomes
- The Organization follows policies and procedures for recognizing and managing organizational financial conflicts of interest.
- Financial conflicts of interest are identified, managed, and minimized or eliminated to maintain protection of research participants, ensure the integrity of the research, and ensure the credibility of the HRPP.
Element I.6.B. The organization has and follows written policies and procedures to identify, manage, and minimize or eliminate individual financial conflicts of interest of Researchers and research staff that could influence the conduct of the research or the integrity of the Human Research Protection Program. The organization works with the Institutional Review Board or Ethics Committee in ensuring that financial conflicts of interest are managed and minimized or eliminated, when appropriate.

Commentary
A financial conflict of interest of a researcher or research staff (defined as anyone involved in the design, conduct, or reporting of research) can be broadly defined as an interest that competes with the researcher’s or research staff’s obligation to protect the rights and welfare of research participants, preserve the integrity of the research, or uphold the credibility of the HRPP. Processes to define financial conflict of interest are generally dictated by laws or regulations, and generally vary in terms of what financial interests must be disclosed and when a financial interest is considered a financial conflict of interest. For example, DHHS regulations refer to significant financial interests whereas other laws and codes of conduct for clinical trials do not reference significant financial interests. Further, laws and regulations vary on their requirements regarding managing and reporting financial conflicts of interests, and enforcement of these procedures and education.

An organization should have a policy and procedure to manage or eliminate the financial conflicts of interest of researchers and research staff that meets the laws, regulations, and codes to which it is bound. They should address the primary components of disclosure (what financial interests must be reported and by whom), evaluation and management, monitoring and enforcement, and reporting, and education. Policy and procedures should be consistent but may vary to meet unique requirements of a particular law, regulations, or code when an organization must follow multiple laws, regulations, or codes.

See AAHRPP Tip Sheet 10.

Required Written Materials

Essential requirements:
- Policies and procedures define the financial interests of researchers and research staff for which the organization requires disclosure.
- Policies and procedures require disclosure of:
  - Financial interests of researchers and research staff.
  - Policies and procedure define the individuals who must disclose financial interests.
  - Financial interests of immediate family members.
  - Policies and procedures define immediate family members.
  - Immediate family members at a minimum include the spouse and each dependent child.
- Policies and procedures describe the process and requirements to educate researchers and research staff about disclosures and responsibilities related to financial conflict of interest.
  - Education is required of each individual initially and at least every four years.
  - Education is required immediately when:
    - Financial conflict of interest policies are revised in a manner that changes researcher requirements.
    - A researcher is new to the organization.
    - A researcher is non-compliant with financial conflict of interest policies and procedures.
- Policies and procedures describe the process the organization uses to obtain financial disclosures from researchers and research staff.
  - Minimum of annual disclosure.
  - Update new significant financial interests within 30 days of acquisition or discovery.
- Policies and procedures describe the process the organization uses to evaluate and manage financial interests.
  - The organizational official(s) or committee designated to evaluate and manage.
  - The definition of significant financial interest.

Regulatory and Guidance References
- PHS: 42 CFR 50
- NSF: Award and Administrative Guide IV.A.
- FDA: 21 CFR 54.2(a)-(d), 21 CFR 54.2(f), 21 CFR 54.4(a)(3), 21 CFR 54.4(b)
- VA: VHA Handbook 1200.1 7, VHA Handbook 1200.05, 9, VHA Handbook 1108.04
• The inclusion of relatedness to research in the definition of significant financial interest.
• Designation of the individual or entity that determines relatedness.
• Examples of strategies to manage financial conflicts of interests.

Policies and procedures establish monitoring and enforcement mechanisms for management plans and provide employee sanctions or other administrative actions to ensure researcher compliance.
• Examples of sanctions or other administrative actions.
• Management may include a retrospective review and a mitigation report if necessary.

If a committee or individual other than the IRB or EC evaluates and manages financial interests of researchers and research staff, policies and procedures describe:
• The process to inform the IRB or EC of the results of this evaluation, including any management plan.
• The process that allow the IRB or EC to have the final authority to decide whether the interest and its management, if any, allows the research to be approved.

Policies and procedures ensure that reporting requirements for funding or regulatory agencies are met.

Policies and procedures have the organization maintain records related to disclosures and management of financial conflicts of interest for at least three years from completion of the research.

When following PHS requirements:
• Policies and procedures describe the process the organization uses to obtain disclosures from researchers and research staff of reimbursed or sponsored travel related to institutional responsibilities.

When following VA requirements:
• Policies and procedures indicate:
  • VA facilities are not required to follow PHS requirements, even when research is funded by a PHS agency (e.g., NIH).
  • Affiliates that serve as IRBs of record for VA facilities must use the VA financial conflict of interest form, and may not create, re-draft, or change this form.

Common Types of Materials That May Be Used to Meet the Element
• Financial disclosure form
• Organizational policy and procedure on researcher conflict of interest
• Reviewer checklist

Outcomes
• Conflicts of interest are identified, managed, and minimized to maintain protections of participants, ensure the integrity of research, and ensure the credibility of the HRPP.
• Management plans are monitored and enforced and when necessary, non-compliance is addressed with sanctions or administrative actions.
• Conflicts of interest are reported to regulatory agencies when required by policies and procedures.
Element I.7.A. When research involves investigational or unlicensed test articles, the organization confirms that the test articles have appropriate regulatory approval or meet exemptions for such approval.

Commentary
This Element applies only to an organization that conducts research or an independent IRB or EC that oversees research involving investigational articles regulated by a national regulatory authority.

When research involves an investigational drug, the organization must ensure researchers have approval from regulatory agencies to use the investigational drug in research, or ensure the drug meets an exemption from this requirement. For example, under the U.S. FDA regulations, research that involves the use of a drug other than a marketed drug in the course of medical practice must have an investigational new drug (IND), unless the research meets one of the five exemptions from this requirement. In other countries, researchers must obtain approval from the regulatory authorities in those countries.

When research involves a device, the organization must ensure researchers have approval from regulatory agencies to use the device in research, or ensure the device meets an exemption from this requirement. For example, under U.S. FDA regulations, research that is conducted to determine the safety or effectiveness of a device must have an IDE issued by the U.S. FDA, unless the device meets the requirements for an abbreviated investigational device exemption (IDE) (21 CFR 812.2(b)(1)) or the research meets one of the five exemptions from the requirement for an IDE (21 CFR 812.2(c)). When device research is conducted in other countries, researchers or the sponsor must obtain approval from the regulatory authorities in those countries.

When research involves the use of an investigational drug or device, the organization must confirm approval from regulatory authorities exists before research may commence. For example, in the U.S., organizations must confirm the drug has an IND or meets an exemption from this requirement, and must confirm a device has an IDE, the device fulfills the requirements for an abbreviated IDE, or the research meets one of the FDA exemptions from the requirement to have an IDE. When research involves a drug or device with an IND or IDE, respectively, the organization should evaluate whether the IND or IDE number is valid. This prevents situations where researchers begin studies that require regulatory authority approval, such as an IND or IDE, before the FDA or other regulatory authority has issued a number. Validation can be done by determining that a approval number granted by the regulatory authority, such as an IND or IDE number, matches the sponsor protocol, or communication from the sponsor, or communication from the relevant government regulatory authority. In the case of a researcher who holds the approval from the government regulatory agency, such as an IND or IDE number, the number should match information provided by the government regulatory agency. An investigator’s brochure may not be used because one investigator brochure often covers multiple government-issued approval numbers, for example, multiple INDs or IDEs.

Regulatory and Guidance References
- VA: VHA Handbook 1108.04, VHA Handbook 1200.05, 39
- ICH-GCP 4.65

Required Written Materials

Essential requirements:
- Policies and procedures describe the legal and regulatory requirements that apply to the use of investigational test articles.
- Policies and procedures describe the process the organization uses to confirm that test articles have appropriate regulatory approval, such as a clinical trial certificate or an IND or...
IDE, or meet exemption requirements for such approvals.

**When following FDA regulations:**

- When research involves the use of a drug other than a marketed drug in the course of medical practice, policies and procedures describe the process to confirm that:
  - The drug has an IND or the research meets one of the FDA exemptions from the requirement to have an IND.
- When research is conducted to determine the safety or effectiveness of a device, policies and procedures describe the process to confirm that the device has an IDE issued by the FDA, the device fulfills the requirements for an abbreviated IDE, or the research meets one of the FDA exemptions from the requirement to have an IDE.
  - The IRB or EC makes a determination whether the device is a significant or non-significant risk device.
- When research involves a drug with an IND or a device with an IDE, policies and procedures describe the process to confirm that the IND or IDE number is valid.
  - For FDA-regulated research involving an investigational drug conducted outside of the U.S., an IND is not required provided the research is conducted under the Declaration of Helsinki (1989) and Good Clinical Practice guidelines.
  - For FDA-regulated research involving an investigational drug, the research does not commence until a valid IND is in place.

**When following VA requirements:**

- Policies and procedures have the researcher:
  - Ensure the local Pharmacy Service or Research Service Investigational Pharmacy receives:
    - Documentation of IRB and any other relevant approvals.
  - A copy of VA Form 10-9012 (if applicable).
  - A copy of the current approval protocol.
  - A copy of the consent document for each participating participant with all appropriate signatures.
  - Documentation of IRB continuing review approval.
  - Copies of sponsor-related correspondence specific to the drugs as appropriate.
  - Copies of all correspondence addressed to the researcher from the FDA specific to the investigational drugs as appropriate.
  - Inform the chief, pharmacy service, the research pharmacy when applicable, and the IRB in writing with a 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 drug pharmacist when requested.

**When following requirements in other countries:**

- Organizations must follow requirements outlined in country law, specified in the country-specific AAHRPP Addenda to the Evaluation Instrument.

**Common Types of Materials That May Be Used to Meet the Element**

- Application form
- Reviewer checklist

**Outcomes**

- Research involving the use of investigational articles complies with regulations governing investigational articles.
Element I.7.B. The organization has and follows written policies and procedures to ensure that the handling of investigational or unlicensed test articles conforms to legal and regulatory requirements.

**Commentary**

This Element applies only to an organization that conducts research with investigational or unlicensed test drugs or devices or an independent IRB or EC that reviews a researcher’s plan to control test articles.

An organization should describe the process for handling investigational or unlicensed test articles so that they are used only in approved protocols and under the direction of approved researchers. Possible methods organizations can use to control investigational drugs and devices are:

- Protocol-by-protocol review and approval of the researcher’s plan to control test articles along with training or evaluation of researchers on knowledge and compliance with the plan.
- Organizational control of test articles. For example, organizations can control investigational drugs by having a pharmacy store them and dispense them only under the prescription of an approved researcher.

Procedures for the control of investigational drugs and devices should apply to all settings in which the organization uses investigational drugs and devices, such as inpatient, outpatient, on-site, and off-site settings.

See AAHRPP Tip Sheet 11.

**Regulatory and Guidance References**

- FDA: 21 CFR 312.61, 21 CFR 312.62, 21 CFR 312.69, 21 CFR 812.100, 21 CFR 812.110, 21 CFR 812.140(a)
- VA Handbook 1108.04
- ICH-GCP: 2.12, 2.13, 4.6.1, 4.6.2 – 4.6.4

**Required Written Materials**

*Essential requirements:*

- Policies and procedures describe the control of investigational drugs.
- Policies and procedures describe the control of investigational devices.

*When following the ICH-GCP (E6) guideline:*

- Policies and procedures include:
  - A description of the manufacturing, handling, and storage in accordance with applicable good manufacturing practice.
  - Where allowed or required, the researcher or organization assigns some or all duties for investigational articles accountability at the clinical trial sites to an appropriate pharmacist or another appropriate individual who is under the supervision of the researcher or organization.
  - The researcher, pharmacist, or other designated individual maintains records of the product's delivery to the clinical trial site, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of unused products. These records include dates, quantities, batch or serial numbers, and expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial participants.
  - The researcher maintains records that document adequately that the participants are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor.

**Outcomes**

- Investigational test articles are used only in approved research protocols and under the direction of approved researchers.
- The organization has a process to ensure the proper handling of investigational test articles.
Element I.7.C. The organization has and follows written policies and procedures for compliance with legal and regulatory requirements governing emergency use of an investigational or unlicensed test article.

**Commentary**
This Element applies only to organizations that use investigational or unlicensed test articles in emergency situations, and the use constitutes research and is regulated. The Element also applies to independent IRBs or ECs that review research involving the emergency use of test articles.

Under the U.S. FDA regulations, the use of an investigational test article in an emergency situation is usually exempt from prior IRB or EC review. This exemption is used in a life-threatening situation in which no standard acceptable treatment is available and in which there is insufficient time to obtain IRB or EC approval.

Even without IRB or EC review, the consent of the participant or the participant’s legally authorized representative should be obtained in order to use the investigational article. There are situations in which an exception can be made to the requirement to obtain consent.

An organization should allow researchers to notify the organization in advance of an emergency use to obtain guidance. The organization should review these notifications to determine whether the circumstances will follow regulatory or legal requirements for the emergency use of a test article.

The IRB or EC should be notified of all emergency uses within five days of the use and notified in writing of all exceptions to the requirement for consent within five days of the exception. IRBs or ECs should review these reports to determine whether the circumstances follow regulatory requirements for the emergency use of a test article, and whether consent was obtained in accordance with regulations or the circumstances met the exception to the requirement for consent.

The organization should monitor the emergency use of test articles to ensure that continued use does not occur, which constitutes research.

**Regulatory and Guidance References**

**Required Written Materials**

**Essential requirements:**
- In order to use a test article in an emergency situation, policies and procedures describe the criteria that permit the emergency use of a test article.
- Policies and procedures indicate consent will be obtained in accordance with regulations or laws or meet the requirements for an exception to obtain consent.
- Policies and procedures describe the role of the IRB or EC as appropriate.

**When following DHHS regulations:**
- Policies and procedures state that patients receiving a test article in an emergency use as defined by FDA regulations may not be considered to be a research participant.
- DHHS regulations do not permit data obtained from patients to be classified as human participants research, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations.

**When following FDA regulations:**
- In order to use a test article in a life-threatening situation without prior IRB or EC review, policies and procedures include the following criteria:
  - The participant is in a life-threatening or severely debilitating situation.
  - No standard acceptable treatment is available.
  - There is not sufficient time to obtain IRB or EC approval.
  - The use is reported to the IRB or EC within five working days.
  - Any subsequent use of the test article is subject to IRB or EC review.
- Policies and procedures indicate consent will be obtained in accordance with FDA regulations, or the circumstances meet the exception to the requirement for consent in FDA regulations.
- Policies and procedures state that under FDA regulations, the emergency use of a test article, other than a medical device, is a clinical...
investigation, the patient is a participant, and the FDA may require data from an emergency use to be reported in a marketing application.

When following VA requirements:

- Policies and procedures state that a patient receiving a test article in an emergency use that is regulated by FDA is not considered to be involved in research and is not a research participant.

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<th>Common Types of Materials That May Be Used to Meet the Element</th>
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<td>• Emergency uses of investigational or unlicensed test articles follow regulations or laws.</td>
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Standard I-8: The organization works with public, industry, and private sponsors to apply the requirements of the Human Research Protection Program to all participants.

Element I.8.A. The organization has a written agreement with the sponsor that addresses medical care for research participants with a research-related injury, when appropriate.

Commentary
When appropriate, arrangements for medical care for research-related injury should be defined before the research starts and communicated to prospective participants. (See Element II.3.F.) This Element does not require any particular party, among the organization, sponsor or its agents, or participant to be responsible for such care; it requires that it be made clear to participants who will provide medical care and who will be responsible to pay for it. This Element primarily applies only to the organization that conducts clinical research. If an organization conducts other types of research in addition to clinical research, this Element is generally not applicable, although there might be instances where research-related injury requiring medical care could occur. The organization should evaluate the risk of injury in the research conducted under its auspices and should make determinations whether medical care for research-related injury might be needed.

See AAHRPP Tip Sheet 25.

Regulatory and Guidance References
- DHHS: 45 CFR 46.116(a)(6), 45 CFR 46.116(a)(7)
- FDA: 21 CFR 50.25(a)(6), 21 CFR 50.25(a)(7)

Required Written Materials

Essential requirements:

- Policies and procedures have contracts or other funding agreements indicate who will provide care and who is responsible to pay for it.
- For independent IRBs:
  - If the organization contracts with sponsors or clinical research organizations, contracts or other funding agreements state that sponsors are required to indicate who will provide care and who is responsible to pay for it.
  - Policies and procedures include the process used to ensure that contracts with the researcher indicate who will provide care and who is responsible to pay for it, such as an attestation or other written statement from the researcher or clinical research organization, for examples master service agreement or work order.

Common Types of Materials That May Be Used to Meet the Element
- Contract template
- Reviewer checklist for contract language

Outcomes
- When appropriate, arrangements for medical care for research-related injury are defined before the research starts.
- For independent IRBs attestations or other written statements or agreements describe who will provide care and who is responsible to pay for it.
Element I.8.B. In studies where sponsors conduct research site monitoring visits or conduct monitoring activities remotely, the organization has a written agreement with the sponsor that the sponsor promptly reports to the organization findings that could affect the safety of participants or influence the conduct of the study.

**Commentary**

This Element does not apply when the sponsor is not responsible for monitoring the research. Monitoring of the research refers to overseeing the progress of a research study. An organization that works directly with a sponsor should require the sponsor or its agents to report to the organization findings of serious or continuing non-compliance detected during the monitoring process that could affect the safety of participants or influence the conduct of the study.

If an independent IRB or EC or an organization does not work directly with the sponsor, the independent IRB or EC or organization should have a mechanism to ensure it receives copies of the monitoring reports that contain findings that could affect the safety of participants or influence the conduct of the study. An organization in this case should make the findings available to the IRB or EC.

See AAHRPP Tip Sheet 25.

**Regulatory and Guidance References**

- None

**Required Written Materials**

*Essential requirements:*

- Policy and procedures have contracts or other funding agreements require the sponsor to promptly report to the organization any findings that could:
  - Affect the safety of participants.
  - Influence the conduct of the study.

*For independent IRBs:*

- If the organization contracts with sponsors or clinical research organizations, contracts or other funding agreements state that sponsors are required to promptly report to the IRB findings that could affect the safety of participants or influence the conduct of the study.

- Policies and procedures include the process used to ensure that contracts with the researcher obligate the sponsor to promptly report any findings of study monitors that could affect the safety of participants or influence the conduct of the study to the researcher or organization conducting the research, such as an attestation or other written statement from the researcher or clinical research organization, for example a master service agreement or work order.

- Policies and procedures require researchers or the organization conducting the research to promptly forward this information to the IRB.

**Common Types of Materials That May Be Used to Meet the Element**

- Contract template
- Reviewer checklist for contract language

**Outcomes**

- Contracts and other funding agreements require the sponsor to promptly report to the organization any findings that could:
  - Affect the safety of participants.
  - Influence the conduct of the study.

- An independent IRB or EC or an organization that does not work directly with the sponsor has a mechanism to receive findings that could affect the safety of participants or influence the conduct of the study. An organization in this case makes the findings available to the IRB or EC.
Element I.8.C. When the sponsor has the responsibility to conduct data and safety monitoring, the organization has a written agreement with the sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to the organization.

Commentary

IRB or ECs have the responsibility to ensure that provisions for data and safety monitoring are adequate and that results from data and safety monitoring justify the continuation of IRB or EC approval of the research study.

When the organization works directly with the sponsor, or its agent, and the sponsor, or its agents, has the responsibility for data and safety monitoring, the contract or funding agreement should include arrangements so that data and safety monitoring plans are provided to the organization, or provided to the researcher who provides them to the IRB or EC. Contracts and funding agreements should stipulate that reports from data and safety monitoring are provided to the researcher who provides them to the IRB or EC.

If an independent IRB does not work directly with the sponsor, it should have a mechanism to ensure it receives the data and safety monitoring plan in order to review the research study and results of the data and safety monitoring to ensure that continuation of IRB or EC approval of the research study is justified.

See AAHRPP Tip Sheet 25.

Regulatory and Guidance References

- None

Required Written Materials

Essential requirements:

- Policies and procedures have contracts or other funding agreements require the sponsor to send data and safety monitoring reports to the organization.

- Contracts or other funding agreements specify the time frame for providing routine and urgent data and safety monitoring reports to the organization.

For independent IRBs:

- If the organization contracts with sponsors or clinical research organizations, contracts or other funding agreements state that sponsors are required to send routine and urgent data and safety monitoring reports to the IRB.

- Policies and procedures include the process used to ensure that contracts obligate the sponsor to send routine and urgent data and safety monitoring reports to the researcher or organization conducting the research, such as an attestation or other written statement from the researcher or clinical research organization, for example a master service agreement or work order.

- Policies and procedures require researchers or the organization conducting the research to forward this information to the IRB.

Outcomes

- Contracts or other funding agreements require the sponsor to provide reports of data and safety monitoring to the organization.

- The independent IRB or EC has a mechanism to ensure it receives data and safety monitoring plans prior to IRB or EC approval of the research.

- The independent IRB or EC has a mechanism to ensure it receives routine and urgent reports of data and safety monitoring.
Element I.8.D. Before initiating research, the organization has a written agreement with the sponsor about plans for disseminating findings from the research and the roles that researchers and sponsors will play in the publication or disclosure of results.

**Commentary**

If the organization has a policy regarding the publication of findings from sponsored research and works directly with a sponsor or its agents, contracts or other funding agreements should require the sponsor to follow that policy and procedure. This Element does not apply to the organization that does not directly work with sponsors or to the organization that has no policy regarding the dissemination of findings from sponsored research. See AAHRPP Tip Sheet 25.

**Regulatory and Guidance References**

- None

**Required Written Materials**

*Essential requirements:*

- Policies and procedures have contracts or other funding agreements require the sponsor to follow the organization’s policies and procedures regarding the publication of findings from sponsored research.

**Outcomes**

- Contracts or other funding agreements require the sponsor to follow the organization’s policies and procedures regarding the publication of findings from sponsored research.
Element I.8.E. When participant safety could be directly affected by study results after the study has ended, the organization has a written agreement with the sponsor that the researcher or organization will be notified of the results in order to consider informing participants.

Commentary
In some cases, findings emerge after a research study has ended that directly affect the safety of past participants and were not anticipated at the time the study was designed or conducted. In such cases, past participants should be notified of the new findings. An organization that works directly with a sponsor or its agents should include in the contract or other agreement how such results will be communicated to the organization. See AAHRPP Tip Sheet 25.

Regulatory and Guidance References
- None

Required Written Materials

Essential requirements:
- Policies and procedures have contracts or other funding agreements describe the steps followed to communicate findings from a closed research study to the researcher or organization when those findings directly affect participant safety.
- Policies and procedures have contracts or other funding agreements specify a time frame after closure of the study during which the sponsor will communicate such findings (e.g., two years). Alternatively, the time frame may be based on a specific triggering event (such as completion of data analysis), or left open-ended or the requirement can be included or referred to in a survivor clause.

For independent IRBs:
- If the organization contracts directly with sponsors or clinical research organizations, contracts or other funding agreements include a requirement that sponsors communicate findings from a closed research study to the IRB when those findings directly affect participant safety.
- Specify a time frame or triggering event after closure of the study during which the sponsor will communicate such findings (e.g., two years; or after the close of data analysis), when appropriate.
- Policies and procedures include the process used to ensure that contracts with the researcher obligate the sponsor to notify the researcher or organization conducting the research any study results after the study has ended that could directly affect participant safety, such as an attestation or other written statement from the researcher or clinical research organization, for example a master service agreement or work order.
- Specify a time frame or triggering event after closure of the study during which the sponsor will communicate such findings (e.g., two years; or after the close of data analysis), when appropriate.
- Policies and procedures require researchers or the organization conducting the research to forward this information to the IRB.

Outcomes
- Contracts and other funding agreements describe the steps followed to communicate results from a research study to former participants when those results directly affect their safety or medical care.
- For independent IRBs attestations or other written statements or agreements describe the steps followed to communicate results from a research study to former participants when those results directly affect their safety or medical care, and to inform the IRB.
Standard I-9: The organization has written policies and procedures to ensure that, when sharing oversight of research with another organization, the rights and welfare of research participants are protected.

Commentary
An organization may rely on IRB or EC review, or other services, such as those of the contracting office or conflict of interest committee, of another organization to supplement its resources. Relying upon the services of one or more other organizations can facilitate research and increase the efficiency and cost-effectiveness of review.

There are multiple models of how organizations work together to share resources: reliance agreements, such as with an independent IRB or EC; reliance upon a central IRB or EC; reliance upon a lead IRB or EC; participating in a group of organizations that form a joint IRB or EC; assuming the role of a reviewing IRB or EC; or some combination of options. The options may be used for review of a single study or for review of all research, and organizations may decide to implement multiple options rather than having to select only one model. Regardless of the approach, the roles and responsibilities of each organization must be described in a written agreement.

If an organization relies on the services of another organization, policies and procedures must describe the steps followed to ensure that the reviewing IRB or EC, or other service, protects the rights and welfare of human research participants. Unless explicitly ceded to the reviewing IRB or EC, the organization retains the organization’s responsibilities defined in Domain I, such as control of investigational drugs.

Relying upon an AAHRPP-accredited IRB or EC ensures the reviewing IRB or EC meets accreditation standards. If the organization relies upon a non-accredited IRB or EC, it should ensure the IRB or EC provides appropriate human participant protections, given the risks of the research.

Some services may be provided by either the relying organization or the reviewing IRB or EC; policies and procedures or a written agreement must define shared responsibilities. AAHRPP strongly supports the notion that resources devoted to the evaluation and management of research – whether internally or externally reviewed – should be calibrated appropriately according to the risks posed by the research. This extends to the content, assessment, and implementation of reliance agreements that the written policies and procedures required under this standard are designed to address. Standards and Elements cited below highlight areas where existing policies may need to be revised to address single IRB or EC review. Requirements listed below describe requirements for IRB or EC review; however, similar considerations exist concerning other shared services. See AAHRPP Tip Sheet 24.

Regulatory and Guidance References
- DHHS: 45 CFR 46.103(b)(2), 45 CFR 46.103(d), 45 CFR 46.109(d), 45 CFR 46.114
- ICH-GCP: 4.2.3

Required Written Materials

Essential requirements for IRB or EC review
For AAHRPP-accredited HRPPs that provide IRB or EC review services to other entities, the relied upon organization must have policies and procedures that describe the roles of the reviewing IRB or EC, including:
- Ensuring the structure and composition of the IRB or EC is appropriate to the research reviewed and complies with applicable laws. This includes ensuring the IRB or EC is properly constituted; members are appropriately qualified; that members do not participate in the review of studies in which they have a conflict of interest; and the IRB or EC follows policy to separate business functions from ethics review services. (Standard II.1)
- Conducting review of research to determine that research is ethically justifiable, according to all applicable regulations and laws, including initial review, continuing review, and review of modifications to previously approved research. (Standards II.2, II.3, and II.4)
- Conducting review of the addition of investigative sites to previously approved protocols. The IRB or EC may decide to review these additions as separate protocols or as modifications to
previously approved research, and they may decide to handle such modifications using the expedited procedure rather than the convened IRB or EC for review. When the expedited procedure is used, the IRB or EC must specify the criteria for when the addition of an investigative site is considered to be a minor modification. (Element II.2.F.)

- Ensuring the IRB or EC has the final authority to decide whether researcher or research staff conflict of interest and its management, if any, allows the research to be approved. (Element I.6.B.)
- Reviewing unanticipated problems involving risks to participants or others. (Element II.2.G.)
- Suspending or terminating IRB or EC approval. (Element II.2.H.)
- Notifying the researcher, and if applicable the organization, of its decisions, consistent with any reliance agreement. (Element II.2.E.)
- Making available relevant IRB or EC records, including but not limited to minutes, approved protocols, consent documents, and other records that document the IRB’s or EC’s determinations to the relying organization upon request. (Element II.5.A.)
- Having authority to request an audit of research being reviewed. (Element I.5.A.)
- Making relevant IRB or EC policies readily available to the relying organization, including HRPP staff, and researchers and research staff, and having a mechanism for communicating to the organization when policies are updated, as appropriate. (Element I.1.D.)
- Specifying the contact person and providing contact information for the reviewing IRB or EC for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the IRB or EC. (Element I.5.C.)

For AAHRPP-accredited HRPPs that rely on another organization’s IRB or EC, the relying organization’s policies and procedures must describe the roles of the organization and researchers when relying upon another organization’s IRB or EC, including:

- Specifying which studies are eligible for review by another organization’s IRB or EC, and describing the mechanism for making the determination. (Element I.1.A.)
- Ensuring, through education or other support, that researchers understand which activities are eligible for review by another IRB or EC. (Element III.1.A.)
- Ensuring that researchers are knowledgeable about the need to obtain any approvals from their own organization prior to seeking review by another IRB or EC, and that researchers know when to seek guidance. (Element III.1.A.)
- Complying with the determinations and requirements of the reviewing IRB or EC. (Element III.2.C.)
- Providing the reviewing IRB or EC with requested information about local requirements or local research context issues relevant to the IRB’s or EC’s determination, prior to IRB or EC review.
- Notifying the reviewing IRB or EC when local policies that impact IRB or EC review are updated. (Element I.1.D.)
- Ensuring that officials of the relying organization may not approve the research subject to the reliance agreement if it has not been approved by the reviewing IRB or EC. (Element I.1.C.)
- Acknowledging that researchers must cooperate in the reviewing IRB’s or EC’s responsibility for initial and continuing review, record keeping, and reporting, and that all information requested by the reviewing IRB or EC must be provided in a timely manner. (Element II.2.D.)
- Requiring researchers and research staff disclose conflicts of interest according to the process agreed upon between the organization and reviewing IRB or EC, and comply with any conflict of interest management plans that may result. (Element III.1.B.)
- Reporting promptly to the reviewing IRB or EC any proposed changes to the research. The investigator cannot implement changes to the research (including changes in the consent document) without prior IRB or EC review and approval, except where necessary to eliminate apparent immediate hazards to the participants. (Element III.2.C.)
- Ensuring researchers will not enroll participants in research prior to review and approval by the reviewing IRB or EC, and meeting all other applicable requirements and approvals for the study. (Element III.1.E.)
- Ensuring that researchers, when responsible for enrolling participants, will obtain, document, and maintain records of consent for each participant or each participant’s legally authorized representative. (Element III.1.F.)
- Reporting promptly to the reviewing IRB or EC any unanticipated problems involving risks to
participants or others according to the requirements specified in the reliance agreement. (Element III.2.D.)

- Ensuring researchers provide to the reviewing IRB or EC data safety monitoring reports they receive, according to the IRB’s or EC’s reporting policy. (Element III.2.D.)

- Ensuring reporting of non-compliance, participant complaints, protocol deviations or other events according to the requirements specified in the reliance agreement. (Elements I.5.D., II.2.G, II.2.H., and III.2.D.)

- Conducting monitoring in addition to, or in cooperation with, the reviewing IRB or EC, when appropriate. (Element I.5.D.)

- Specifying the contact person and providing contact information for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the use of the reviewing IRB or EC. (Element I.5.C.)

- Ensuring researchers and research staff have appropriate qualifications and expertise to conduct the research, are knowledgeable about laws, regulations, codes and guidance governing their research, and are knowledgeable about the organization’s policies and procedures. (Element III.2.A.)

**When there is a reliance relationship for IRB or EC review, a written agreement or policies and procedures must describe whether the organization conducting the IRB or EC review, or the relying organization, is responsible for the following:**

- Providing education to researchers and research staff. (Element I.1.E.)

- Conducting scientific review. (Element I.1.F.)

- Ensuring concordance between any applicable grant and the IRB or EC application. (Element II.2.E.)

- Reviewing potential non-compliance, including complaints, protocol deviations, and results of audits:
  - Identifying which organization is responsible for deciding whether each allegation of non-compliance has a basis in fact.
  - Identifying which organization’s process is used to decide whether each incident of non-compliance is serious or continuing. (Element I.5.D.)

- Obtaining management plans for researcher and research staff conflicts of interest. If the relying organization maintains responsibility for this issue, the management plan must be provided to the IRB or EC in a timely manner prior to the decision by the IRB or EC. (Element I.6.B.)

- Managing organizational conflict of interest related to the research. (Element I.6.A.)

- Ensuring that, should termination of a reliance agreement occur, one of the parties clearly is responsible for continued oversight of active studies until closure or a mutually agreed upon transfer of the studies.

- When following DHHS and FDA regulations, policies and procedures or a written agreement must define the responsibilities of the relying organization and reviewing IRB or EC, including but not limited to:
  - Determining whether the relying organization applies its FWA to some or all research, and ensuring the IRB or EC review is consistent with requirements in the relying organization’s FWA.
  - Determining which organization is responsible for obtaining any additional approvals from DHHS when the research involves pregnant women, fetuses, and neonates; or children; or prisoners.
  - Determining which organization is responsible for reporting serious or continuing non-compliance; unanticipated problems involving risks to participants or others; and suspensions or terminations of IRB or EC approval. Reporting may be done by the reviewing IRB or EC, the relying organization, or jointly, but must be clearly defined in policies or a written agreement. (Elements I.5.D., II.2.G., II.2.H., and III.2.D.)

When following NIH policy, policies and procedures must describe responsibilities for single IRB review, including:

- Defining “authorization agreements” as the agreement, also called a reliance agreement, which documents respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

- Specifying in policies and procedures:
  - That the requirement for single IRB review applies to awardees in the United States and participating research sites in the United States.
  - That the requirement for single IRB review does not apply to organizations outside the United States.
• That awardee organizations are responsible for ensuring authorization agreements are in place, and that documentation is maintained.

• Who is responsible for meeting the additional requirements of the NIH Genomic Data Sharing Policy. (Element II.2.E.)

• That 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.

**When relying upon an IRB or EC that is not AAHRPP-accredited, policies and procedures must also define:**

• The process ensuring research is being reviewed appropriately and complies with applicable law and regulations.

• Criteria describing the extent of the review to confirm compliance with the organization’s ethical standards and with applicable law and regulations. The extent of the review of the non-accredited IRB or EC can vary, depending upon the level of risk to participants in the research.

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**Essential requirements for other reviews required by the HRPP**

• When additional reviews relevant to the HRPP are conducted by an external organization, including but not limited to biosafety review, radiation safety review, recombinant DNA research review, human stem cell research review, and conflict of interest review, the relying organization must have policies and procedures describing:
  
  • How the review is documented and communicated to the IRB or EC or other relevant part of the HRPP. (Element I.1.F.)

• The process for the relying organization to inform the external organization of circumstances when the external review must take into account additional regulatory requirements, for example, those of DoD or DoJ. (Element I.1.F.)

• Education for researchers when using these additional reviews. (Element I.1.E.)

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**Outcomes**

• The organization protects the rights and welfare of participants when collaborating with other organizations for oversight of research.
Commentary

Within a Human Research Protection Program (HRPP), responsibilities must be delegated for providing ethical review and oversight of research. These responsibilities are distributed differently in different organizations; in many organizations, the Institutional Review Board (IRB) or Ethics Committee (EC), along with the support personnel and systems, provide these functions. In more complex organizations, there might be multiple IRBs and a general oversight office. This Domain of Standards sets forth requirements for the ethical oversight of research.

An IRB or EC is a body established generally under laws, regulations, codes, and guidance to protect the rights and welfare of human research participants. The HRPP must have mechanisms in place to ensure the independence of its ethics review and oversight functions from other units within the organization, particularly with respect to decision-making regarding the ethics of research involving human participants. IRB or EC structure, composition, operations, and review standards are set forth in laws, regulations, codes, and guidance.

Standard II-1: The structure and composition of the IRB or EC are appropriate to the amount and nature of the research reviewed and in accordance with requirements of applicable laws, regulations, codes, and guidance.

Element II.1.A. The IRB or EC membership permits appropriate representation at the meeting for the types of research under review, and this is reflected on the IRB or EC roster. The IRB or EC has one or more unaffiliated members; one or more members who represent the general perspective of participants; one or more members who do not have scientific expertise; one or more members who have scientific or scholarly expertise; and, when the IRB or EC regularly reviews research that involves vulnerable participants, one or more members who are knowledgeable about or experienced in working with such participants.

Commentary

Laws, regulations, codes, and guidance usually define the requirements of the IRB or EC membership roster. The information in this roster should be used to provide for effective review of research and management of the IRB or EC. For example, if the IRB or EC directs protocols to primary reviewers with scientific or scholarly expertise (professional competence), the information in the IRB or EC roster should be sufficient to implement this function. The IRB or EC roster should include at least one member who represents the perspective of research participants, such as a former or current research participant or a research participant advocate.

At least one individual whose primary interest is scientific, and at least one individual whose primary interest is non-scientific and at least one non-affiliated member should attend meetings. IRB or EC minutes should demonstrate that IRB or EC meetings were convened with members appropriately representing regulatory or legal requirements and the general perspective of participants.

When the IRB or EC reviews research that involves categories of participants vulnerable to coercion or undue influence, if there is not at least one person who is knowledgeable about or experienced in working with such participants present at the meeting, the IRB or EC should defer review until such expertise can be obtained through membership or consultation.

See AAHRPP Tip Sheet 18.
See AAHRPP Tip Sheet 22.
Regulatory and Guidance References

- DHHS: 45 CFR 46.103(b)(3), 45 CFR 46.108(b), OHRP Step-by-Step Instructions on Registering an Institutional Review Board (IRB) or Independent EC (IEC)
- ICH-GCP: 3.2.1, 3.2.3, 3.2.4

Required Written Materials

**Essential requirements:**

- IRB or EC rosters include:
  - Names.
  - Earned degrees.
  - Representative capacities.
  - Scientific/nonscientific status.
  - Affiliation status (whether the IRB or EC member or an immediate family member of the IRB or EC member is affiliated with the organization).
  - Indications of experience sufficient to describe each IRB or EC member's chief anticipated contributions.
  - Employment or other relationship between each IRB or EC member and the organization.
  - Alternate members.
  - The primary members or class of primary members for whom each alternate member can substitute.

- According to IRB or EC rosters:
  - Each IRB or EC has at least five members with varying backgrounds to promote complete and adequate review of research commonly conducted by the organization.
  - No IRB or EC has members who are all males or all females.
  - No IRB or EC has members who represent a single profession.
  - Each IRB or EC has at least one member whose primary concerns are in scientific areas.
  - Each IRB or EC has at least one member whose primary concerns are in nonscientific areas.
  - Each IRB or EC has at least one member who is not otherwise affiliated with the organization and who is not part of the immediate family of a person who is affiliated with the organization.
  - Each IRB or EC has at least one member who represents the perspective of research participants.

**When following VA requirements:**

- For a VA using an academic affiliate’s IRB or other local VA facility’s IRB, policies and procedures indicate:
  - The IRB includes at least two VA employees who hold a minimum of 1/8ths VA-compensated appointments to serve as voting members to each IRB of record, except the VA Central IRB or the central IRB of another federal agency (e.g., National Cancer Institute Central IRB). VA facilities with fewer than ten active protocols are only required to appoint one voting member and one alternate member. Members appointed to affiliate IRBs may be scientific or non-scientific members.
  - Alternate members must have qualifications similar to the member they replace. Alternate members may not serve for a class of members (for example a physician may not serve for all physician regular members, but must be designated to serve for a specific physician member). The individual the alternate is serving for must be referenced specifically by name.
  - At least one VA voting member of the IRB must be in attendance when VA research is discussed at a convened meeting.
  - IRBs serving VA should consider including a veteran or veteran's representative.
  - Physicians, dentists, nurses, pharmacists, social workers, other clinicians, statisticians, and allied health professionals are considered scientists.
  - Veterans whose only relationship with the VA facility is receiving care at a VA facility or receiving benefits from the Veterans Benefits Administration are not considered to be affiliated for the purpose of being an IRB member. Individuals who perform occasional volunteer activities without compensation (WOC) are not considered affiliated. However, those who hold a WOC appointment for volunteer activities other than IRB service are considered to be affiliated. Individuals who have retired from the VA and who are...
receiving VA retirement benefits are considered affiliated.

• The facility director, administrative staff, chief of staff, other senior administrators such as associate or assistant directors, or chief nurse, may observe meetings but not serve as voting or non-voting members of the facility’s IRB. Research office staff including, but not limited to, the associate chief of staff for research and development, the administrative officer for research and development, and IRB administrative staff, may not serve as voting members of the IRB.

• The facility director appoints the privacy officer and information security officer as non-voting members or consultants of the IRB or research and development committee.

• The research compliance officer may serve as a non-voting consultant, as needed, to the VA facility’s IRB. The research compliance officer may not serve as a voting or non-voting member of the IRB. The research compliance officer may attend meetings of the IRB when requested by the IRB or as specified by local procedure. These requirements are also relevant for an affiliate IRB.

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<tr>
<th>Common Types of Materials That May Be Used to Meet the Element</th>
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<td>• IRB or EC roster</td>
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<th>Outcomes</th>
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<tr>
<td>• The IRB or EC roster contains all the required categories and information.</td>
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Element II.1.B. The IRB or EC has qualified leadership (e.g., chair and vice chair) and qualified members and staff. Membership and composition of the IRB or EC are periodically reviewed and adjusted as appropriate.

Commentary
IRB or EC chairs, members, and staff involved in review should have the knowledge, skills, and abilities necessary to carry out the function of the IRB or EC. The membership of the IRB or EC must be qualified through the experience and expertise, or the use of consultants (See Element II.1.E.) to review the research. Which individuals have this expertise is unimportant, provided the expertise is available and applied.

Policies and procedures should define the requirements to be an IRB or EC chair, member, staff, and describe the periodic evaluation of their performance. Policies and procedures should describe the periodic review and adjustment of the membership and composition of the IRB or EC.

See AAHRPP Tip Sheet 7.

Regulatory and Guidance References
- DHHS: 45 CFR 46.107, 45 CFR 46.304, OHRP Guidance on Written Institutional Review Board (IRB) Procedures
- FDA: 21 CFR 56.107, FDA Information Sheets: Non-Local IRB Review, IRB Membership
- VA: 38 CFR 16.107, VHA Handbook 1200.05, 12
- ICH-GCP: 3.2.1, 3.3.1

Required Written Materials

Essential requirements:
- Policies and procedures describe the appointment of:
  - IRB or EC members.
  - IRB or EC chairs and vice-chairs when appropriate.
  - Alternate members.
- Policies and procedures describe the function of alternate members.
- Policies and procedures describe the periodic assessment and feedback provided to:
  - IRB or EC members.
  - IRB or EC chairs, and vice-chairs when appropriate.
  - IRB or EC staff.

When following VA requirements
- Policies and procedures indicate:
  - The facility director is responsible for appointing the IRB chair (or co-chairs, or chair and vice chair), and IRB voting members in writing.
  - IRB members are appointed for a period of up to three years. They may be re-appointed to a new terms of up to three years without a break in service at the end of each term. There is not a maximum number of terms for IRB members as long as the composition of the IRB meets all requirements.
  - The IRB chair (or co-chairs, or chair and vice chair) are appointed for a term of up to three years, and may be re-appointed indefinitely.
  - There may be one IRB chair, co-chairs, or a chair and a vice chair.
  - The IRB chair, co-chairs, and vice-chairs are voting members of the IRB.
  - The IRB chair at the VA facility must be a paid VA employee.

Outcomes
- The IRB or EC is sufficiently qualified through the experience, expertise (professional competence), and diversity of its members to protect the rights and welfare of research participants.
- IRB or EC chairs, members, and staff are knowledgeable.
- The composition of the IRB or EC is periodically evaluated and, when necessary, adjusted so that the membership and composition of the IRB or EC meet legal or regulatory and organizational requirements.
- IRB chairs, vice-chairs and members are periodically evaluated and provided feedback.
Commentary
The IRB or EC review process should be free of conflict of interest so that the IRB or EC member’s obligation to protect participants or ensure the integrity of the review process is not compromised by competing business interests. Competing business interests can influence the review process when individuals responsible for business development serve on the IRB or EC or are involved in the day-to-day operations of the IRB or EC. For example, the director of grants and contracting, the vice president for research, or deans of research who are responsible for raising funds or garnering support for research should not serve as IRB or EC members or be involved in the daily operations of the IRB or EC. For-profit independent IRBs or ECs should separate the business function of the company from the ethics review function. IRB or EC members should not own equity in the company and senior officers in the company who are responsible for business development should not be involved in the daily operation of the review process, such as reviewing or triaging protocols.

Regulatory and Guidance References
- None

Required Written Materials

Essential requirements:
- Policies and procedures prohibit individuals who are responsible for business development from:
  - Serving as members on the IRB or EC.
  - Carrying out day-to-day operations of the review process.
- Policies and procedures prohibit IRB or EC members from owning equity in the organization, if appropriate.

Outcomes
- The organization separates the business functions from the ethics review function.
- Individuals involved in the business function or in research development do not serve as members of the IRB or EC and do not carry out the day-to-day operations of the review process.
Element II.1.D. The IRB or EC has and follows written policies and procedures so that members and consultants do not participate in the review of research protocols or plans in which they have a conflict of interest, except to provide information requested by the IRB or EC.

Commentary

The primary goal of the conflict of interest policy should be to prevent conflicting interests from interfering with the review process either by competing with an IRB or EC member’s or consultant’s obligation to protect participants or by compromising the credibility of the review process. Unlike financial conflict of interest of researchers and research Staff, there is no latitude for the management of an IRB or EC member’s conflict of interest. IRB or EC members must not participate in the review of any protocol in which they have a conflict of interest, except to provide information requested by the IRB or EC.

From time to time, IRBs or ECs use consultants to supplement the review process. Consultants should be queried as to whether they have a conflict of interest. If a consultant has a conflict of interest and is allowed to review the protocol, the IRB or EC should determine by what means the conflict of interest will be disclosed to the convened IRB or EC. An organization should define the criteria for determining whether an IRB or EC member or a consultant has a conflict of interest. This definition should be designed to capture all conflicts of interest that might affect review. When IRB or EC members or consultants have a conflict of interest, they may remain in the room to provide information requested by the IRB or EC. However, they should leave the room before deliberation and voting.

The definition of a conflict of interest should consider both financial and non-financial interests of IRB or EC members and consultants. For example, a non-financial conflict of interest exists when an IRB or EC member or consultant who reviews research is the spouse of the researcher. For financial interests, the level of interest considered to be a conflict should be at least as stringent as the level of a researcher’s financial interest that requires evaluation as a possible conflict of interest.

See AAHRPP Tip Sheet 13.

Regulatory and Guidance References

- DHHS: 45 CFR 46.107(e)
- FDA: 21 CFR 56.107(e)
- VA: 38 CFR 16.107(e), VHA Handbook 1200.05, 3, 12, 28
- ICH-GCP: 3.2.1, 3.2.4, 3.2.5, 3.2.6

Required Written Materials

Essential requirements:

- Policies and procedures indicate IRB or EC members and consultants do not participate in any review in which they have a conflict of interest, except to provide information requested by the IRB or EC.
- Policies and procedures define when an IRB or EC member has a conflict of interest.
  - The definition considers financial issues.
  - The definition considers non-financial issues.
  - The definition is at least as stringent as the level of a researcher’s financial interest that requires evaluation as a possible financial conflict of interest.
- Policies and procedures describe the process to identify IRB or EC members and consultants with a conflict of interest. These policies cover each type of review, such as:
  - Review by a convened IRB or EC.
  - Review by the expedited procedure.
  - Review of unanticipated problems involving risks to participants or others.
  - Review of non-compliance with regulations or laws or the requirements of the IRB or EC.
- Policies and procedures indicate IRB or EC members and consultants with a conflict of interest:
  - Are excluded from discussion except to provide information requested by the IRB or EC.
  - Are excluded from voting except to provide information requested by the IRB or EC.
  - Leave the meeting room for discussion and voting.
  - Are not counted towards quorum.
- IRB members with a conflict are documented in the minutes as being absent with an
indication that a conflict of interest was the reason for the absence.

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<tbody>
<tr>
<td>• Disclosure form</td>
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<td>• Reviewer checklist</td>
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<tr>
<td>• IRB or EC agenda</td>
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<td>• Announcement regarding conflict of interest</td>
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<th>Outcomes</th>
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<tr>
<td>• Conflicts of interest of IRB or EC members and consultants are identified and disclosed.</td>
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<tr>
<td>• IRB or EC members and consultants do not participate in the review of any protocol in which they have a conflict of interest, except to provide information requested by the IRB or EC.</td>
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Element II.1.E. The IRB or EC has and follows written policies and procedures requiring research protocols or plans to be reviewed by individuals with appropriate scientific or scholarly expertise and other expertise or knowledge as required to review the research protocol or plan.

Commentary
The IRB or EC should have the competence and knowledge to review research so that it can protect the rights and welfare of research participants.

To review research, the IRB or EC should have or acquire the scientific or scholarly expertise and other expertise or knowledge to understand the protocol. Policies and procedures should describe the steps to follow so that each protocol undergoes an in-depth review by individuals with relevant expertise and knowledge.

Policies and procedures should describe the steps the IRB or EC uses to assess the scientific or scholarly expertise or other expertise or knowledge required for each protocol submitted for review so that one or more IRB or EC members or consultants with appropriate expertise perform an in-depth review. In the case of an organization with multiple IRBs, this might involve directing the protocol to the IRB or EC with relevant expertise. In the case of an organization that uses a primary reviewer system, this might involve directing the protocol to one or more primary reviewers with relevant expertise. In the case of an organization with multiple IRBs and primary reviewer systems, this might involve both strategies.

If there is not at least one person on the IRB or EC with appropriate scientific or scholarly expertise or other expertise or knowledge to conduct an in-depth review of the protocol, the IRB or EC should defer review until such expertise can be obtained through membership or consultation.

When additional expertise is needed, policies and procedures should describe the steps followed to obtain consultation and communicate the results of the consultation to the IRB or EC.

IRB or EC members may obtain consultations by directly contacting colleagues for information. Such consultations are acceptable provided they are described in policies and procedures and the information is documented.

Required Written Materials

Essential requirements:

- Policies and procedures describe the process so that at least one person with appropriate scientific or scholarly expertise conducts an in-depth review of the protocol.
- Policies and procedures describe the process to determine whether other types of expertise or knowledge are required in order to conduct an in-depth review of the protocol.
- Policies and procedures have the IRB or EC defer to another meeting, IRB or EC, or obtain consultation if there is not at least one person on the IRB or EC with appropriate scientific or scholarly expertise or other expertise or knowledge to conduct an in-depth review of the protocol.
- Policies and procedures describe who evaluates each protocol to determine whether a consultant is needed.
- Policies and procedures describe the process to obtain consultants.
- Policies and procedures indicate consultants do not vote with IRB or EC members.
- Policies and procedures describe the ways in which information provided by consultants is documented.

When following Department of Education (ED) requirements:

- Policies and procedures include that for research funded by the National Institute on Disability and Rehabilitation Research, when an IRB or EC reviews research that purposefully requires inclusion of children with disabilities or individuals with mental disabilities as research participants, the IRB or EC must include at least one person primarily concerned with the welfare of these research participants.

Outcomes

- At least one IRB or EC member or consultant with appropriate scientific or scholarly expertise reviews each protocol in depth.
• When required by the circumstances of the research, at least one IRB or EC member or consultant with appropriate expertise or knowledge other than scientific or scholarly expertise reviews the protocol in depth.

• When the IRB or EC needs additional expertise, the IRB or EC obtains consultation.

• When a consultant is obtained, the IRB or EC is made aware of the information provided by the consultant.
Standard II-2: The IRB or EC evaluates each research protocol or plan to ensure the protection of participants.

Element II.2.A. The IRB or EC has and follows written policies and procedures for determining when activities are exempt from applicable laws and regulations, when permitted by law or regulation and exercised by the IRB or EC. Such policies and procedures indicate that exemption determinations are not to be made by researchers or others who might have a conflict of interest regarding the studies.

Commentary
If the laws, regulations, codes, and guidance under which an organization conducts research involving human participants permit the use of exemptions, the organization should have policies to differentiate between research involving human participants that is exempt and research involving human participants that is not exempt. A determination of exemption should consider the criteria for exemption of all applicable laws, regulations, codes, and guidance, because activities that are exempt from one set of rules might not be exempt from another set of rules. For example, laws and regulations in some countries do not allow exemptions, and in that case even though the research may be covered by DHHS regulations, exemptions would not be allowed.

When research is not covered by DHHS regulations, or other laws or regulations that limit exemptions to specific exemption categories, organizations may define additional exemption categories beyond those specified in regulation. Written materials should define equivalent protections when creating additional exemptions.

The organization should provide written decisions and maintain records of exemption determinations. The person making a decision about whether an activity is exempt should have the authority to represent the organization, and have no direct involvement in the activity he or she is examining. The person making a decision should be familiar with laws, regulations, codes, and guidance governing the research, organizational policies, and the nature of the research to make sound judgments. Policies and procedures should describe the communication of exemption determinations to researchers.

An organization may elect to restrict or not use the categories of exemption, and to require such research to meet all regulatory criteria for approval. If so, this should be stated in policies and procedures.

Generally, the authority to make exemptions determinations rests with the IRB or EC. However, this is not a requirement to meet this Element. For example, exemption determinations may be made by qualified staff who are not members of the IRB or EC. Organizations may choose to delegate to an entity other than the IRB or EC or an individual the authority to make exemption determinations.

For organizations that follow DHHS regulations, when the revised Common Rule goes into effect, some exemption determinations may not be made by staff, but will require a limited IRB review by an IRB or EC member. (See Element II.2.C.)

See AAHRPP Tip Sheet 8.
See AAHRPP Tip Sheet 9.
See AAHRPP Tip Sheet 18.

Regulatory and Guidance References
- FDA: 21 CFR 56.104(c)-(d)

Required Written Materials

Essential requirements:
• Policies and procedures identify the entity or individuals who are authorized to make exemption determinations.
• Policies and procedures define which research studies involving human participants are exempt.
• Policies and procedures inform researchers:
  • Whom to ask for an authoritative decision about whether research involving human participants is exempt from regulation.
  • What information to submit.
• Policies and procedures describe the process to provide determinations about whether research involving human participants is exempt from regulation that includes:
  • Specific titles of persons or offices authorized to make determinations.
  • Criteria used to make determinations.
  • The process used to communicate determinations.
• Exemption determinations may not be made solely by the researcher, or someone with a conflict of interest in the research.

When following DHHS regulations:
• The criteria for exemptions are consistent with:
  • Subpart A of the DHHS regulations.
  • Subpart B of the DHHS regulations.
  • Subpart D of the DHHS regulations.
When following the revised Common Rule when it goes into effect:
• Written materials define benign behavioral intervention, consistent with the organization’s research portfolio.

• When permitted, the IRB or EC may conduct a limited review of the research. (See Element II.2.C.)

When following FDA regulations:
• The criteria for exemptions are consistent with FDA regulations.

When following VA requirements:
• Policies and procedures designate who is authorized to make exemption determinations. Exemption determinations may be made by the research and development committee or a subcommittee, the IRB chair, an experienced voting member of the IRB, IRB administrators, or IRB staff with appropriate qualifications.
• Exemption determinations may not be made solely by the researcher, or someone with a conflict of interest in the research.

Common Types of Materials That May Be Used to Meet the Element
• Application form
• Reviewer checklist
• Template letters to researchers

Outcomes
• The IRB or EC recognizes the difference between exemption criteria that are requirements of laws, regulations, codes, and guidance and additional criteria based on local policy.
• Decisions about whether research involving human participants is exempt are made promptly.
• Decisions about whether research involving human participants is exempt are made accurately.
### Table II.2.A.1. Criteria Allowing Exemption from US Federal Regulations

When following DHHS regulations, written materials should include the following exemption categories when the revised Common Rule goes into effect.

#### Category 1

- The research is conducted in established or commonly accepted educational settings.
- The research involves normal educational practices that are not likely to adversely impact students’ opportunity to learn required educational content or the assessment of educators who provide instruction, such as:
  - Research on regular and special education instructional strategies.
  - Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
- Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
- The research is not regulated by the US FDA.
- For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws).

#### Category 2

*See Element II.2.C. and Table II.2.C.1. regarding requirements for limited IRB or EC review.*

- The research only involves interactions involving one or more of the following:
  - Educational tests (cognitive, diagnostic, aptitude, achievement).
  - Survey procedures.
  - Interview procedures.
  - Observation of public behavior (including visual or auditory recording).
- One of the following conditions are met:
  - The information obtained is recorded in such a manner that participants cannot be identified, directly or indirectly through identifiers linked to the participants.
    - When the research involves children, this exemption only applies to educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed.
  - Any disclosure of the participants’ responses outside the research would not reasonably place the participants at risk of criminal or civil liability or be damaging to the participants’ financial standing, employability, or reputation.
    - When the research involves children, this exemption only applies to educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed.
  - The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB or EC review of the research. (See Element II.2.C.)
    - This condition cannot be applied when research is subject to Subpart D.
- If the research is regulated by the Department of Veterans Affairs:
  - If any disclosure of the participants’ responses outside the research could reasonably place the participants at risk of loss of insurability.
  - Information obtained is not recorded in such a manner that human participants can be identified, directly or through identifiers linked to the participants.
- Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
- The research is not regulated by the US FDA.
- For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)

### Category 3

*See Element II.2.C. and Table II.2.C.1. regarding requirements for limited IRB or EC review.*

Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection.

- Benign behavioral interventions are:
  - Brief in duration.
  - Harmless.
  - Painless.
  - Not physically invasive.
  - Not likely to have a significant adverse lasting impact on the participants.
- The researcher has no reason to think the subjects will find the interventions offensive or embarrassing.
- At least one of the following criteria is met:
  - The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subject; or
  - Any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; or
  - If the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, an IRB conducts a limited IRB review.
- If the research involves deception of participants regarding the nature or purposes of the research:
  - The participant authorizes the deception through a prospective agreement to participate in research in circumstances in which the participant is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.
- Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
- The research is not regulated by the US FDA.
- For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)

### Category 4

Secondary research uses of identifiable private or identifiable biospecimens, if at least one of the following criteria are met:

- The identifiable private information or identifiable biospecimens are publicly available, or
- Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects, or
- The research involves only information collection and analysis, that either:
  - Involves the researcher’s use of identifiable health information when that use is regulated under HIPAA for the purposes of “health care operations,” or “research” or public health activities and purposes as defined in HIPAA.
  - Involves research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section
- Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
- The research is not regulated by the US FDA.
- For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)

### Category 5

- The project is a research or demonstration project.
- The research is conducted by or subject to the approval of a US federal Department or Agency head.
- The research is designed to study, evaluate, improve, or other examine a program that delivers 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) and includes one or more of the following:
  - Procedures for obtaining benefits or services under those programs.
  - Possible changes in or alternatives to those programs or procedures.
  - Possible changes in methods or levels of payment for benefits or services under those programs.
- The research is conducted pursuant to specific statutory authority of the US federal government.
- There is no statutory requirement that an IRB or EC review the research.
- Research does not involve significant physical invasions or intrusions upon the privacy of participants.
- Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
- The research is not regulated by the US FDA.
- For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)

### Category 6

- The research involves taste and food quality evaluation or is a consumer acceptance study.
- Either of the following is true:
  - Wholesome foods without additives are consumed.
  - If a food is consumed that contains a food ingredient or an agricultural chemical or environmental contaminant, the food ingredient or agricultural chemical or environmental contaminant is at or below the level and for a use found to be safe by one of the following:
    - The Food and Drug Administration.
    - The Environmental Protection Agency.
    - The Food Safety and Inspection Service of the U.S. Department of Agriculture.
- Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
- For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)

### Category 7

*See Element II.2.C. and Table II.2.C.1. regarding requirements for limited IRB or EC review.*

Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use:
- The research has undergone limited IRB review by an IRB or EC member.
The researcher plans to obtain broad consent (See Table II.2.C.2.) for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens, including the following disclosures:

- A description of any reasonably foreseeable risks or discomforts to the subject.
- A description of any benefits to the subject or to others that may reasonably be expected from the research.
- A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. (May be omitted if confidentiality will not be maintained.)
- A statement that participation is voluntary.
- A statement that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.
- A statement that the participant may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
- Whether the subject will or will not share in any commercial profit.
- For research involving biospecimens: whether the research will (if known) or might include whole genome sequencing.
- One of the following statements:
  - 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.
- Documentation of consent or waiver of consent was obtained. (See Elements II.3.F. and II.3.G.)
- The researcher does not plan on providing individual research results to participants, unless otherwise required by law.
- If there is a change made for research purposes in the way identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy interests of participants and the confidentiality of data. (See Elements II.3.D. and II.3.E.)
- When some or all of the subjects 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, additional safeguards have been included in the study to protect the rights and welfare of these participants.
- Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
- The research is not regulated by the US FDA.
- For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)

**Category 8**

See Element II.2.C. and Table II.2.C.1. regarding requirements for limited IRB or EC review. Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

- The research has undergone limited IRB review by an IRB or EC member.
- The researcher plans to obtain broad consent (See Table II.2.C.2.) for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens, including the following disclosures:
  - A description of any reasonably foreseeable risks or discomforts to the subject.
  - A description of any benefits to the subject or to others that may reasonably be expected from the research.
• A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. (May be omitted if confidentiality will not be maintained.)
• A statement that participation is voluntary.
• A statement that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.
• A statement that the participant may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.
• Whether the subject will or will not share in any commercial profit.
• For research involving specimens: Whether the research will (if known) or might include whole genome sequencing.
• One of the following statements:
  • 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.
• Documentation of consent or waiver of consent is obtained. (See Elements II.3.F. and II.3.G.)
• The researcher does not plan on providing individual research results to participants, unless otherwise required by law.
• If there is a change made for research purposes in the way identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy interests of participants and the confidentiality of data. (See Element II.3.E.)
• When some or all of the subjects 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, additional safeguards have been included in the study to protect the rights and welfare of these participants.
• Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
• The research is not regulated by the US FDA.
• For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)
Element II.2.B. The IRB or EC has and follows written policies and procedures for addressing protection of participants in research that is exempt from applicable laws and regulations. These functions may be delegated to an entity other than the IRB or EC.

Commentary
Generally, when a research study is determined to be exempt, it is exempt from the laws, regulations, codes, or guidance that govern the research, and there are no required provisions to protect the participants enrolled in the research study. For example, there may be no requirement for IRB review, or only a requirement for a limited IRB or EC review. There may be no requirement for consent, and no prohibition against the use of coercion, undue influence, or deception to recruit participants. Although most exempt research requires no further oversight to be conducted ethically, some exempt research raises ethical concerns or requires measures to protect participants.

This Element looks for a process to address the ethical concerns of research that is exempt. The person who makes determinations of exemption may also conduct the ethical evaluation of exempt research.

See AAHRPP Tip Sheet 8.
See AAHRPP Tip Sheet 9.
See AAHRPP Tip Sheet 18.

Regulatory and Guidance References
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)

Required Written Materials
Essential requirements:
- Policies and procedures describe the evaluation of exempt research as to whether it fulfills the organization’s ethical standards. Such an evaluation might include:
  - The research holds out no more than minimal risk to participants.
  - Selection of participants is equitable.
  - If there is recording of identifiable information, there are adequate provisions to maintain the confidentiality of the data.
  - If there are interactions with participants, the IRB or EC should determine whether there should be a consent process that will disclose such information as:
    - That the activity involves research.
    - A description of the procedures.
    - That participation is voluntary.
    - Name and contact information for the researcher.
  - There are adequate provisions to maintain the privacy interests of participants.

When following the revised Common Rule when it goes into effect:
- When permitted, the IRB or EC may conduct a limited review of the research. (See Element II.2.C.)

When following DOE requirements:
- When conducting classified research, the use of exemptions is prohibited. The fact that research meets a particular exemption category may be noted, but review by a convened IRB is required.

Common Types of Materials That May Be Used to Meet the Element
- Reviewer checklist

Outcomes
- When appropriate, participants involved in exempt research are provided additional protections.
Commentary

When the revised Common Rule goes into effect, organizations that are covered by DHHS regulations may conduct a “limited IRB review” by IRB or EC members of certain exempt research. Limited IRB review is a new requirement created under the revised DHHS regulations, and is unique to DHHS regulations. Under the revised DHHS regulations, some “exempt” research is no longer exempt from requirements for IRB or EC review, but requires limited IRB review. Limited IRB review may not be conducted by staff – it must be conducted by a member of the IRB, and has different requirements from other exempt research. (see Elements II.2.A. and II.2.B.)

For research requiring limited IRB review, there are two different review standards. (See Table II.2.C.1.) Some exempt categories require the IRB or EC reviewer to determine that there are adequate protections for privacy interests of participants and the confidentiality of identifiable data, but other exempt categories require review of broad consent.

When the revised Common Rule goes into effect, written materials should describe a procedure for conducting limited IRB or EC review. Written materials should specify what research is eligible for limited review, the process for limited IRB review, and the required determinations by the reviewer conducting limited IRB review.

Regulatory and Guidance References

• DHHS: 45 CFR 46.111(a)(8)

Required Written Materials

Essential requirements:

• Policies and procedures describe what research is eligible for limited IRB review. (See Table II.2.C.1.)
  • Eligible research is deemed to be no more than minimal risk.
  • If an IRB or EC member reviewing the research finds that research is greater than minimal risk, the reviewer must document the rationale for this determination and the rationale for review by the convened IRB or EC.

• Written materials specify the information that researchers must submit for limited IRB review, including:
  • The full protocol, application, or a protocol summary containing the relevant information to determine whether the proposed research fulfills the criteria for approval.
  • Proposed consent document.
  • Recruitment materials.

• Written materials specify that IRB or EC members conducting limited IRB review may not disapprove research.

• Written materials specify the required determinations when conducting limited IRB or EC review.

• For exemption Categories 2 and 3, there are adequate protections for privacy interests of participants and the confidentiality of identifiable data. (See Table II.2.C.1.)

• For exemption Category 7, broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained. (See Element II.3.F. and Table II.3.F.1.)

• For exemption Category 8, broad consent is appropriately documented or a waiver of documentation is appropriate. (See Element II.3.F. and Element II.3.G., and Table II.3.F.2.)

• Written materials describe the evaluation of exempt research under limited IRB review to whether it fulfills the organization’s ethical standards. (See Element II.2.B.)

• Written materials specify that continuing review is not required for studies that qualify for a limited review.

• Written materials specify that the organization retains the authority to suspend or terminate IRB or EC approval of research approved with a limited review.

Common Types of Materials That May Be Used to Meet the Element

• Application form
• Reviewer checklist

Outcomes

• Reviewers conducting limited IRB or EC review are experienced IRB or EC members.
• Research protocols or plans reviewed by the limited IRB or EC review were eligible for such review and did not require review by a convened IRB or EC or the expedited procedure.
• Research approved through the limited IRB or EC review procedure meets the required criteria for approval.
Table II.2.C.1. Required Determinations for Limited IRB or EC Review

When following DHHS regulations, written materials should include the following exemption categories when the revised Common Rule goes into effect.

- See Element II.2.A. and Table II.2.A.1. for a complete listing of exemption categories and required determinations.
- This table lists only the exemption categories where limited IRB review is required.

Category 2

- Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) where:
  - The information obtained is recorded by the researcher in such a manner that the identity of human participants can be readily ascertained, directly or through identifiers linked to the participants. (§104.104(2)(iii))
  - Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
  - Research does not involve children.
  - The research is not regulated by the US FDA.
  - For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)
  - The IRB or EC must determine there are adequate provisions to protect the privacy interests of research participants and the confidentiality of identifiable data. (See Elements II.3.D. and II.3.E.)

Category 3

- Research involving benign behavioral interventions in conjunction with the collection of information from adult participants through verbal or written responses (including data entry) or audiovisual recording if the participant prospectively agrees to the intervention and where:
  - The information obtained is recorded by the researcher in such a manner that the identity of human participants can be readily ascertained, directly or through identifiers linked to the participants. (§104.104(3)(i)(C))
  - Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
  - The research is not regulated by the US FDA.
  - For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)
  - The IRB or EC must determine there are adequate provisions to protect the privacy interests of research participants and the confidentiality of identifiable data. (See Elements II.3.D. and II.3.E.)

Category 7

- Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use. (§104.104(7))
  - The researcher plans to obtain broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens, including all required disclosures. (See Table II.2.C.2.)
  - Documentation of consent or waiver of consent was obtained. (See Elements II.3.F. and II.3.G.)
• If there is a change made for research purposes in the way identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy interests of participants and the confidentiality of data. (See Elements II.3.D. and II.3.E.)
• When some or all of the subjects 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, additional safeguards have been included in the study to protect the rights and welfare of these participants.
• Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
• The research is not regulated by the US FDA.
• For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)
• The IRB or EC must determine the requirements for broad consent are met, but does not need to determine that other criteria for approval (See Standard II-3) are met.

**Category 8**

• Research involving the use of identifiable private information or identifiable biospecimens for secondary research use. (§____.104(8))
  • There are adequate plans to protect the privacy of participants and the confidentiality of participants’ data.
  • The researcher plans to obtain broad consent (See Table II.2.C.2.) for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens, including the required disclosures. (See Table II.2.C.2.)
  • Documentation of consent or waiver of consent was obtained. (See Elements II.3.F. and II.3.G.)
  • If there is a change made for research purposes in the way identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy interests of participants and the confidentiality of data. (See Element II.3.E.)
  • When some or all of the subjects 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, additional safeguards have been included in the study to protect the rights and welfare of these participants.
  • Research does not involve prisoners, except for research aimed at involving a broader participant population that only incidentally includes prisoners.
  • The research is not regulated by the US FDA.
  • For organizations located outside the US, the research is eligible for an exemption under the laws of that country. (See AAHRPP Addenda for discussion of country-specific laws)
  • The IRB or EC must determine the requirements for broad consent are met, but does not need to determine that other criteria for approval (see Standard II-3) are met.
Element II.2.D. The IRB or EC has and follows written policies and procedures for conducting meetings by the convened IRB or EC.

Commentary
The IRB or EC should have policies and procedures describing the conduct of meetings of the convened IRB or EC. These policies and procedures should allow the IRB or EC to carry out its functions effectively and consistently according to applicable laws, regulations, codes, and guidance and the organization’s policies and procedures.
The IRB or EC should have policies and procedures for developing the meeting agenda and describing functions of the meeting agenda. This should include how the volume of the agenda is controlled or limited to allow for adequate time for discussion of all items on the agenda. If the agenda is used for purposes such as informing members of research protocols or plans approved using the expedited procedure, or identification of member conflict of interest, these uses should be described in policies and procedures.
Meeting agendas should be designed to allow for adequate discussion of each item on the agenda, resolution of controverted issues, and IRB or EC determinations.
The process of IRB or EC review takes time. The definition of timely review depends on organizational culture and the expectations of researchers and those involved with the IRB or EC. Reviews should be timely within the context of the organizational culture.
IRB or EC meetings should be scheduled regularly based on the volume of research to be reviewed. The schedule should promote timely review or re-review of research.
The establishment and maintenance of quorum is essential for the IRB or EC to review and approve research during a meeting. This involves not only appropriate numbers of members, but composition (e.g., a non-scientist must be present). Policies and procedures should describe who determines quorum is established and how it is documented at the beginning and during a meeting.
The widespread use of technology in IRB or EC meetings has necessitated the development of policies and procedures to integrate the use of these technologies in the conduct of meetings and in accordance with any legal or regulatory requirements. This includes policies and procedures for teleconferencing or videoconferencing, or the use of technology or other materials to meet responsibilities, such as displaying and confirming the criteria for approval of research.
Policies and procedures should describe how votes are taken and recorded. For example, votes may be taken by a show of hands, voice vote, or electronic polling. An affirmative vote may be by majority or by consensus.
The role of the IRB or EC chair and vice-chair, if any, should be described in policies and procedures, including whether they vote and have any specific role.
See AAHRPP Tip Sheet 16.
See AAHRPP Tip Sheet 18.

Regulatory and Guidance References
- DHHS: 45 CFR 46.108(b), OHRP Guidance on Written Institutional Review Board (IRB) Procedures
- FDA: 21 CFR 56.108
- VA: 38 CFR 16.107, VHA Handbook 1200.05, 7
- ICH-GCP: 3.3.2
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)

Required Written Materials
Essential requirements:
- Policies and procedures describe:
  - The timing of document distribution before convened IRB or EC meetings.
  - The timing and scheduling of IRB or EC meetings.
  - Limits placed on the number of items on the agenda, if any.
  - Other functions of the agenda, e.g., informing IRB or EC members of research protocols approved using the expedited process.
- Policies and procedures indicate that at convened meetings:
  - A majority of IRB or EC members has to be present.
  - At least one member whose primary concerns are in non-scientific areas has to be present.
For research to be approved it has to receive the approval of a majority of members present at the meeting.

If quorum is lost during a meeting, the IRB or EC cannot take votes until the quorum is restored.

When the convened IRB or EC reviews research involving prisoners, the prisoner representative is present.

At least one unaffiliated member is generally present at convened meetings.

This may be accomplished by one of the following:

- Requiring an unaffiliated member as part of quorum.
- Placing an attendance requirement on the unaffiliated member (e.g., attend 10 of 12 meeting per year).
- Documenting the general attendance of the unaffiliated member (e.g., minutes indicate attendance at 10 of 12 meetings).

At least one member who represents the perspective of participants is generally present at convened meetings.

This may be accomplished by one of the following:

- Requiring a member who represents the perspective of participants as part of quorum.
- Placing an attendance requirement on the member (e.g., attend 10 of 12 meeting per year).
- Documenting the general attendance of the member (e.g., minutes indicate attendance at 10 of 12 meetings).

If the IRB or EC reviews research that involves categories of participants vulnerable to coercion or undue influence, one or more individuals who are knowledgeable about or experienced in working with such participants are present.

Policies and procedures describe who determines quorum is established and how it is documented.

Policies and procedures state that if quorum is lost during a meeting, the IRB or EC cannot take votes until the quorum is restored.

If required members (e.g. non-scientific) leave the room and quorum is lost votes cannot be taken until the quorum is restored, even if half of the members are still present.

Policies and procedures describe the use of any materials or technology used to conduct meeting or meet regulatory requirements. For example, all members have laptop computers to access materials; handouts, posters, or projections contain the criteria for approval; or meetings are conducted over the Internet.

Policies and procedures describe how votes are taken and documented, and what constitutes approval.

Policies and procedures describe the role of the chair and vice-chair, if there are vice-chairs:

- Voting responsibilities.
- Role of the chair and vice-chair prior to, during, and after the meeting.

When following VA requirements:

- When the IRB of record is an affiliate’s IRB, policies and procedure indicate that at least one of the VA members has to be present during the review of VA research.

When following DOE requirements:

- When conducting classified research, the IRB must have a voting quorum of at least five members, which must include both a non-scientist and a non-affiliated member.
- The non-affiliated member must be a non-governmental member with the appropriate security clearances. This individual cannot be a current federal employee or contractor.
- Any IRB member can appeal a vote to approve research to the Institutional Official, Secretary of Energy, and Director of the Office of Science and Technology, in that order.

Common Types of Materials That May Be Used to Meet the Element

- Policies and procedures
- Meeting materials

Outcomes

- The IRB or EC conducts convened meetings according to policies and procedures.
- IRB or EC members receive materials in enough time prior to the meeting to review them.
- The IRB or EC meets regularly to promote timely reviews.
- Meeting agendas allow for adequate discussion and determinations for all research under review.
- During a meeting, the IRB or EC votes and takes actions only when there is a quorum.
• The chair and vice-chair, if any, fulfill their roles according to policies and procedures.
Element II.2.E. The IRB or EC has and follows written policies and procedures to conduct reviews by the convened IRB or EC.

Element II.2.E.1. – Initial review
Element II.2.E.2. – Continuing review
Element II.2.E.3. – Review of proposed modifications to previously approved research

Commentary
The IRB or EC should have policies and procedures that describe the review of research at convened meetings, including initial review, continuing review, and review of modifications to previously approved research.

The IRB or EC should obtain and review sufficient information to conduct initial review of research, continuing review, and review or modifications to previously reviewed research in accordance with the regulations and the organization’s written materials. When they are scheduled to attend an IRB or EC meeting, all members (including alternate members) should review enough information so that they will be able to determine whether the research meets the regulatory criteria for approval.

Written materials should describe the information provided to all IRB or EC members and the information provided to all primary reviewers with the expectation that IRB or EC members will review the materials and the primary reviewer will conduct an in-depth review. When an organization has an electronic system that provides members access to materials, policies and procedures should describe what information primary reviewers are expected to review and what information all other members are expected to review.

When the convened IRB or EC requires modifications to research to secure approval (sometimes referred to as “approval with conditions” or “conditional approval” or “contingent approval”), verification of those modifications may be made by a staff member or IRB or EC member designated by the IRB or EC chair, or by the IRB or EC chair. Verification of modifications is not considered review using an expedited procedure. When the IRB or EC grants conditional approval, the IRB or EC should provide the researcher specific modifications required to secure approval. For example, “Participants must be 18 years or older” or “Drop the placebo controlled arm of this study.”

The convened IRB or EC should not grant approval contingent upon clarifications or modifications directly relevant to criteria for approval specified in regulations. Such requests include: “Explain why participants younger than 18 years of age will be allowed to participate,” “Provide additional justification for the use of placebo,” or “Clarify whether participants will be offered counseling services at the end of the study.” The convened IRB or EC should review responses to requests for substantive modifications relevant to the criteria for approval.

An IRB or EC serving as a single IRB for a multi-site study, should have a policy and procedure for reviewing the addition of investigative sites to previously approved protocols. When serving as a single IRB for a multi-site study, the independent the IRB or EC may decide to review these additions as separate protocols or as modifications to previously approved research, and they may decide to handle such modifications using the expedited procedure rather than the convened IRB or EC for review. When the expedited procedure is used, the independent IRB or EC written materials should specify the criteria for when the addition of an investigative site is considered to be a minor modification.

See AAHRPP Tip Sheet 16.

Regulatory and Guidance References

- DoD: Instruction 3216.02 4.b.4
- ICH-GCP: 3.2.2, 3.2.3, 3.3.3, 3.3.4

Required Written Materials

Essential requirements:

- Policies and procedures describe the process the IRB or EC uses to review research for initial review, continuing review, and review of modifications to previously approved research:
  - The primary reviewer system used, if any.
  - The process used to supplement the IRB’s or EC’s review.
- The range of possible actions that the IRB or EC is allowed to take.
• If the IRB approves research with conditions:
  • Substantive changes or requirements, requests for more information for IRB consideration, and other issues related to the criteria for approval require review and approval by the convened IRB or EC.
  • Minor or prescriptive changes or requirements may be reviewed for approval by a staff member or IRB or EC member designated by the IRB or EC chair, or by the IRB or EC chair.
  • Written materials describe how the date of approval is calculated, consistent with applicable law, regulations, and guidance.
  • Written materials describe a process for the IRB or EC to determine which protocols need review more often than annually. The IRB or EC should consider:
    • The nature of and any risks posed by the clinical investigation.
    • The degree of uncertainty regarding the risks involved.
    • The vulnerability of the participants.
    • The experience of the clinical investigator in conducting clinical research.
    • The IRB’s or EC’s previous experience with that researcher or sponsor (e.g., compliance history, previous problems with the researcher obtaining informed consent, prior complaints from participants about the researcher).
    • The projected rate of enrollment.
    • Whether the study involve novel therapies.
  For initial review of research by a convened IRB, policies and procedures indicate that when they are scheduled to attend an IRB or EC meeting, all members (including attending alternate members) are provided and review:
    • The full protocol, application, or a protocol summary containing the relevant information to determine whether the proposed research fulfills the criteria for approval.
    • Proposed consent document.
    • Recruitment materials.
  At least one member is provided and reviews the investigator’s brochure (when one exists).
  • For continuing review of research by a convened IRB or EC, policies and procedures indicate that, when they are scheduled to attend an IRB or EC meeting, all IRB or EC members (including alternate members) are provided and review:
    • The full protocol, application, or a protocol summary containing the relevant information necessary to determine whether the proposed research continues to fulfill the criteria for approval.
    • The current consent document.
    • Any newly proposed consent document.
    • A status report on the progress of the research.
  • For continuing review of research by a convened IRB or EC, policies and procedures indicate that at least one IRB or EC member is provided and reviews the complete protocol including any protocol modifications previously approved by the IRB or EC.
  • The status report on the progress of the research includes:
    • The number of participants accrued.
    • A summary since the last IRB review of:
      • Adverse events and adverse outcomes experienced by participants.
      • Unanticipated problems involving risks to participants or others.
      • Participant withdrawals.
      • The reasons for withdrawals.
      • Complaints about the research.
      • Amendments or modifications.
      • Any relevant recent literature.
      • Any interim findings.
      • Any relevant multi-center trial reports.
    • The researcher’s current risk-potential benefit assessment based on study results.
  • Policies and procedures have the IRB or EC use the required criteria for approval for all reviews of research, including initial review, continuing review, and review of a modification to previously approved research (when the modification affects a criterion for approval).
  • Policies and procedures have the IRB or EC determine whether continuing review should occur at an interval less than one year, when continuing review is required.
  • Policies and procedures describe:
    • Whether the expiration date is the last date that the protocol is approved or the first date that the protocol is no longer approved.
    • The calculation of the expiration date.
  • If the IRB approves research with conditions:
    • Substantive changes or requirements, requests for more information for IRB consideration, and other issues related to the criteria for approval require review and approval by the convened IRB or EC.
    • Minor or prescriptive changes or requirements may be reviewed for approval by a staff member
or IRB or EC member designated by the IRB or EC chair, or by the IRB or EC chair.

- Written materials describe how the date of approval is calculated, consistent with applicable law, regulations, and guidance.

- If the research expires before the conditions are reviewed and approved, written materials:
  - Have all research activities stop.
  - Have interventions and interactions on current participants stop, unless the IRB or EC finds an over-riding safety concern or ethical issue involved such that it is in the best interests of individual participants to continue participating.
  - Do not allow new enrollment of participants to occur.

- Policies and procedures describe:
  - The organizational offices and officials who are notified of the findings of the IRB or EC and the method of notification.
  - The person or office that is responsible for further approval or disapproval of research that is approved by the IRB or EC.
  - The process the IRB or EC uses for reporting its findings and actions to researchers in writing, including:
    - The decision to approve, disapprove, or require modifications to secure approval.
    - Any modifications or clarifications required by the IRB as a condition for IRB approval.
    - If an IRB decides to disapprove a research activity, a statement of the reasons for its decision and giving the researcher an opportunity to respond in person or in writing.
  - The review of researchers’ responses.

- For continuing review of research, policies and procedures have the IRB or EC determine:
  - That the protocol needs verification from sources other than the researchers that no material changes had occurred since previous IRB or EC review.
  - That the current consent document is still accurate and complete.
  - That any significant new findings that arise from the review process and that might relate to participants’ willingness to continue participation will be provided to participants.

- If a researcher does not provide continuing review information to the IRB or EC or the IRB or EC has not approved a protocol by the expiration date, written materials:
  - Have all research activities stop.
  - Have interventions and interactions on current participants stop, unless the IRB or EC finds an over-riding safety concern or ethical issue involved such that it is in the best interests of individual participants to continue participating.
  - Do not allow new enrollment of participants to occur.

- For review of modifications to previously approved research by a convened IRB or EC, policies and procedures indicate that, when they are scheduled to attend a meeting, all members (including alternate members) receive and review all modified documents.

- Policies and procedures have:
  - The IRB or EC use the criteria to approve modifications to previously approved research when the modifications affect one or more criteria.
  - The IRB or EC determine that any significant new findings that arise from the review process and that might relate to participants’ willingness to continue participation are provided to participants.
  - Changes in approved research that are initiated without IRB or EC approval to eliminate apparent immediate hazards to the participant:
    - Are promptly reported to the IRB or EC.
    - Are reviewed by the IRB or EC to determine whether each change was consistent with ensuring the participants’ continued welfare.
  - Researchers report to the IRB or EC proposed changes in a research study.
  - Researchers report to the IRB or EC the premature completion of a study.

- Policies and procedures describe actions taken to ensure that proposed changes in approved research during the period for which IRB or EC approval had already been given cannot be initiated without IRB approval.

**When following DHHS regulations:**

- For initial review of research by a convened IRB or EC, policies and procedures indicate that at least one member is provided and reviews:
  - The DHHS-approved sample consent document (when one exists).
  - The complete DHHS-approved protocol (when one exists).

**When following VA requirements:**

- Policies and procedures indicate:
  - If a researcher does not provide continuing review information to the IRB or the IRB has not
approved a protocol by the expiration date, policies and procedures:

- Stop all research activities including, but not limited to, enrollment of new participants, analysis of individually identifiable data, and research interventions or interactions with currently enrolled participants, except where stopping such interventions or interactions could be harmful to participants.
- Immediately submit to the IRB chair a list of research participants who could be harmed by stopping study procedures.
- The IRB chair, with appropriate consultation with the chief of staff, determines within two business days whether participants on the list may continue participating in the research interventions or interactions.

When following DoD requirements:

- Surveys 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.
- For DoD-supported research, the following must be promptly (within 30 days) reported to the DoD human research protection officer:
  - When significant changes to the research protocol are approved by the IRB.
  - The results of the IRB continuing review.
  - Change of reviewing IRB.
  - When the organization 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.

Common Types of Materials That May Be Used to Meet the Element

- Reviewer checklist
- Template letters for notifications

Outcomes

- All IRB or EC members (including alternate members) review materials in enough depth to discuss the information when they are present at the convened meeting.
- At least one IRB or EC member conducts an in-depth review of all submitted materials.
- IRB or EC members can obtain information provided to any individual reviewer.
- Each approved research protocol or plan meets the required criteria for approval.
- The approval period for research is no longer than one year, when continuing review is required.
- The IRB or EC communicates its findings to the organization and researchers.
Element II.2. The IRB or EC has and follows written policies and procedures to conduct reviews by an expedited procedure, if such procedure is used.

Element II.2.F.1. – Initial review
Element II.2.F.2. – Continuing review
Element II.2.F.3. – Review of proposed modifications to previously approved research

Commentary
If the laws, regulations, codes, and guidance under which an organization conducts research involving human participants permit one or more IRB or EC members to conduct review of research outside of a convened IRB or EC meeting, written materials should describe a procedure for “expedited review.” In general, requirements and criteria to conduct review using the expedited procedure are identical to those for review by the convened IRB or EC. Written materials should specify what research is eligible for expedited review, and whether any additional IRB or EC review is required after initial review and approval.

If laws, codes, and regulations do not require continuing review of the research by the IRB or EC, nevertheless, written materials must describe an alternate process, such as staff review, for the organization to maintain oversight over the research initially reviewed using the expedited procedure, as long as the research is ongoing. When the IRB or EC is not required to conduct continuing review, records must provide a rationale for any decisions to conduct continuing review of research otherwise eligible for review using the expedited procedure.

When research is not covered by DHHS regulations or other laws or regulations that specify that only certain categories of research are eligible for expedited review, organizations may define additional categories of research beyond those specified in regulation to conduct expedited review. Written materials should define equivalent protections when creating additional categories of research that may be reviewed using an expedited procedure.

See AAHRPP Tip Sheet 17.
See AAHRPP Tip Sheet 18.

Regulatory and Guidance References
- FDA: FDA Information Sheets: Continuing Review after Study Approval
- DoD: Instruction 3216.02 4.b.4., SECNAVINST 3900.39D, para. 6e; OPNAVINST 5300.8B
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)
- ICH-GCP: 3.3.5
- VA: 38 CFR 46.110, 45 CFR 46.110, 21 CFR 56.110, VHA Handbook 1200.05, 10, 22, 44

Required Written Materials

Essential requirements:
- Policies and procedures describe:
  - That only experienced IRB or EC members may conduct reviews using the expedited procedure.
  - “Experienced” is defined in terms of professional competence.
- The conduct of:
  - Initial review.
  - Continuing review, when required by law or regulation.
  - Review of modifications using the expedited procedure, when required by law or regulation.
- Modifications that are “minor” are defined.
- The information that researchers have to submit for review using the expedited procedure.
- That at least one reviewer receives and reviews the same materials that the convened IRB or EC receives for protocols reviewed by the convened IRB or EC. (See Element II.2.E.)
- The evaluation by the reviewer of research undergoing initial review and continuing review, when required by law or regulation, using the expedited procedure.
- The criteria for approval using the expedited procedure are the same as those for review by
a convened IRB or EC, unless otherwise specified in law or regulation.

• The prohibition of the reviewer to disapprove research.

• The process for informing IRB or EC members about approvals by review using the expedited procedure, including:
  • Initial review.
  • Continuing review, when required by law or regulation.
  • Review of modifications to previously approved research.

• When continuing review of research is required by law or regulation, policies and procedures indicate that at least one IRB or EC member is provided and reviews the complete protocol, including any protocol modifications previously approved by the IRB or EC.

• The status report on the progress of the research includes:
  • Number of participants accrued.
  • A summary since the last IRB review of:
    • Adverse events, untoward events, and adverse outcomes experienced by participants.
    • Unanticipated problems involving risks to participants or others.
    • Participant withdrawals.
    • The reasons for withdrawals.
    • Complaints about the research.
    • Amendments or modifications.
    • Any relevant recent literature.
    • Any interim findings.
    • Any relevant multi-center trial reports.
    • The researcher’s current risk-potential benefit assessment based on study results.

• When continuing review of research is required by law or regulation, policies and procedures have the IRB or EC members determine:
  • That the protocol needs verification from sources other than the researchers that no material changes had occurred since previous IRB or EC review.
  • That the current consent document is still accurate and complete.
  • That any significant new findings that arise from the review process and that might relate to participants’ willingness to continue participation will be provided to participants.

• When continuing review is required by law or regulation, if a researcher does not provide continuing review information to the IRB or EC or the IRB or EC has not approved a protocol by the expiration date, policies and procedures:
  • Have all research activities stop.
  • Have interventions and interactions on current participants stop, unless the IRB or EC finds an over-riding safety concern or ethical issue involved such that it is in the best interests of individual participants to continue participating.
  • Do not allow new enrollment of participants to occur.

When following DHHS regulations:

• Policies and procedures describe:
  • The designation by the IRB or EC chair of IRB or EC members who may conduct review using the expedited procedure.
  • The evaluation by the reviewer of whether research undergoing initial review and continuing review using the expedited procedure:
    • Meets all applicability criteria.
    • Represents one or more approvable categories of research.
  • Continuing review of research is required at least annually.

When following the revised Common Rule when it goes into effect:

• Policies and procedures describe:
  • The designation by the IRB or EC chair of IRB or EC members who may conduct review using the expedited procedure.
  • Written materials describe the conduct initial review using the expedited procedure, including the following required regulatory determinations.

  When the research:
  • Does not involve more than minimal risk.
  • Research appearing on the list of expedited review categories is deemed to be no more than minimal risk.
  • If a reviewer finds that research appearing on the expedited review list is greater than minimal risk, the reviewer must document the rationale for this determination and the rationale for review by the convened IRB or EC.
  • Represents one or more approvable categories of research.
• Does not include activities where identification of the subjects 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.
• Does not involve classified research.

• Continuing review of research must occur at intervals appropriate to the degree of risk, but not less than once a year.
• The IRB or EC must determine which clinical investigations require review more than annually.
• The IRB or EC must determine which clinical investigations need verification from sources other than the clinical investigator that no material changes in the research have occurred since the previous IRB or EC review. The IRB or EC should consider:
  • The nature of and any risks posed by the clinical investigation.
  • The degree of uncertainty regarding the risks involved.
  • The vulnerability of the participants.
  • The experience of the clinical investigator in conducting clinical research.
  • The IRB’s or EC’s previous experience with that researcher or sponsor (e.g., compliance history, previous problems with the researcher obtaining informed consent, prior complaints from participants about the researcher).
  • The projected rate of enrollment.
  • Whether the study involve novel therapies.

When following 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, policies and procedures:
  • Stop all research activities including, but not limited to enrollment of new participants, continuation of research interventions or interactions with currently enrolled participants, and data analysis.
  • Immediately submit to the IRB chair a list of research participants who could be harmed by stopping study procedures.
  • The IRB chair, with appropriate consultation with the chief of staff, determines whether participants on the list may continue participating in the research interventions or interactions.

When following DoD requirements:

Written materials specify that continuing review by the IRB or EC or an expedited reviewer is not required when:
• Research meets one or more categories of research that qualify for expedited review.
• Research has progressed to the point that it involves only one or both of the following:
  • 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.
• The IRB or EC must justify the decision to conduct continuing review of research originally reviewed using the expedited procedure.

When following FDA regulations:
• Written materials describe:
  • The designation by the IRB or EC chair of IRB or EC members who may conduct review using the expedited procedure.
  • The evaluation by the reviewer of whether research undergoing initial review and continuing review using the expedited procedure:
    • Represents one or more approvable categories of research.
    • Does not include activities where identification of the subjects 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.
• Does not involve classified research.
Surveys 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.

For any DoD-supported researcher, the following must be promptly (within 30 days) reported to the DoD human research protection officer:

- When significant changes to the research protocol are approved by the IRB.
- The results of the IRB continuing review.
- Change of reviewing IRB.
- When the organization 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.

When following DOE requirements:

- When conducting classified research, the use of the expedited review procedure is prohibited.

**Common Types of Materials That May Be Used to Meet the Element**

- Application form
- Reviewer checklist

**Outcomes**

- Reviewers using the expedited procedures are experienced IRB or EC members.
- Research protocols or plans reviewed by the expedited procedure were eligible for such review and did not require review by a convened IRB or EC.
- Research approved by the expedited procedure meets the required criteria for approval.
<table>
<thead>
<tr>
<th>Table II.2.F.1. Expedited Review Criteria</th>
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<tr>
<td>When following DHHS regulations, written materials should include the following expedited categories when the revised Common Rule goes into effect.</td>
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</table>

**Category 1**

Clinical studies of drugs and medical devices only when condition (a) or (b) is met.

- Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (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.)
- Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

**Category 2**

Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

- from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
- 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. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

**Category 3**

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

- hair and nail clippings in a nondisfiguring manner;
- 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;
- excreta and external secretions (including sweat);
- uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue;
- placenta removed at delivery;
- amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;
- 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;
- mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
- sputum collected after saline mist nebulization.

**Category 4**

Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:

- 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.

<table>
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<tr>
<th>Category 5</th>
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<tr>
<td>Research involving materials (data, documents, records, or specimens) that:</td>
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<tr>
<td>- have been collected for nonresearch purposes (such as medical treatment or diagnosis), or</td>
</tr>
<tr>
<td>- will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).</td>
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(Some research in this category may be exempt from the DHHS regulations for the protection of human subjects.)

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<tr>
<th>Category 6</th>
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<tr>
<td>Collection of data from voice, video, digital, or image recordings made for research purposes.</td>
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<th>Category 7</th>
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<tr>
<td>Research on individual or group characteristics or behavior including, but not limited to:</td>
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<td>- research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or</td>
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<td>- research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.</td>
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<th>Category 8</th>
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<td>Continuing review of research previously approved by the convened IRB as follows:</td>
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<td>- the research is permanently closed to the enrollment of new subjects;</td>
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<td>- all subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subjects; or</td>
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<td>- where no subjects have been enrolled and no additional risks have been identified; or</td>
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<td>- where the remaining research activities are limited to data analysis.</td>
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(When following the revised DHHS regulations, when the revised Common Rule goes into effect, continuing review is not required for research reviewed using the expedited procedure, and the IRB or EC must provide justification for conducting continuing review of research deemed to meet expedited criteria.)

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<th>Category 9</th>
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<td>Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.</td>
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Element II.2.G. The IRB or EC has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and for reporting these actions, when appropriate.

Commentary

An organization should have an effective policy and procedure to ensure prompt reporting to the IRB or EC, appropriate organizational officials, and regulatory agencies of unanticipated problems involving risks to participants or others. The policy must inform researchers of the type of information that needs to be reported to the IRB or EC. Each item of information reported by researchers might or might not be an unanticipated problem involving risks to participants or others. For example, an IRB or EC might ask researchers to report all breaches of confidentiality. The IRB or EC determines that some of these are unanticipated problems involving risks to participants or others and others are not.

When the IRB or EC obtains new information, including adverse event reports, publications, complaints, revised package inserts, data monitoring reports, breaches of confidentiality, or other material, it should decide whether the information represents an unanticipated problem involving risks to participants or others. If so, the IRB or EC should decide what actions need to be taken and then report the outcome to regulatory agencies and appropriate organizational officials. If not, no further evaluation is needed (unless the problem involves non-compliance).

An organization should develop a process for managing adverse event reports as they relate to unanticipated problems involving risks to participants or others. An organization should limit the information reported to the IRB or EC to adverse events that are unexpected, involve increased risks, and are related to the research.

See AAHRPP Tip Sheet 11.
See AAHRPP Tip Sheet 15.
See AAHRPP Tip Sheet 21.
See AAHRPP Tip Sheet 23.

Required Written Materials

Essential requirements:

- Policies and procedures define the problems researchers have to report to the IRB or EC and the time frame for reporting.
- The list of problems that need reporting includes:
  - Internal adverse events that are unexpected, involve new or increased risks, and are related to the research.
  - External adverse events that are unanticipated problems involving risks to participants or others.
  - Changes made to the research without prior IRB or EC approval in order to eliminate apparent immediate harm.
  - Other unanticipated information that is related to the research and indicates that participants or others might be at increased risk of harm.
- Policies and procedures define unanticipated problems involving risks to participants or others.
- Policies and procedures describe:
  - The review of problems reported by researchers.
  - The determination of whether each reported problem is an unanticipated problem involving risks to participants or others.

Regulatory and Guidance References

- DHHS: 45 CFR 46.103(b)(5)(i), 45 CFR 46.116(b)(5), OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, OHRP Guidance on Reporting Incidents to OHRP
- DoD: Instruction 3216.02 4.b.4., SECNAVINST 3900.39D, para. 8d(2), para. 8e(6), and para. 8g(6)
- VA: 38 CFR 16.103(b)(5)(i), 38 CFR 16.116(b)(5), VHA Handbook 1058.01, VHA Handbook 1200.05, 11,14,42; Guidance: Examples and a Brief Guide for Reporting Apparently Serious or Apparently Continuing Noncompliance in Human Research That May Be Reportable to ORO under VHA Handbook 1058.01
- ICH-GCP: 3.3.8, 4.5.2, 4.5.3, 4.5.4, 4.10.2
Policies and procedures describe the review process of unanticipated problems involving no more than minimal risks to participants or others.

Policies and procedures describe the convened IRB’s or EC’s review of unanticipated problems involving more than minimal risks to participants or others, including:
- If a primary reviewer system is used, documents distributed to primary reviewers.
- Documents distributed to all IRB or EC members.

Policies and procedures describe the range of actions considered by the IRB or EC:
- Required actions:
  - Suspension of the research.
  - Termination of the research.
  - Notification of current participants when such information may relate to participants’ willingness to continue to take part in the research.
- Optional actions:
  - Modification of the protocol.
  - Modification of the information disclosed during the consent process.
  - Providing additional information to past participants.
  - Requiring current participants to re-consent to participation.
  - Modification of the continuing review schedule.
  - Monitoring of the research.
  - Monitoring of the consent process.
  - Referral to other organizational entities.

Policies and procedures describe the reporting of problems determined to represent unanticipated problems involving risks to participants or others, including:
- The distribution of the report to:
  - Specific organizational officials.
  - Regulatory agencies, when the research is overseen by those agencies, and they require separate reporting.
- The maximum time allowed between the recognition of a reportable event and fulfilling reporting requirements.

When following DHHS regulations:
- When research is covered by DHHS regulations, the report of unanticipated problems involving risks to participants or others be not to be reported to OHRP.
- When research is not covered by DHHS regulations, written materials specify that reports of unanticipated problems involving risks to participants or others are not to be reported to OHRP.

When following FDA regulations:
- Policies and procedures include a requirement that the report of unanticipated problems involving risks to participants or others be sent to the FDA, when the research is FDA-regulated.
- When research is not covered by FDA regulations, written materials specify that reports of unanticipated problems involving risks to participants or others are not to be reported to FDA.

When following VA requirements:
- Policies and procedures describe:
  - 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.
  - For unanticipated problems involving risks to participants or others, members of the VA research community are required to ensure that all unanticipated problems involving risks to participants or others in research are reported promptly to the IRB.
  - For serious unanticipated problems involving risks to participants or others, within five business days of becoming aware of any serious unanticipated problem involving risks to participants or others in VA research, members of the VA research community are required to ensure that the problem has been reported in writing to the IRB. Serious unanticipated problems involving risks to participants or others include:
  - Interruptions of participant enrollments or other research activities due to concerns about the safety, rights, or welfare of human research participants, research staff, or others.
  - 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 individuals, or leads to serious complications or death.

- Any VA National Pharmacy Benefits Management (PBM) Bulletins or Communications (sometimes referred to as PBM Safety Alerts) relevant to one or more of the VA facility’s research projects.
- Any data monitoring committee, data and safety monitoring board or data and safety monitoring committee report describing a safety problem.
- Any sponsor analysis describing a safety problem for which action at the VA facility might be warranted.
- Any unanticipated problem involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research participants, research staff, or others.
- Any problem reflecting a deficiency that substantively compromises the effectiveness of the VA facility’s HRPP.

Local unanticipated serious adverse events.

- Policies and procedures indicate that within five business days of becoming aware of any local (i.e., occurring in the reporting individual’s own facility) unanticipated serious adverse events in VA research, members of the VA research community are required to ensure that the serious adverse event has been reported in writing to the IRB.
  - This requirement is in addition to other applicable reporting requirements (e.g., reporting to the sponsor under FDA regulations).
  - The unfounded classification of an serious adverse event as “anticipated” constitutes serious non-compliance.

IRB review of serious unanticipated problems and unanticipated serious adverse events.

- Policies and procedures indicate that within five business days after a report of a serious unanticipated problem involving risks to participants or others, or of a local unanticipated serious adverse event, the convened IRB or a qualified IRB member-reviewer must determine and document whether the reported incident was serious and unanticipated and related to the research.
  - “Related” means the event or problem may reasonably be regarded as caused by, or probably caused by, the research.

- If the convened IRB or the IRB reviewer determines that the problem or event was serious, unanticipated, and related to the research, the IRB chair or designee must report in writing the unanticipated problem or event within five business days after the determination to:
  - Facility director.
  - Associate chief of staff for research.
  - The Research and Development Committee.
  - The facility director must report the problem or event to the appropriate Office of Research Oversight research officer within five business days after receiving such notification.

- If the convened IRB or the IRB reviewer determines that the problem or event was serious, unanticipated, and related to the research, a simultaneous determination is required regarding the need for any action (e.g., suspension of activities; notification of participants) necessary to prevent an immediate hazard to participants in accordance with VA regulations.

- All determinations of the IRB reviewer (regardless of outcome) must be reported to the IRB at its next convened meeting.

- If it was determined that the problem or event is serious, unanticipated, and related to the research, the convened IRB must determine and document whether a protocol or consent document modification is warranted.

- If the convened IRB determines that a protocol or consent document modification is warranted, the IRB must also determine and document:
  - Whether previously enrolled participants must be notified of the modification.
  - When such notification must take place and how such notification must be documented.

- Policies and procedures include a requirement that the report of unanticipated problems involving risks to participants or others be sent to:
  - The Office of Research and Development, if VA-funded.
  - The Regional Office of Research Oversight.
  - The VA Privacy Office, when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information.
• The VHA Information Security Officer when the report involves violations of VA information security requirements.
• IRBs of academic affiliates and the IRB of record for VA facilities must follow these requirements.

When following DoD requirements:
• Any unanticipated problems involving risks to participants or others for any DoD-supported research must be promptly (within 30 days) reported to the DoD human research protection officer.

When following the ICH-GCP (E6) guideline:
• Policies and procedures define the problems researchers have to report to the IRB or EC to include:
  - New information that may affect adversely the safety of the participants or the conduct of the clinical trial.
  - Any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.

Outcomes
• The IRB or EC evaluates each reported problem to determine whether it is an unanticipated problem involving risks to participants or others.
• The IRB or EC reviews problems that are unanticipated problems involving more than minimal risks to participants or others.
• The IRB or EC or an organizational official reports unanticipated problems involving risks to participants or others to appropriate organizational officials and applicable regulatory agencies.
Commentary
The IRB or EC has and follows written policies and procedures for suspending or terminating IRB or EC approval of research, if warranted, and for reporting these actions, when appropriate.

Required Written Materials

**Essential requirements:**
- Policies and procedures define:
  - Suspension of IRB approval.
  - Termination of IRB approval.
- Policies and procedures indicate that the IRB or EC can suspend or terminate approval of research that:
  - Is not being conducted in accordance with the IRB’s or EC’s requirements.
  - Has been associated with unexpected serious harm to participants.
- Policies and procedures describe who is authorized to suspend or terminate research.
- Policies and procedures describe who can suspend or terminate IRB approval on an urgent basis.
- Policies and procedures have suspensions and terminations by someone other than the convened IRB reported to and reviewed by the convened IRB.
- When study approval is suspended or terminated, policies and procedures have the IRB or EC or the person ordering the suspension or termination:
  - Consider actions to protect the rights and welfare of currently enrolled participants.
  - Consider whether procedures for withdrawal of enrolled participants take into account their rights and welfare (e.g., making arrangements for medical care outside of a research study, transfer to another researcher, and continuation in the research under independent monitoring).
  - Consider informing current participants of the termination or suspension.
  - Have any adverse events or outcomes reported to the IRB or EC.
- Policies and procedures describe the prompt reporting of suspensions and terminations of IRB or EC approval.
  - The maximum time allowed between the recognition of a reportable event and fulfilling reporting requirements.
  - The distribution of the report to:
    - Specific organizational officials.

Regulatory and Guidance References
- DHHS: 45 CFR 46.103(b)(5)(ii), 45 CFR 46.113, OHRP Guidance on Reporting Incidents to OHRP
- FDA: 21 CFR 56.108(b)(3), 21 CFR 56.113, FDA Information Sheets: Continuing Review After Study Approval
- DoD: Instruction 3216.02 4.b.4

See AHRPP Tip Sheet 14.
See AHRPP Tip Sheet 15.
See AHRPP Tip Sheet 21.
• Regulatory agencies when the research is overseen by to those agencies, and they require reporting.

When following DHHS regulations:
• Policies and procedures describe the prompt reporting of suspensions and terminations of IRB or EC approval to OHRP.

When following FDA regulations:
• Policies and procedures describe the prompt reporting of suspensions and terminations of IRB or EC approval to FDA.

When following VA requirements:
• Policies and procedures include the following definitions, procedures and timeframes:
  • The research and development committee and facility director have the authority to suspend or terminate their approval of research.
  • Reporting of terminations or suspensions of research.
  • Any termination or suspension of research (e.g., by the IRB or other research review committee, or by the associate chief of staff for research or other VA facility official) related to concerns about the safety, rights, or welfare of human research participants, research staff, or others must be reported in writing within five business days after the termination or suspension occurs to:
    • Facility director.
    • Associate chief of staff for research.
    • Research and Development Committee.
    • IRB.
    • Other relevant research review committee.
  • The facility director must report the termination or suspension to the appropriate Office of Research Oversight research officer within five business days after receiving such notification.
  • Policies and procedures describe the prompt reporting of suspensions and terminations of IRB or EC approval to:
    • The Office of Research and Development, if VA-funded.
    • The Regional Office of Research Oversight.
    • The Privacy Office, when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information.
    • The Information Security Officer when the report involves violations of information security requirements.
    • IRBs of academic affiliates that are the IRB of record for a VA facility must follow these requirements.

When following DoD requirements:
• Any suspension or termination of DoD-supported research is promptly (within 30 days) reported to the DoD human research protection officer.

Outcomes
• The IRB or EC suspends or terminates approval of research in its policies and procedures.
• When the IRB or EC suspends or terminates approval of research, the rights and welfare of enrolled participants are protected.
• The IRB or EC or organizational official reports suspensions and terminations of approval of research to appropriate organizational officials and applicable regulatory agencies.
Element II.2.I. The IRB or EC has and follows policies and procedures for managing multi-site research by defining the responsibilities of participating sites that are relevant to the protection of research participants, such as reporting of unanticipated problems or interim results.

Commentary
This Element applies when the IRB or EC reviews research where the researcher under the oversight of the HRP is responsible for the overall conduct of the study. That is, the researcher is the lead researcher of a multi-site study or provides study-wide services such as for data coordination. In such cases, policies and procedures should describe the steps the IRB or EC follows to communicate among the sites involved in the multi-site study on issues other than IRB or EC review. Such communications might include reporting of unanticipated problems, protocol modifications, and interim results.

See AAHRPP Tip Sheet 1.

Regulatory and Guidance References
- VA: VHA Handbook 1200.05, 9; VHA Handbook 1200.01
- DoD: Instruction 3216.02 2 (3) (b); SECNAVINST 3900.39D 6f

Required Written Materials

Essential requirements:
- When the researcher is the lead researcher of a multi-site study, policies and procedures have applications include information about the management of information that is relevant to the protection of participants, such as:
  - Unanticipated problems involving risks to participants or others.
  - Interim results.
  - Protocol modifications.
- When the researcher is the lead researcher of a multi-site study, policies and procedures have the IRB or EC evaluate whether the management of information that is relevant to the protection of participants is adequate.

When following VA requirements:
- Policies and procedures indicate that for a VA multi-site study, not only the principal researcher, but also all local site researchers, must obtain written approvals from the relevant local VA facilities’ IRBs of record and all other local committees, subcommittees, and other approvals according to the respective applicable local, VA and other federal requirements.
- Research cannot be initiated at any given site until the local researcher has obtained written notification that the research can be initiated from the local associate chief of staff for research and development.
- Policies and procedures include a definition of collaborative research.
- Policies and procedures indicate that collaboration is encouraged when non-VA researchers have a substantial role in the design, conduct, or analysis of research.
- Policies and procedures indicate that collaborative research may not be undertaken without a signed agreement that addresses the responsibilities of each party, including ownership of data and re-use of data for other research.

When following DoD requirements:
- When conducting multi-site research, policies and procedures indicate that a formal agreement between organizations is required to specify the roles and responsibilities of each party.

Outcomes
- There is communication among the IRBs of sites participating in a multi-site study.
Standard II-3: The IRB or EC approves each research protocol or plan according to criteria based on applicable laws, regulations, codes, and guidance.

Element II.3.A. The IRB or EC has and follows written policies and procedures for identifying and analyzing risks and identifying measures to minimize such risks. The analysis of risk includes a determination that the risks to participants are reasonable in relation to the potential benefits to participants and to society.

Commentary

- Minimization of risks
  A criterion for approval of research is that risks to participants are minimized by using procedures that are consistent with sound research design and do not unnecessarily expose participants to risk, and whenever appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes. The IRB or EC should evaluate whether research submitted for review satisfies this criterion. IRB or EC members should understand how to apply this criterion. They should recognize risks whose probability or magnitude can be reduced by using procedures that are consistent with sound research design and that do not unnecessarily expose participants to risk. If the research context involves procedures already being performed for diagnostic or treatment purposes, the IRB or EC should recognize risks whose probability or magnitude can be reduced by using those procedures. If the research context does not involve such procedures, this strategy for minimizing risks is not applicable.

- Risk-potential benefit analysis
  Another criterion for approval of research is that risks to participants are reasonable in relation to potential benefits, if any, to participants, and the importance of the knowledge that may reasonably be expected to result. The IRB or EC should evaluate whether research submitted for review satisfies this criterion. The IRB or EC should be able to recognize the likelihood and magnitude of harms and benefits, and understand the importance of the knowledge reasonably expected to result. The IRB or EC should be cognizant of the range of harms, including physical, social, economic, psychological, and legal harm. The IRB or EC should also be cognizant of the range of benefits. Direct benefits to participants can take the form of therapy, education, information, resources, or empowerment.

In all research, the IRB or EC should evaluate the importance of the knowledge that is likely to result from the research.

- Resources
  The IRB or EC should evaluate each research study to ensure that it has the resources necessary to protect research participants. Such resources include staffing and personnel, in terms of availability, number, expertise, and experience; psychological, social, or medical services, including counseling or social support services that may be required because of research participation; psychological, social, or medical monitoring, ancillary care, equipment needed to protect participants, and resources for participant communication, such as language translation services.

An organization, such as an independent review board, that does not provide all necessary resources should evaluate the resources of the local site. This might be accomplished by a case-by-case review of resources at each site. For example, an IRB can evaluate the adequacy of resources based on a description of facilities and personnel provided by the researcher. The precise resources required are protocol specific.

See AAHRPP Tip Sheet 1.
See AAHRPP Tip Sheet 20.

Regulatory and Guidance References

- DoD: Instruction 3216.02 6.b
- ICH-GCP: 2.2, 2.3, 3.13,4.2.1, 4.2.2, 4.2.3

Required Written Materials

Essential requirements:
Applications include information allowing the IRB or EC to conduct an analysis of the risks and potential benefits, such as:

- The purposes of the research.
- The scientific or scholarly rationale.
- The procedures to be performed.
- A description of the procedures being performed already for diagnostic or treatment purposes.
- The risks and potential benefits of the research to participants.

In order to approve research, policies and procedures have the IRB or EC determine that:

- Risks to participants are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose participants to risk.
- Risks to participants are minimized, when appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.
- Risks to participants are reasonable in relationship to the potential benefits, if any, to participants, and the importance of the knowledge that may be expected to result.
- Research studies have the resources necessary to protect participants:
  - Adequate time for the researchers to conduct and complete the research.
  - Adequate number of qualified staff.
  - Adequate facilities.
  - Access to a population that will allow recruitment of the necessary number of participants.
  - Availability of medical or psychosocial resources that participants may need as a consequence of the research.

When following DoD requirements:

- The definition of the minimal risk based on the phrase “ordinarily encountered in daily life or during the performance of routine physical or physiological examinations or tests” must not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects 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).

Common Types of Materials That May Be Used to Meet the Element

- Application form
- Reviewer checklist

Outcomes

- IRB or EC members approve research according to the criteria of approval pertaining to risks and potential benefits.
- When considering risks, the IRB or EC considers physical, psychological, social, economic, and legal risks.
- When considering benefits, the IRB or EC considers direct benefits, if any, to participants and the importance of the knowledge likely to result from the research.
- Research studies have the resources necessary to protect participants.
Element II.3.B. The IRB or EC has and follows written policies and procedures for reviewing the plans for data and safety monitoring, when applicable, and determines that the data and safety monitoring plan provides adequate protection for participants.

Commentary
A criterion for approval of research is that when appropriate, the research protocol or plan makes adequate provisions for monitoring the data to ensure the safety of participants. The IRB or EC should evaluate whether research submitted for review satisfies this criterion.

For clinical research involving no more than minimal risk and for most behavioral and social science research (because most involves no more than minimal risk), provisions for data and safety monitoring are not needed to protect participants. IRB or EC members should have criteria for determining when such monitoring is necessary.

IRB or EC members should understand the range of possible options for monitoring and that monitoring might occur at specific points in time, after a specific number of participants have been enrolled, or upon recognition of harm. IRB or EC members should understand that monitoring might be conducted by the researcher, the sponsor (e.g., medical monitor, safety monitoring committee), or by an independent monitoring board.

See AAHRPP Tip Sheet 1.
See AAHRPP Tip Sheet 6.
See AAHRPP Tip Sheet 20.

Regulatory and Guidance References
- DHHS: 45 CFR 46.111(a)(6)
- FDA: 21 CFR 56.111(a)(6)
- VA: 38 CFR 16.111(a)(6), VHA Handbook 1200.05, 10, 17, 22
- DoD: Instruction 3216.02 8; SECNAVINST 3900.39D, para. 6c
- ICH-GCP: 5.1.6

Required Written Materials

Essential requirements:
- Policies and procedures describe when the IRB or EC considers provisions for monitoring data to ensure the safety of participants to be appropriate.

When the IRB or EC considers provisions for monitoring data to ensure the safety of participants to be appropriate, policies and procedures have applications include descriptions of such provisions.

- In order to approve research in which the IRB or EC considers provisions for monitoring data to ensure the safety of participants to be appropriate, policies and procedures have the IRB or EC determine that the research plan makes adequate provisions. The IRB might consider provisions such as:
  - What safety information will be collected, including serious adverse events.
  - How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).
  - The frequency of data collection, including when safety data collection starts.
  - The frequency or periodicity of review of cumulative safety data.
  - The plan might include establishing a data monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor.
  - For studies that do not have or are not required to have a data monitoring committee and are blinded, have multiple sites, enter vulnerable populations, or employ high-risk interventions, the IRB or EC needs to carefully review the data and safety monitoring plan and determine whether a data monitoring committee is needed.
  - If not using a data monitoring committee, and if applicable, statistical tests for analyzing the safety data to determine whether harm is occurring;
  - Provisions for the oversight of safety data (e.g., by a data monitoring committee).
  - Conditions that trigger an immediate suspension of the research, if applicable.

When following DoD requirements:
- Policies and procedures have the IRB or EC consider the appointment of a research monitor:
- Required for research involve greater than minimal risk, although the IRB or EC or organizational official can require this for a portion of the research or studies involving no more than minimal risk, if appropriate.
• The research monitor is appointed by name and must be independent of the team conducting the research.
• There may be more than one research monitor (e.g., if different skills or experience are needed).
• The monitor may be an ombudsman or a member of the data safety monitoring board. The IRB must approve a written summary of the monitors’ duties, authorities, and responsibilities.
• The IRB or HRPP official must communicate with research monitors to confirm their duties, authorities, and responsibilities.
• The duties of the research monitor are determined on the basis of specific risks or concerns about the research.
  • May perform oversight functions (e.g., observe recruitment, enrollment procedures, and the consent process, oversee study interventions and interactions, review monitoring plans and unanticipated problems involving risks to participants or others, oversee data matching, data collection, and analysis).
  • May discuss the research protocol with researchers, interview human subjects, and consult with others outside of the study.
• Report observations and findings to the IRB or a designated official.
• The research monitor has the authority to:
  • Stop a research study in progress.
  • Remove individuals from study.
  • Take any steps to protect the safety and well-being of participants until the IRB or EC can assess.

Common Types of Materials That May Be Used to Meet the Element

• Application form
• Reviewer checklist

Outcomes

• IRB or EC members articulate when provisions for data and safety monitoring are required.
• IRB or EC members determine that research protocols or plans include adequate provisions for monitoring the data to provide for the safety of participants.
Element II.3.C. The IRB or EC has and follows written policies and procedures to evaluate the equitable selection of participants.

Element II.3.C.1. The IRB or EC has and follows written policies and procedures to review proposed participant recruitment methods, advertising materials, and payment arrangements and determines whether such arrangements are fair, accurate, and appropriate.

Commentary

A criterion for approval of research is that selection of participants is equitable. The IRB or EC should evaluate whether research submitted for review satisfies this criterion. IRB or EC members should understand how to apply this criterion. In evaluating this criterion, IRB or EC members should consider both the selection (inclusion and exclusion) criteria and the proposed plans for recruitment of participants. IRB members should evaluate whether selection criteria and recruitment practices meet this criterion.

Recruitment methods, including advertisements, and participant payment arrangements affect the equitable selection of participants and an appropriate consent process.

A research study might have fair selection criteria, but use recruitment methods or payment arrangements that lead to inequitable selection. For example, recruitment methods, advertisements, or payment arrangements that target economically disadvantaged participants can lead to unfair selection of participants despite reasonable selection criteria. Therefore, the IRB or EC should evaluate whether recruitment processes, advertisements, and payment arrangements affect the equitable selection of participants.

Recruitment methods, advertising materials, and payment arrangements also represent a part of the consent process. Recruitment methods and advertisements are the beginning of the consent negotiations; payments for participation are provided to reimburse participants for their time, effort, or other expenses. Recruitment methods, advertisements, or payment arrangements that are misleading, inaccurate, exculpatory, coercive, or unduly influential violate ethical requirements for consent. Therefore, the IRB or EC should review proposed recruitment processes and advertising materials to judge whether they fulfill the requirements for consent.

Payment arrangements can place participants at risk of coercion or undue influence or cause inequitable selection. Two situations should be examined: finder’s fees and recruitment bonuses. A finder’s fee or referral is a payment from the researcher or sponsor to a person who refers a prospective participant. Recruitment bonuses are payments from the sponsor to a researcher or organization based on the rate or timing of recruitment. For example, a sponsor might contract to pay the researcher or organization a fixed fee for each participant but promise an additional payment if more than a certain number of participants are enrolled in the first week or if the site has the highest enrollment at the end of the month. Policies and procedures should describe acceptable and unacceptable payment arrangements among the sponsor, organization, researcher, and those referring research participants.

See AAHRPP Tip Sheet 1.
See AAHRPP Tip Sheet 20.

Regulatory and Guidance References

- DoD: Instruction 3216.02 11., Dual Compensation Act, 24 U.S.C 301, DoD 3216.2, para. 4.4.4; SECNAVINST 3900.39D, para. 6a(6)
- DOJ: 28 CFR 512.11(4,5)
- ICH-GCP: 3.1.8

Required Written Materials

Essential requirements:

- Applications include information that allows the IRB or EC to determine whether selection of participants will be equitable, such as:
  - The purposes of the research.
  - The setting in which the research will be conducted.
  - Whether prospective participants will be vulnerable to coercion or undue influence.
  - The selection (inclusion/exclusion) criteria.
• Participant recruitment and enrollment procedures.
• The amount and timing of payments to participants.

In order to approve research, policies and procedures have the IRB or EC determine that selection of participants is equitable.

In making an assessment about whether selection of participants is equitable, policies and procedures have the IRB or EC take into account:
• The purposes of the research.
• The setting in which the research will be conducted.
• Whether prospective participants will be vulnerable to coercion or undue influence.
• The selection (inclusion/exclusion) criteria.
• Participant recruitment and enrollment procedures.
• The influence of payments to participants.

Policies and procedures have the IRB or EC review:
• The information contained in the advertisement.
• The mode of its communication.
• The final copy of printed advertisements.
• The final audio or video taped advertisements.

Policies and procedures have the IRB or EC review advertising to ensure that advertisements do not:
• State or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
• Include exculpatory language.
• Emphasize the payment or the amount to be paid, by such means as larger or bold type.
• Promise “free treatment” when the intent is only to say participants will not be charged for taking part in the investigation.

Policies and procedures have advertisements limited to the information prospective participants need to determine their eligibility and interest, such as:
• The name and address of the researcher or research facility.
• The purpose of the research or the condition under study.
• In summary form, the criteria that will be used to determine eligibility for the study.
• A brief list of benefits to participants, if any.

When following FDA regulations:
• Policies and procedures have the IRB or EC review 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.
  • 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.

When following VA requirements:
• Policies and procedures have the IRB consider the relevance of the research to the mission of VA and the Veteran population it serves.

• Policies and procedures have the protocol and related materials justify the inclusion of non-Veterans. Non-veterans may be enrolled in VA-approved research studies, including the provision of outpatient or hospital care for research participants, only when there are insufficient veterans available to complete the study or when the researcher can present a compelling argument to the IRB for the inclusion of non-veterans (e.g., survey of VA employees; study of active duty military; study involving veterans’ family members), and the research is relevant to the care of veterans or active duty military personnel.

• To improve veterans’ access to non-VA research, advertisements for research not conducted at a VA facility may be posted, provided facility director ensures there is a formal process to review and approve recruiting documents, flyers, and advertisements prior to being posted or distributed.

• A VA facility may not use Facebook as a method of advertising non-VA studies.

When following DoD requirements:

• When research involves U.S. military personnel, policies and procedures include additional protections for military research participants to minimize undue influence. Superiors of service members (e.g., unit officers, senior NCOs, and equivalent civilians):
  • Are not permitted to influence the decision of their subordinates.
  • May not be present at the time of recruitment.
  • Have a separate opportunity to participate, when applicable.
  • When recruitment occurs in a group setting, the IRB shall appoint an ombudsman.

• When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:
  • Prohibit an individual from receiving pay of compensation for research during duty hours.
  • An individual 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 participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

When following DOJ requirements:

• Policies and procedures indicate that for research conducted within the Bureau of Prisons:
  • The selection of participants within any one organization must be equitable.
  • Incentives may not be offered to help persuade inmate participants to participate. However, soft drinks and snacks to be consumed at the test setting may be offered.
  • Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research participants who are both:
    • No longer in Bureau of Prisons custody.
    • Participating in authorized research being conducted by Bureau employees or contractors.

Common Types of Materials That May Be Used to Meet the Element

• Application form
• Reviewer checklist

Outcomes

• IRB or EC members determine that selection of participants is equitable.

• IRB or EC members determine that advertisements:
  • Provide prospective participants with sufficient opportunity to consider whether to participate.
  • Do not include any exculpatory language through which the participant or the legally authorized representative is made to waive or appear to waive any of the participant’s legal rights, or releases or appears to release the researcher, the sponsor, or the institution, or its agents from liability for negligence.

• IRB or EC members determine that payment arrangements:
  • Provide prospective participants with sufficient opportunity to consider whether to participate.
  • Minimize the possibility of coercion or undue influence of participants.
  • Based on the timing or rate of participant enrollment (often known as bonus payments or finder’s fees), are prohibited unless they are judged not to interfere with providing
prospective participants with sufficient opportunity to consider whether to participate and do not increase the possibility of coercion or undue influence on researchers or participants.
Element II.3.D. The IRB or EC has and follows written policies and procedures to evaluate the proposed arrangements for protecting the privacy interests of research participants, when appropriate, during their involvement in the research.

Commentary
A criterion for approval of research is that there are adequate provisions to protect the privacy interests of participants. The IRB or EC should evaluate whether research submitted for review satisfies this criterion. IRB or EC members should understand how to apply this criterion.

Privacy refers to persons and their interest in controlling the access of others to themselves. (Confidentiality refers to the agreement between the researcher and participant on how data will be managed and used.) For example, based on their privacy interests, people want to control:

- The time and place where they give information.
- The nature of the information they give.
- The nature of the experiences that are given to them.
- Who receives and can use the information.

For example, persons might not want to be seen entering a place that might stigmatize them, such as a pregnancy counseling center that is clearly identified as such by signs on the front of the building.

What is private depends on the individual and can vary according to gender, ethnicity, age, socio-economic class, education, ability level, social or verbal skill, health status, legal status, nationality, intelligence, personality, and the individual’s relationship to the researcher. For example, protecting the privacy interests of a young child might mean having a parent present at a session with a researcher. Protecting the privacy interests of a teenager might mean having a parent absent.

IRB members should understand the concept of privacy and how it differs from confidentiality. IRB or EC members should know strategies to protect privacy interests relating to contact with prospective participants and access to private information.

See AAHRPP Tip Sheet 1.
See AAHRPP Tip Sheet 5.
See AAHRPP Tip Sheet 20.

Regulatory and Guidance References
- DHHS: 45 CFR 46.111(a)(7)
- FDA: 21 CFR 56.111(a)(7)
- VA: 38 CFR 16.111(a)(7), VHA Handbook 1200.05, 10, 12, 17

Required Written Materials

**Essential requirements:**
- Applications include a description of provisions to protect the privacy interests of participants.
- In order to approve research, policies and procedures have the IRB or EC determine that the research protocol or plan contains adequate provisions to protect the privacy interests of participants.

Common Types of Materials That May Be Used to Meet the Element
- Application form
- Reviewer checklist

Outcomes
- IRB or EC members understand the concept of privacy.
- IRB or EC members determine that the research protocol or plan contains adequate provisions to protect the privacy interests of participants.
Element II.3.E. The IRB or EC has and follows written policies and procedures to evaluate proposed arrangements for maintaining the confidentiality of identifiable data, when appropriate, preliminary to the research, during the research, and after the conclusion of the research.

Commentary
A criterion for approval of research is that there are adequate provisions to maintain the confidentiality of identifiable data. The IRB or EC should evaluate whether research submitted for review satisfies this criterion. IRB or EC members should understand how to apply this criterion.

Confidentiality refers to maintenance of the researcher’s agreement with the participant about how the participant’s identifiable private information will be handled, managed, and disseminated. IRB or EC members should understand the concept of confidentiality and how it differs from privacy. IRB or EC members should be knowledgeable about strategies to maintain confidentiality of identifiable data, including controls on storage, handling, and sharing of data.

When appropriate, the IRB or EC should also know how certificates of confidentiality can be used to maintain the confidentiality of identifiable data. When appropriate, the IRB or EC should also be aware of other standard methods to protect confidentiality, such as inter-file linkage, error inoculation, top coding, bracketing, and data brokering.

The confidentiality protections include information obtained preliminary to research; for example, information collected from personal records to determine potential sample size, as well as the maintenance of the confidentiality of information after the study has ended, when identifiable information is maintained.

See AAHRPP Tip Sheet 1.
See AAHRPP Tip Sheet 4.
See AAHRPP Tip Sheet 20.

Regulatory and Guidance References
- DHHS: 45 CFR 46.111(a)(7)
- FDA: 21 CFR 56.111(a)(7)
- VA: 38 CFR 16.111(a)(7), VHA Handbook 1200.05, 10, 12, 17, 38
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)
- DOJ: 28 CFR 22, 28 CFR 512.11,12,13,15
- ICH-GCP: 2.11

Required Written Materials
Essential requirements:
- Applications include a description of provisions to maintain the confidentiality of data.
- In order to approve research policies and procedures have the IRB or EC determine that, when appropriate, the research protocol or plan contains adequate provisions to maintain the confidentiality of data.

When following DHHS regulations:
- Written materials specify that research is automatically covered by a certificate of confidentiality whenever the study is funded in whole or in part by the NIH and involves identifiable, sensitive information.
- Written materials define “identifiable sensitive information.”
- Examples of research automatically covered by a certificate of confidentiality include:
  - Biomedical, behavioral, clinical or other research, including exempt research, except where the information obtained is recorded in such a manner that human participants cannot be identified or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects.
  - The collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual.
  - The generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained.
  - Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the

- NIH Policy for Issuing Certificates of Confidentiality (Effective October 1, 2017)
Researchers may also apply for a certificate of confidentiality for non-federally funded research.

Written materials specify that when research is covered by a certificate of confidentiality, researchers:

- May not disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or

- May disclose information only when:
  - Required by Federal, State, or local laws (e.g., as required by the Federal Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding.
  - Necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual;
  - Made with the consent of the individual to whom the information, document, or biospecimen pertains; or
  - Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

Written materials require that when research is covered by a certificate of confidentiality, researchers must inform participants (for example, in the consent document) of the protections and limitations of certificates of confidentiality.

This requirement also applies to existing studies active on after December 13, 2016. For existing studies, researchers must notify participants that the research is now covered by a certificate of confidentiality. However, because a certificate of confidentiality reduces risks, the IRB does not need to require the researcher to obtain consent again based on this information, and can simply notify participants of this change.

Written materials require that researchers conducting NIH-supported research covered by a certificate of confidentiality must ensure that if identifiable, sensitive information is provided to other researchers or organizations, regardless of whether or not the research is federally funded, the other researcher or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.

When following DOE requirements:

- Written materials require the IRB or EC to review and ensure that research protocols submitted to the IRB for review comply with the DOE requirements for protecting personally identifiable information (PII). Additional information can be found at: http://science.energy.gov/ber/human-subjects/regulations-and-requirements/doe-special-requirements/#ProtectionOfData

When following DOJ requirements:

- Written materials indicate that for National Institute of Justice (NIJ)-funded research:
  - All projects are required to have a privacy certificate approved by the NIJ human subjects protection officer.
  - All researchers and research staff are required to sign employee confidentiality statements, which are maintained by the responsible researcher.

- Written materials indicate that for research conducted with the Bureau of Prisons:
  - A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency.
  - Except as noted in the consent statement to the participant, the researcher must not provide research information that identifies a participant to any person without that participant’s prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.

- Except for computerized data records maintained at an official U.S. Department of Justice site, records
that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system.

- If the researcher is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint project involving ORE, the researcher may be asked to provide ORE with the computerized research data, not identifiable to individual participants, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.

When following VA requirements where research involves a certificate of confidentiality:

- For studies that do not involve a medical intervention, no annotation may be made in the medical record.
- For studies involving a medical intervention, a progress note in the medical record should be made, indicating the individual has been enrolled in a research study, any details that would impact clinical care, and the name and contact information of the researcher conducting the study.

Common Types of Materials That May Be Used to Meet the Element

- Application form
- Reviewer checklist

Outcomes

- IRB or EC members understand the concept of confidentiality.
- IRB or EC members determine that, when appropriate, the research protocol or plan contains adequate provisions to maintain the confidentiality of identifiable data in accordance with agreements between researchers and participants.
Element II.3.F. The IRB or EC has and follows written policies and procedures to evaluate the consent process and to require that the researcher appropriately document the consent process.

Commentary
To approve research, the IRB or EC has to determine that the consent process meets these criteria for approval of research:

- The researcher obtains the legally effective consent of the participant or the participant’s legally authorized representative.
- The consent process provides sufficient opportunity for the participant or the participant’s legally authorized representative to consider whether to participate.
- The consent process minimizes the possibility of coercion or undue influence.
- The consent discussion is in language understandable to the participant or the representative.
- The consent discussion is free of exculpatory language through which the participant or the legally authorized representative is made to waive or appear to waive any of the participant’s legal rights.
- Documentation of consent contains all applicable basic and additional elements of disclosure (See Table II.3.F.), and meets requirements in law and regulation, either with a long-form consent document, or a short-form consent document, or a broad consent document.

The IRB or EC should evaluate whether a research study satisfies these criteria. This cannot be accomplished solely by evaluating a written consent document, since the consent process is an ongoing discussion that should be culturally and linguistically appropriate to the study population, and not simply a consent document. Instead, the IRB or EC should know the nature and circumstances of the consent process, such as who will conduct the consent interview, the timing of obtaining consent, and any waiting period between informing the participant and obtaining consent, and based on this information determine whether the criteria for approval of research are met.

Another criterion for approval of research is that researchers inform prospective participants of required disclosures. The IRB or EC should evaluate whether research submitted for review satisfies this criterion. This cannot be accomplished solely by evaluation of a written consent document, because the consent document does not reflect all the information communicated to the participant during the consent process. Therefore, the IRB or EC should evaluate the information that will be communicated to the participant during the consent process, and determine which information will be disclosed.

When reviewing research, the IRB or EC should evaluate whether the consent process will be documented using a consent document.

See AAHRPP Tip Sheet 1.
See AAHRPP Tip Sheet 11.
See AAHRPP Tip Sheet 19.
See AAHRPP Tip Sheet 20.

Regulatory and Guidance References
- DoD: Instruction 3216.2, para. 5.3.4; SECNAVINST 3900.39D, para. 6a(5)
- DOJ: 28 CFR 512.16
- ICH-GCP: 2.9, 3.1.5, 3.1.9, 4.3.4, 4.8.1-4.8.9, 4.8.11
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)
Required Written Materials

Essential requirements:

- Applications include a description of the consent process including:
  - The person who will conduct the consent interview.
  - The person who will provide consent or permission.
  - Any waiting period between informing the prospective participant and obtaining consent.
  - Steps taken to minimize the possibility of coercion or undue influence.
  - The language used by those obtaining consent.
  - The language understood by the prospective participant or the legally authorized representative.
  - The information to be communicated to the prospective participant or the legally authorized representative.

- In order to approve research, policies and procedures have the IRB or EC determine:
  - The researcher will obtain the legally effective consent of the participant or the participant’s legally authorized representative.
  - The circumstances of the consent process provide the prospective participant or the legally authorized representative sufficient opportunity to consider whether to participate.
  - The circumstances of the consent process minimize the possibility of coercion or undue influence.
  - The individuals communicating information to the participant or the legally authorized representative during the consent process will provide that information in language understandable to the participant or the representative.
  - The information being communicated to the participant or the representative during the consent process will not include exculpatory language through which the participant or the legally authorized representative is made to waive or appear to waive any of the participant’s legal rights.

- In order to approve research, policies and procedures have the IRB or EC determine that in seeking consent, the required disclosures (See Table II.3.F.) will be provided to each participant or a legally authorized representative in accordance with legal and regulatory requirements. (See Tip Sheet 1: Criteria for Approval)

- Policies and procedures have the IRB or EC consider whether additional disclosures (See Table II.3.F.) are required for inclusion in the consent process.

- Policies and procedures have the IRB or EC determine that the consent process will be documented according to legal and regulatory requirements, or equivalent protections.

When following DHHS regulations:

- Written materials have the IRB or EC determine:
  - The required and appropriate additional elements of disclosure are included in the consent process.
  - To allow use of the long form of consent documentation, policies and procedures have the IRB or EC determine that:
    - The consent document embodies the basic and required additional elements of disclosure.
    - The participant or the participant’s legally authorized representative will sign the consent document.
    - A copy of the consent document will be given to the person signing the consent document.
    - The researcher will give either the participant or the representative adequate opportunity to read the consent document before it is signed.
  - To allow the use of the short form of consent documentation, policies and procedures have the IRB or EC determine that:
    - The consent document states that the elements of disclosure required by regulations have been presented orally to the participant or the participant’s legally authorized representative.
    - A written summary embodies the basic and required additional elements of disclosure.
    - There will be a witness to the oral presentation.
    - For participants who do not speak English, the witness is conversant in both English and the language of the participant.
    - The participant or the participant’s legally authorized representative will sign the consent document.
    - The witness will sign both the short form and a copy of the summary.
• The person actually obtaining consent will sign a copy of the summary.
• A copy of the signed short form will be given to the participant or the legally authorized representative.
• A copy of the signed summary will be given to the participant or the legally authorized representative.

When following the revised Common Rule when it goes into effect:
• Written materials have the IRB or EC determine:
  • The required and appropriate additional elements of disclosure are included in the consent process.
  • The consent document begins with a concise and focused presentation of key information that is most likely to assist a prospective participant or legally authorized representative in understanding the reasons why one might or might not want to participate in the research.
  • Written materials define for researchers what the organization considers “key information”.
  • Written materials specify what the organization considers a “concise” presentation of key information.
  • The consent process and documentation as a whole presents information in sufficient detail, and facilitates the prospective participant’s or legally authorized representative’s understanding.

Long form of consent documentation
• To allow use of the long form of consent documentation, policies and procedures have the IRB or EC determine that:
  • The consent document embodies the basic and appropriate additional elements of disclosure, including required disclosures when the research involves private identifiable information or identifiable biospecimens. (See Table II.3.F.1.) have been presented orally to the participant or the participant’s legally authorized representative, including required disclosures when the research involves private identifiable information or identifiable biospecimens. (See Tip Sheet 1: Criteria for Approval)
  • A written summary embodies the basic and appropriate additional elements of disclosure. (See Table II.3.F.)
  • There will be a witness to the oral presentation.
  • For participants who do not speak English, the witness is conversant in both English and the language of the participant.
  • The participant or the participant’s legally authorized representative will sign the consent document.
  • The witness will sign both the short form and a copy of the summary.
  • The person actually obtaining consent will sign a copy of the summary.
  • A copy of the signed short form will be given to the participant or the legally authorized representative.
  • A copy of the signed summary will be given to the participant or the legally authorized representative.

Short-form Consent
• To allow use of the short form of consent documentation, policies and procedures have the IRB or EC determine that:
  • The consent document states that the basic and appropriate additional elements of disclosure have been presented orally to the participant or the participant’s legally authorized representative, including required disclosures when the research involves private identifiable information or identifiable biospecimens. (See Tip Sheet 1: Criteria for Approval)
  • A written summary embodies the basic and appropriate additional elements of disclosure. (See Table II.3.F.)
  • There will be a witness to the oral presentation.
  • The participant or the participant’s legally authorized representative will sign the consent document.
  • The witness will sign both the short form and a copy of the summary.
  • The person actually obtaining consent will sign a copy of the summary.
  • A copy of the signed short form will be given to the participant or the legally authorized representative.

Broad consent
• To allow use of broad consent, policies and procedures have the IRB or EC determine that:
  • The study is limited to the storage, maintenance, and secondary research use of identifiable private information and identifiable biospecimens (collected for either research studies other than the proposed research, or non-research purposes).
  • The study has undergone limited IRB review and meets requirements for exempt Category 7 or Category 8. (See Elements II.2.A. and II.2.C.)
  • Researchers must provide all required disclosures for broad consent to each participant or participant’s legally authorized representative. (See Table II.3.F.1.)
• If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Posting of clinical trial consent form

• Written materials must describe the process for posting one IRB-approved consent form for each clinical trial conducted or supported by a Federal department or agency on a website specified by the US Federal government.
• Written materials specify the person or role responsible for posting the consent form.
• The consent form must be posted on the website after the clinical trial is closed to recruitment, but no later than 60 days after the last study visit by any participant, as required by the protocol.
• Written materials must describe the process to request from the Federal funding agency an exception to the requirement to post the consent document, and the process to redact confidential commercial information from the consent form.

When following FDA regulations:

• Policies and procedures have the IRB or EC determine that the required and appropriate additional elements of disclosure are included in the consent process.
• Policies and procedures have the IRB or EC determine that:
  • The consent document embodies the basic and required additional elements of disclosure.
  • There is a statement noting the possibility that the FDA may inspect the records that will be provided to each participant.
  • There is a statement that a description of the clinical trial will be available on http://www.clinicaltrials.gov as required by U.S. law. The website will not include information that can identify the participant. At most the website will include a summary of the results. The participant can reach the website at any time.
• The participant or the participant’s legally authorized representative will sign and date the consent document.
• The researcher will give either the participant or the legally authorized representative adequate opportunity to read the consent document before it is signed.

Short-form Consent When Following FDA Regulations

• To allow the use of the short form of consent documentation when following FDA regulations, policies and procedures have the IRB or EC determine that:
  • The consent document states that the elements of disclosure (See Table II.3.F.1.) required by regulations have been presented orally to the participant or the participant’s legally authorized representative.
  • A written summary embodies the basic and appropriate additional elements of disclosure.
  • There will be a witness to the oral presentation.
  • For participants who do not speak English, the witness is conversant in both English and the language of the participant.
  • The participant or the participant’s legally authorized representative will sign the consent document.
  • The witness will sign both the short form and a copy of the summary.
• The person actually obtaining consent will sign a copy of the summary.
• A copy of the signed short form will be given to the participant or the legally authorized representative.
• A copy of the signed summary will be given to the participant or the legally authorized representative.

• With regard to data retention when participants withdraw from a clinical trial, policies and procedures have the IRB or EC:
  • When a 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 data removed.
  • A researcher 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 this circumstance, the discussion with the participant distinguishes 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 researcher must obtain the participant’s consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB or EC must approve the consent document.
- 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 researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant’s consent. However, a researcher 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.

**When following VA requirements:**
- The consent document must include all required disclosures, but does not need to use a specific template.
- The consent document must be signed and dated by the participant or legally authorized representative, and by the person obtaining consent. The IRB may waive the requirement for the signature of the person obtaining consent when there is no physical contact with the participant (e.g., where the only contact with the participant is through telephone or mail).
- The consent document must indicate the date of IRB approval, but the date does not need to appear on each page of the consent document.
- Consent may be obtained and documented electronically so long as there are appropriate authentication controls to provide assurance the consent is rendered by the appropriate individual, and the participant dates the consent, or software provides the current date when signed.
- Consent to take a photograph, video, or audio recording for research cannot be waived by the IRB.
- Consent documents must include additional VA elements of disclosure. (See Table II.3.F.)

**When following DoD requirements:**
- Policies and procedures have the IRB or EC determine that the disclosure for research-related injury follow the requirements of the DoD component.
- Consent documents must include additional DoD elements of disclosure. (See Table II.3.F.)

**When following DOE requirements:**
- When the research is classified, the IRB must determine if participants need access to classified information to make a valid consent decision.
- Consent documents must include additional DoE elements of disclosure. (See Table II.3.F.1.)

**When following DOJ requirements:**
- Policies and procedures indicate that for National Institute of Justice-funded research:
  - Under a privacy certificate, researchers and research staff do not have to report child abuse unless the participant signs another consent document to allow child abuse reporting.
- Consent documents must include additional DoE elements of disclosure. (See Table II.3.F.)

**When following the ICH-GCP (E6) guideline:**
- Consent documents must include additional DoE elements of disclosure. (See Table II.3.F.)
- Policies and procedures on documentation of the consent process include:
  - Prior to a participant’s participation in the trial, the written consent document should be signed and personally dated by the participant or by the participant’s legally acceptable representative.
  - Prior to a participant’s participation in the trial, the written consent document should be signed and personally dated by the person who conducted the informed consent discussion.
  - If a participant is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion.
  - After the written consent document and any other written information to be provided to participants is read and explained to the participant or the participant’s legally acceptable representative, and after the participant or the participant’s legally acceptable representative has orally consented to the participant’s participation in the trial and, if capable of doing so, has signed and personally dated the consent document, the witness should sign and personally date the consent document.
• By signing the consent document, the witness attests that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant or the participant’s legally acceptable representative, and that consent was freely given by the participant or the participant’s legally acceptable representative.

• Prior to participation in the trial, the participant or the participant’s legally acceptable representative should receive a copy of the signed and dated written consent document and any other written information provided to the participants.

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**Common Types of Materials That May Be Used to Meet the Element**

- Application form
- Reviewer checklist
- Consent template

**Outcomes**

- Unless waived, IRB or EC members determine that the consent process will seek the legally effective consent of participants or their legally authorized representatives.
- IRB or EC members determine that the required and additional elements of disclosure, when appropriate, are included in the consent process.
- IRB or EC members determine that the consent process will be documented as required.
Table II.3.F.1. Elements of Consent Disclosure

### Basic Elements of Consent Disclosure for Long form and Short Form Consent Documents

<table>
<thead>
<tr>
<th>Long form consent document</th>
<th>Short form consent document</th>
</tr>
</thead>
<tbody>
<tr>
<td>A statement that the study involves research.</td>
<td>An explanation of whom to contact for answers to pertinent questions about the research.</td>
</tr>
<tr>
<td>An explanation of the purposes of the research.</td>
<td>An explanation of whom to contact for answers to pertinent questions about the research participants’ rights.</td>
</tr>
<tr>
<td>An explanation of the expected duration of the participant’s participation.</td>
<td>An explanation of whom to contact in the event of a research-related injury to the participant. (May not be omitted just because the research involves no more than minimal risk.)</td>
</tr>
<tr>
<td>A description of the procedures to be followed.</td>
<td>Contact information for the research team for questions, concerns, or complaints. (Element III.I.G.)</td>
</tr>
<tr>
<td>Identification of any procedures that are experimental. (May be omitted if there are none.)</td>
<td>Contact information for someone independent of the research team for problems, concerns, questions, information, or input. (Element I.4.A.)</td>
</tr>
<tr>
<td>A description of any reasonably foreseeable risks or discomforts to the participant. (May be omitted if there are none.)</td>
<td>A statement that participation is voluntary.</td>
</tr>
<tr>
<td>A description of any benefits to the participant or to others, which may reasonably be expected from the research. (May be omitted if there are none.)</td>
<td>A statement that refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled.</td>
</tr>
<tr>
<td>A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the participant. (May be omitted if there are none.)</td>
<td>If research involves the collection of identifiable information or identifiable biospecimens, an explanation of potential future use. (May be omitted if the research does not involve collection of identifiable information or identifiable biospecimens):</td>
</tr>
<tr>
<td>A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained. (May be omitted if confidentiality will not be maintained.)</td>
<td>- 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 researcher for future research studies without additional informed consent from the participant or legally authorized representative, if this might be possible; or</td>
</tr>
<tr>
<td>An explanation as to whether compensation is available if injury occurs. (May be omitted if the research involves no more than minimal risk.)</td>
<td>- A statement that the participant’s information or specimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.</td>
</tr>
<tr>
<td>If compensation is available when injury occurs, an explanation as to what it consists of or where further information may be obtained. (May be omitted if the research involves no more than minimal risk.)</td>
<td>Additional elements of disclosure</td>
</tr>
<tr>
<td>An explanation as to whether any medical treatments are available if injury occurs. (May be omitted if the research involves no more than minimal risk.)</td>
<td>A statement that the particular treatment or procedure may involve risks to the participant, which are currently unforeseeable.</td>
</tr>
<tr>
<td>If medical treatments are available when injury occurs, an explanation as to what it consists of or where further information may be obtained. (May be omitted if the research involves no more than minimal risk.)</td>
<td>A statement that if the participant is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable.</td>
</tr>
<tr>
<td>A statement that significant new findings developed during the course of the research which may relate to the participant’s willingness to continue participation will be provided to the participant.</td>
<td>Anticipated circumstances under which the participant’s participation may be terminated by the investigator without regard to the participant’s consent.</td>
</tr>
<tr>
<td>The approximate number of participants involved in the study.</td>
<td>Any additional costs to the participant that may result from participation in the research.</td>
</tr>
<tr>
<td>A statement that the participant’s biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in this commercial profit.</td>
<td>The consequences of a participant’s decision to withdraw from the research.</td>
</tr>
<tr>
<td>A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to the participant, and if so, under what conditions.</td>
<td>Procedures for orderly termination of participation by the participant.</td>
</tr>
<tr>
<td>For research involving biospecimens, a statement specifying whether the research will (if known) or might include whole genome sequencing.</td>
<td></td>
</tr>
</tbody>
</table>

### Additional elements of disclosure

- A statement that the particular treatment or procedure may involve risks to the participant, which are currently unforeseeable.
- A statement that if the participant is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable.
- Anticipated circumstances under which the participant’s participation may be terminated by the investigator without regard to the participant’s consent.
- Any additional costs to the participant that may result from participation in the research.
- The consequences of a participant’s decision to withdraw from the research.
- Procedures for orderly termination of participation by the participant.

### Additional requirements for FDA-regulated research

- A statement that significant new findings developed during the course of the research which may relate to the participant’s willingness to continue participation will be provided to the participant.
- The approximate number of participants involved in the study.
- A statement that the participant’s biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in this commercial profit.
- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to the participant, and if so, under what conditions.
- For research involving biospecimens, a statement specifying whether the research will (if known) or might include whole genome sequencing.
**Additional requirements when following the ICH-GCP (E6) guideline**

- The approval or favorable opinion by the IRB.
- The probability for random assignment to each treatment.
- The participant’s responsibilities.
- When applicable, the reasonably foreseeable risks or inconveniences to an embryo, fetus, or nursing infant.
- The important potential benefits and risks of the alternative procedures or courses of treatment that may be available to the participant.
- When there is no intended clinical benefit to the participant, the participant should be made aware of this.

**A statement that the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the participant’s original medical records for verification of clinical trial procedures and data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the participant or the participant’s legally authorized representative is authorizing such access.
- If the results of the trial are published, the participant’s identity will remain confidential.

**Additional requirements for DoD research**

- A statement that the DoD or a DoD organization is funding the study.

**Additional requirements for DoE research**

- The identity of the sponsoring agency, unless the sponsor requests that it not be done, because doing so could compromise intelligence sources or methods; the research involves no more than minimal risk to participants; and the IRB determines that by not disclosing the identity, the investigators will not adversely affect the participants.

**Additional Requirements for DOJ Research**

- When research is classified, consent documents must state the project is classified, and what it means for the purposes of the research project.

**Additional requirements for VA research**

- A statement that the results of the research will be posted on clinicaltrials.gov.
- A statement that notes the possibility that the Food and Drug Administration may inspect the records.
- A statement that the results of the research will be posted on clinicaltrials.gov.
- When research is sponsored by the Bureau of Prisoners, consent documents must disclose:
  - The identity of the researchers.
  - Anticipated uses of the results of the research.
  - A statement that participation is completely voluntary and that the participant may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable).
  - A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, a researcher may not guarantee confidentiality when the participant indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the participant is an inmate, indicates intent to leave the facility without authorization.
  - A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility.
  - A statement that informs VA research subjects that they or their insurance will not be charged for any costs related to the research.
  - A statement that a veteran-participant will not be required to pay for care received as a participant in a VA research project except in accordance with federal law and that certain veterans were required to pay co-payments for medical care and services provided by VA. Consent for research must describe any photographs, video, or audio recordings obtained for research purposes; how they will be used, and whether they will be disclosed outside the VA.
Broad consent for the storage, maintenance, and secondary use of identifiable private information and identifiable biospecimens

When following DHHS regulations, written materials should include the following requirements for broad consent when the revised Common Rule goes into effect.

- A statement that the study involves research.
- A description of any reasonably foreseeable risks or discomforts to the participant. (May be omitted if there are none.)
- A description of any benefits to the participant or to others which may reasonably be expected from the research. (May be omitted if there are none.)
- A statement describing the extent, if any, to which confidentiality of records identifying the participant will be maintained. (May be omitted if confidentiality will not be maintained.)
- A statement that participation is voluntary.
- A statement that refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled.
- A statement that the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.
- A statement that the participant’s biospecimens (even if identifiers are removed) may be used for commercial profit and whether the participant will or will not share in this commercial profit.
- Information about future use of private 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 researcher for future research studies without additional informed consent from the participant or legally authorized representative, if this might be possible; or
  - A statement that the participant’s information or specimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.
- A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens, such that a reasonable person would expect the broad consent would permit the types of research conducted.
- A description of the identifiable private information or identifiable biospecimens that might be used in the research.
- Whether sharing of identifiable private information or identifiable biospecimens might occur.

- The types of organizations or researchers that might conduct research with the identifiable private information or identifiable biospecimens.
- The period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite).
- The time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period could be indefinite).
- Unless the participant or legally authorized representative will be provided details about the specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the participant’s identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might not have chosen to consent to some of those specific research studies.
- Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the participant in all circumstances, a statement that such results might not be disclosed to the participant.
- For research involving biospecimens, a statement specifying whether the research will (if known) or might include whole genome sequencing.
- An explanation of whom to contact for answers to pertinent questions about the research participant’s rights.
- An explanation of whom to contact for answers to questions about storage and use of the participant’s identifiable information or biospecimens.
- An explanation of whom to contact in the event of a research-related injury to the participant. (May not be omitted just because the research involves no more than minimal risk.)
- Contact information for the research team for questions, concerns, or complaints. (Element III.1.G.)
- Contact information for someone independent of the research team for problems, concerns, questions, information, or input. (Element I.4.A.)
Element II.3.G. The IRB or EC has and follows written policies and procedures for approving waivers or alterations of the consent process and waivers of consent documentation.

**Commentary**

**Waiver or alteration of the consent process**

In certain situations, the IRB or EC may waive or alter the consent process in accordance with laws, regulations, codes, and guidance. When an IRB or EC waives the requirement to obtain consent, it waives the entire requirement for consent, both the attributes of the consent process and the elements of disclosure. When an IRB or EC alters the consent process, consent is still obtained, but the consent process or elements of disclosure differ from what is generally required. When the IRB or EC approves a waiver or alteration of the consent process, records should document why the IRB or EC judged that each criterion was met for the specific protocol being reviewed.

IRBs or ECs sometimes use the terms “passive consent,” “deferred consent,” or “implied consent” to describe consent processes that do not follow one or more requirements for the consent process. Each of these cases represents a waiver or alteration in the consent process. Research that proposes these consent procedures cannot be approved unless the IRB or EC approves a waiver or alteration of the consent process.

**Waiver of consent documentation**

In certain situations, the IRB or EC may waive the requirement to document the consent process. When the IRB or EC approves a waiver of the requirement to document the consent process, records should document the protocol-specific reasons justifying the waiver. An IRB or EC might require that a written statement describing the research be provided to participants, such as a copy of a consent document that might be used if the participant requests written documentation of the consent process.

See AAHRPP Tip Sheet 1.
See AAHRPPTip Sheet 19.
See AAHRPP Tip Sheet 20.

**Regulatory and Guidance References**

- DHHS: 45 CFR 46.116(c), 45 CFR 46.116(d), 45 CFR 46.117(c), OHRP Guidance on Informed Consent Legally Effective and Prospectively Obtained
- VA: 38 CFR 16.116(c), 38 CFR 16.116(d), 38 CFR 16.117(c), VHA Handbook 1200.05, 34
- DoD: Instruction 3216.02 9. (2.1.1), 10 USC 980(a,b)
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)
- ED: 343 CFR 99

**Required Written Materials**

**Essential requirements:**

- Policies and procedures allow the IRB or EC to waive or alter the consent process by determining that the criteria for waivers or alterations are met.
- Policies and procedures allow the IRB or EC to waive parental permission by determining that the criteria for waivers or alterations are met.
- Policies and procedures allow the IRB or EC to waive the requirement for written documentation of the consent process by determining that the criteria for waivers are met.
- Policies and procedures have the IRB or EC document its findings justifying the waiver or alteration.

**When following DHHS regulations:**

- Policies and procedures allow the IRB or EC to waive the requirement to document the consent process by determining that the regulatory criteria for waivers or alterations of the consent process are met. (See Table II.3.G.1.)
- Written materials allow the IRB or EC to waive the requirement to document the consent process by determining that the regulatory criteria for waivers are met. (See Table II.3.G.1.)
  - When the IRB or EC considers waiving the requirement to obtain written documentation of the consent process, policies and procedures have the IRB or EC review a written description of the information that will be provided to participants.
  - When granting waivers of the requirement to obtain written documentation of the consent process, policies and procedures have the IRB or EC consider requiring the researcher to
provide participants with a written statement regarding the research.

- If the participants or LAR are members of a distinct cultural group or community in which signing forms is not the norm, documentation of consent may be waived if the research presents no more than minimal risk of harm to the participants, and provided there is an appropriate alternative mechanism for documenting consent was obtained.

When following the revised Common Rule when it goes into effect:

- If a broad consent procedure is used:
  - An IRB may not omit or alter any of the required elements of disclosure, and when appropriate, any of the additional elements of disclosure.
  - If a study requests broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens, and refused to consent, an IRB or EC cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

When following FDA regulations:

- Policies and procedures allow the IRB or EC to waive or alter the consent process by determining that the regulatory criteria for waivers or alterations of the consent process are met. (See Table II.3.G.2.)
- Policies and procedures allow the IRB or EC to waive the requirement to document the consent process by determining that the regulatory criteria for waivers are met. (See Table II.3.G.2.)
- When the IRB or EC considers waiving the requirement to obtain written documentation of the consent process, policies and procedures have the IRB or EC review a written description of the information that will be provided to participants.
- When granting waivers of the requirement to obtain written documentation of the consent process, policies and procedures have the IRB or EC consider requiring the researcher to provide participants with a written statement regarding the research.

When following VA requirements:

- Policies and procedures require the IRB to document the reason when it waives the requirement to obtain written documentation of the consent process.

When following DoD requirements:

- When research supported by DoD-appropriated funds involves experimental subjects as defined in DODI 3216.02, consent must be obtained in advance, unless waived.
- The Assistant Secretary for 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 may 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” as defined in DODI 3216.02, policies and procedures allow the IRB or EC to waive the consent process.

When following ED requirements:

- Policies and procedures include a process to comply with the Family Educational Rights and Privacy Act (FERPA). This process may occur outside the IRB or EC.
- FERPA applies when researchers obtain student records or personal education information from an education program as defined as any program principally engaged in the provision of education, including, but not limited to, early childhood education, elementary and secondary education, postsecondary education, special education, job training, career and technical education, and adult education.
- The organization has in policies and procedures, a process to grant exceptions to parental or student consent to release student records for research. This responsibility may be delegated to the IRB or EC, another individual, or component of the organization (e.g., a FERPA committee).
- An educational agency or institution may disclose personally identifiable information from an education record of a student without consent if the disclosure is part of an agreement between organizations or researchers conducting studies for, or on behalf of, educational agencies or institutions to:
  - Develop, validate, or administer predictive tests.
  - Administer student aid programs.
• Improve instruction.

• A school district or postsecondary institution that uses this exception is required to enter into a written agreement with the organization or researcher conducting the research that specifies:
  • The determination of the exception.
  • The purpose, scope, and duration of the study.
  • The information to be disclosed.
  • That 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 U.S. Department of Education regulations on redisclosure and destruction of information.
  • That the study will be conducted in a manner that does not permit personal identification of parents and students by anyone other than representatives of the organization with legitimate interests.
  • That the organization is required to destroy or return all personally identifiable information when no longer needed for the purposes of the study.
  • The time period during which the organization must either destroy or return the information.

• Education records may be released without consent 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.

When following DOE requirements:

• Policies and procedures specify that when conducting classified research the IRB may not grant a waiver of the consent process or waiver of documentation of consent.

Outcomes

• IRB or EC members waive the requirement to document the consent process according to criteria for waivers.
### Table II.3.G.1. Waivers and Alterations of Consent under US DHHS Regulations

#### Waiver of the Consent Process – Public Demonstration Project
- The research is conducted by or subject to the approval of state or local government officials.
- The research or demonstration protocol 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.
  - Possible changes in methods or levels of payment for benefits or services under those programs.
- The research cannot practicably be carried out without the waiver or alteration.
- The research is not regulated by the US FDA.

#### Waiver or Alteration of Consent Process – Obtaining Consent Not Practicable
- The research involves no more than minimal risk to the participants.
- The waiver or alteration will not adversely affect the rights and welfare of the participants.
- The research cannot practicably be carried out without the waiver or alteration.
- When appropriate, the participants will be provided with additional pertinent information after participation.

#### Waiver of Documentation of the Consent Process – Minimal Risk
- The research presents no more than minimal risk of harm to participants.
- The research involves no procedures for which written document of the consent process is normally required outside of the research context.
- The oral or written information provided to participants includes all required and appropriate additional elements of consent disclosure.
- The IRB or EC has determined whether the researcher should provide participants with a written statement regarding the research.
(Also applies to research regulated by the US FDA; See Table II.3.G.2.)

#### Waiver of Documentation of the Consent Process – Based on Harm
- The only record linking the participant and the research will be the consent document.
- The principal risk will be potential harm resulting from a breach of confidentiality.
- Each participant will be asked whether the participant wants documentation linking the participant with the research, and the participant’s wishes will govern.
- The oral or written information provided to participants includes all required and appropriate additional elements of consent disclosure.
- The IRB or EC has determined whether the participant should be provided written information.
(Also applies to research regulated by the US FDA; See Table II.3.G.2.)

See Element II.4.C. Planned Emergency Research
<table>
<thead>
<tr>
<th>Table II.3.G.2. Waivers and Alterations of Consent under US FDA Regulations</th>
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<tr>
<td>- The clinical investigation involves no more than minimal risk to the participants.</td>
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<td><strong>See Element II.4.C. Planned Emergency Research</strong></td>
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</table>
Standard II-4: The IRB or EC provides additional protections for individuals who are vulnerable to coercion or undue influence and participate in research.

Element II.4.A. The IRB or EC has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable laws, regulations, codes, and guidance.

Commentary
The IRB or EC should evaluate research to judge whether the research involves participants who are vulnerable to coercion or undue influence. When some or all of the participants are likely to be vulnerable, the IRB or EC should ensure that additional safeguards are included in the research design to protect the rights and welfare of these participants. If the IRB or EC reviews research that involves children; pregnant women, fetuses, or neonates; prisoners; or adults who lack the ability to consent, or the IRB or EC regularly reviews research that involves other vulnerable individuals (for example, students, employees, or economically or educationally disadvantaged persons, or homeless persons), the IRB or EC should have written policies and procedures regarding additional protections for these categories.

It is impractical to have specific policies for every vulnerable population that might be involved in research. Therefore, when a research study involves vulnerable populations not otherwise covered by specific policies and procedures, policies and procedures should describe in general the steps followed by the IRB or EC to evaluate such research to determine the need for additional protections.

In research involving no more than minimal risk and vulnerable populations, the IRB or EC may decide that existing protections are sufficient and no additional protections are warranted. Conversely, sometimes when research involves no more than minimal risk, additional protections for vulnerable populations might be appropriate.

If additional protections for vulnerable populations are not required under laws, regulations, codes, and guidance, then policies and procedures should describe equivalent protections. Equivalent protections ensure safeguards are in place to protect vulnerable populations, while allowing flexibility in review.

See AAHRPP Tip Sheet 1.
See AAHRPP Tip Sheet 11.
See AAHRPP Tip Sheet 18.

See AAHRPP Tip Sheet 20.
See AAHRPP Tip Sheet 26.

Regulatory and Guidance References
- FDA: 21 CFR 50.3, 21 CFR 50 Subpart D, 21 CFR 56.111(b), 21 CFR 56.111(c)
- DoD: Instruction 3216.02 7.; SECNAVINST 3900.39D, para. 6a(8), DoDD 3216.2, para. 4.4.1; SECNAVINST 3900.39D, para. 6a(6), DoDD 3216.2, para. 4.2; SECNAVINST 3900.39D, para. 6a(3);10 U.S.C. 980
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)
- ICH-GCP: 4.8.13, 4.8.14

Required Written Materials

Essential requirements:
- Applications include whether some or all of the participants are likely to be vulnerable to coercion or undue influence.
- When some or all of the participants are likely to be vulnerable, applications include a description of
additional safeguards included in the protocol to protect their rights and welfare.

- In order to approve research where some or all of the participants are likely to be vulnerable, policies and procedures have the IRB or EC determine whether additional safeguards have been included in the protocol to protect their rights and welfare.
- If research involves pregnant women, fetuses, or neonates, policies and procedures have the IRB or EC follow Subpart B of the DHHS regulations or equivalent protections as allowed by law.
  - If the organization chooses not to apply Subpart B to all research regardless of funding, policies and procedures include equivalent protections for participants in non-funded research.
- If research involves prisoners as participants, policies and procedures have the IRB follow Subpart C of the DHHS or equivalent protections as allowed by law.
  - If the organization chooses not to apply Subpart C to all research regardless of funding, procedures include equivalent protections for participants in non-funded research.
- If the convened IRB or EC reviews research that involves prisoners, policies and procedures indicate that one or more individuals who are prisoners or prisoner representatives have to be present at the meeting.
- If research involves children as participants, policies and procedures have the IRB or EC follow Subpart D of the DHHS or equivalent protections as allowed by law.
  - If the organization chooses not to apply Subpart D to all research regardless of funding, procedures include equivalent protections for participants in non-funded research.
- If research involves adults unable to consent, policies and procedures have the IRB or EC consider specific criteria for approval of such research that provides additional safeguards to protect their rights and welfare.
- If the IRB or EC regularly reviews research that involves other vulnerable populations, policies and procedures describe the steps the IRB or EC follows to evaluate whether additional safeguards are included in research to protect the rights and welfare of these participants.

When following DHHS regulations:

- Policies and procedures have the IRB or EC follow the requirements specified in Subpart B for research involving pregnant women, fetuses, or neonates; Subpart C for research involving prisoners; and Subpart D for research involving children.

When following FDA regulations:

- Policies and procedures have the IRB or EC follow the requirements specified in Subpart D for research involving children.

When following VA requirements:

- Policies and procedures have the IRB find and document in the minutes or IRB records specific findings in accordance with VA requirements.
- Policies and procedures indicate:
  - Research involving stem cells shall be governed by the policy set by NIH.
  - Research involving the provision of *in vitro* fertilization services is not allowed.
  - Research in which the focus is either a fetus, human fetal tissue, in-utero, or ex-utero, is not allowed.
  - Interventional research involving neonates is not allowed. Prospective observational or retrospective record review studies that involve neonates or neonatal outcomes are permitted.
  - Research involving pregnant women as participants is not allowed unless the IRB determines the requirements in 45 CRR 46.204 are met, and the facility director certifies the facility has sufficient expertise in women’s health to conduct the proposed research.
  - Research involving prisoners as participants is not allowed unless a waiver has been granted by the chief research and development officer.
  - Research involving children as participants is not allowed unless a waiver has been granted by the facility director. Research involving children may not pose greater than minimal risk to the child.
  - Biological specimens and data obtained from children is considered research involving children even if de-identified.
  - International research is not initiated unless permission is obtained from the facility director.
  - Research involving adults who are unable to consent may occur only when the IRB determines the proposed research:
    - Does not present greater than minimal risk, or
    - Presents a greater probability of direct benefit to the participant than harm to the participant, or
    - Poses greater than minimal risk and no prospect of direct benefit to individual participants, but is likely to yield generalizable knowledge about the participant’s disorder or condition that is of vital importance to understanding or amelioration of the participant’s disorder or condition.
- In addition, the IRB determines the research cannot be performed solely on adults who can consent, and the focus of the research is the disorder leading to the lack of decision-making capacity, or
- Where the subject of the research is not directly related to the participant’s lack of decision-making capacity, the researcher has presented a compelling reason for including adults unable to consent.

*When following DoD requirements:*
- Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C, and D.
- For purposes of applying Subpart B, the phrase “biomedical knowledge” must be replaced with “generalizable knowledge.”
- The applicability of Subpart B is limited to research involving pregnant women as participants in research that is more than minimal risk and included interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.
- Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.
- Research involving prisoners cannot be reviewed by the expedited procedure.
- When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum. The prisoner representative may be a prisoner, an employee of the prison, or an individual not affiliated with the prison.
- In addition to allowable categories of research on prisoners in Subpart C, epidemiological research is also allowable when:
  - The research describes the prevalence or incidence of a disease by identifying all cases or studies potential risk factor association for a disease.
  - The research presents no more than minimal risk.
  - The research presents no more than an inconvenience to the participant.
- When a previously enrolled human participant becomes a prisoner, if the researcher asserts to the IRB that it is in the best interest of the prisoner-participant to continue to participate in the research while a prisoner, the IRB chair may determine that the prisoner-participant may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the organizational official and DoD Component office review the IRB’s approval to change the research protocol. Otherwise, the IRB chair must require that all research interactions and interventions with the prisoner-subject (including obtaining identifiable private information) cease until the convened IRB can review this request to approve a change in the research protocol. The convened IRB, upon receipt of notification that a previously enrolled human participant has become a prisoner, must promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy. The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative. If the prisoner-participant can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-participant’s confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human participants from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-participant to continue to participate in the research. This approval is limited to the individual prisoner-participant and does not allow recruitment of prisoners as participants.
- Research involving a detainee as a human participant is prohibited.
  - This prohibition does not apply to research involving investigational drugs and devices when the same products would be offered to US military personnel in the same location for the same condition.
- The exemption for research involving survey or interview procedures or observation of public behavior, does not apply to research with children, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed.
- Policies and procedures prohibit research involving prisoners of war.
- The IRB or EC is aware of the definition of “prisoner of war” for the DoD component granting the addendum.

*When following DOE requirements:*
- Policies must indicate that employees and contractors are considered vulnerable participants.
- Policies must include direction for the IRB to consider if additional protections are required for research involving employees and contractors.

*When following EPA regulations:*
- Policies and procedures include that for research conducted or supported by the EPA, research
involving intentional exposure of pregnant women or children to any substance is prohibited and not approved by the IRB or EC.

- Policies and procedures include that for research intended for submission to the EPA, research involving intentional exposure of pregnant women or children to any substance is prohibited and not approved by the IRB or EC.

- Policies and procedures have the IRB review observational research involving pregnant women and fetuses using 40 CFR 26 and 45 CFR 46 Subpart B.

- Policies and procedures allow the IRB to review and approve observational research involving children that does not involve greater than minimal risk only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 26.406.

- Policies and procedures allow the IRB to review and approve observational research involving children that involves greater than minimal risk but presenting the prospect of direct benefit to the individual participants if the IRB finds and documents that:
  - The intervention or procedure holds out the prospect of direct benefit to the individual participant or is likely to contribute to the participant's well-being.
  - The risk is justified by the anticipated benefit to the participants.
  - The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.
  - Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 26.406.

When following the ICH-GCP (E6) guideline:

- When adults are unable to consent, policies and procedures have the IRB or EC determine:
  - A non-therapeutic clinical trial (i.e., a trial in which there is no anticipated direct clinical benefit to the participant) should be conducted in participants who personally give consent and who sign and date the written consent document.

- Non-therapeutic clinical trials may be conducted in participants with consent of a legally acceptable representative provided the following conditions are fulfilled: a) The objectives of the clinical trial cannot be met by means of a trial in participants who can give consent personally; b) The foreseeable risks to the participants are low; c) The negative impact on the participant's well-being is minimized and low; d) The clinical trial is not prohibited by law; and e) The opinion of the IRB or EC is expressly sought on the inclusion of such participants, and the written opinion covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

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<tr>
<th>Common Types of Materials That May Be Used to Meet the Element</th>
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<tr>
<td>Application form</td>
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<td>Reviewer checklist</td>
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<th>Outcomes</th>
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<tr>
<td>IRB or EC members determine whether additional safeguards are required in research that involves vulnerable individuals in order to protect their rights and welfare.</td>
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<tr>
<td>The IRB or EC documents required determinations and provides protocol-specific findings justifying the determinations.</td>
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</tbody>
</table>
Element II.4.B. The IRB or EC has and follows written policies and procedures requiring appropriate protections for prospective participants who cannot give consent or whose decision-making capacity is in question.

Commentary
The IRB or EC should determine whether the research involves participants whose decision-making capacity is in question. When some or all of the participants are likely to have diminished decision-making capacity, the IRB or EC should consider whether additional safeguards are needed as part of the consent process. The IRB or EC should evaluate whether research submitted for review satisfies this criterion. If the IRB or EC reviews research that involves children, fetuses, neonates, prisoners, or adults who lack the ability to consent, or the IRB or EC regularly reviews research involving other populations who have diminished decision-making capacity, the IRB or EC should have written policies and procedures regarding the consent process for these individuals. When a research study involves a population that has a diminished decision-making capacity not otherwise covered by specific policies and procedures, policies and procedures should describe in general the steps the IRB or EC uses to evaluate the consent process in this population.

See AAHRPP Tip Sheet 1.
See AAHRPP Tip Sheet 18.
See AAHRPP Tip Sheet 20.
See AAHRPP Tip Sheet 26.

Regulatory and Guidance References
- DHHS: 45 CFR 46.204, 45 CFR 46.205, 45 CFR 46.305, 45 CFR 46.402(a)-(c), 45 CFR 46.408
- FDA: 21 CFR 50.3(l), 21 CFR 50.3(n), 21 CFR 50.55
- VA: VHA Handbook 1200.05, 36, 45, 46, 47, 48, 49
- DoD: Instruction 3216.02 9
- ED: 34 CFR 98.4
- ICH-GCP: 3.1.6, 4.8.12, 4.8.13, Public Law 107-110 Jan. 8, 2002 Part E

Required Written Materials
Essential requirements:
- Policies and procedures have the IRB or EC evaluate whether the research involves participants who have diminished decision-making capacity and, if so, provide additional safeguards to ensure an appropriate consent process.
- When a research study involves populations with diminished decision-making capacity not covered by specific policies and procedures, policies and procedures describe, in general, the steps followed by the IRB or EC to evaluate the consent process for these populations.
- When research involves pregnant women, fetuses, or neonates, policies and procedures have the IRB or EC follow Subpart B of the DHHS regulations or equivalent laws or regulations to approve an appropriate consent process.
- When research involves prisoners as participants, policies and procedures have the IRB or EC follow Subpart C of the DHHS regulations or equivalent laws or regulations to approve an appropriate consent process that includes a determination that:
  - The information will be presented in language that is understandable to prisoners.
  - Each prisoner will be informed in advance that participation in the research will have no effect on his or her parole.
- When research involves children as participants, policies and procedures have the IRB or EC follow Subpart D of the DHHS or FDA regulations or equivalent laws or regulations to approve an appropriate consent process for children and consent process for parents or guardians.
- When researchers are likely to approach adults who lack the ability to consent, policies and procedures have the IRB evaluate whether:
  - The proposed plan for the assessment of the capacity to consent is adequate.
  - Assent of the participants is a requirement, and, if so, whether the plan for assent is adequate.

When following DHHS regulations:
- When research involves pregnant women, policies and procedures have the IRB or EC determine that the consent of the pregnant women is required if the research holds out:
  - The prospect of direct benefit to the pregnant woman.
• The prospect of direct benefit both to the pregnant woman and the fetus.
• No prospect of benefit for the woman or the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.
• When research involves pregnant women and holds out the prospect of direct benefit solely to the fetus, policies and procedures have the IRB or EC determine that the consent of the pregnant woman and the father is required, except that the father’s consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest if the research holds out the prospect of direct benefit solely to the fetus.
• When the research involves neonates of uncertain viability, policies and procedures have the IRB or EC determine that the consent of either parent of the neonate is required or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective consent of either parent’s legally authorized representative is required, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.
• When the research involves non-viable neonates, policies and procedures have the IRB or EC determine that the consent of both parents is required, except:
  • If either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the consent of one parent is required.
  • If the pregnancy resulted from rape or incest the consent of the father need not be obtained.
• When the research involves non-viable neonates, policies and procedures did not allow the IRB or EC to approve the consent of a legally authorized representative.

When following DHHS or FDA regulations:
• When research involves children, policies and procedures have the IRB or EC following the requirements in Subpart D pertaining to obtaining assent of children and permission of the parents or guardian.
• For research that involves no more than minimal risk or more than minimal risk with the prospect of direct benefit to the individual children, policies and procedures have the IRB or EC determine whether:
  • The permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child, or the permission of one parent is sufficient.
  • For research that involves more than minimal risk without the prospect of direct benefit to the individual children, policies and procedures have the IRB or EC determine that the permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
• Policies and procedures have the IRB or EC determine and document that assent is a requirement of:
  • All children.
  • Some children.
  • None of the children.
• When the IRB or EC determines that assent is not a requirement of some children, policies and procedures have the IRB or EC determine and document which children are not required to assent.
• When the IRB or EC determines that assent is not a requirement for some or all children, policies and procedures have the IRB or EC determine and document one or more of the following:
  • The children are not capable of providing assent based on the age, maturity, or psychological state.
  • The capability of the children is so limited that they cannot reasonably be consulted.
  • The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of the research.
• Assent can be waived using the criteria for waiver of the consent process.
• When the IRB or EC determines that assent is a requirement, policies and procedures have the IRB determine whether:
  • Assent will be documented.
  • If so, the process to document assent.

When following VA requirements:
• When research involves children, policies and procedures have the IRB or EC following the requirements in Subpart D pertaining to obtaining assent of children and permission of the parents or guardian.
• For research that involves no more than minimal risk or more than minimal risk with the prospect of direct benefit to the individual children,
Policies and procedures indicate:

- Consent by a legally authorized representative is limited to situations where the prospective participant is incompetent or has impaired decision-making capacity, as determined and documented in the person’s medical record in a signed and dated progress note.

- Consent from the legally authorized representative of the participant can only be obtained from the following: a healthcare agent (i.e., an individual named by an individual in a durable power of attorney for health care); 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; or close friend, unless otherwise specified by applicable state law.

- If there is any question as to whether a potential adult participant has decision-making capacity, and there is no documentation in the medical record that the individual lacks decision-making capacity, and the individual has not been ruled incompetent by a court of law, the researcher must consult with a qualified practitioner (who may be a member of the research team) about the individual’s decision-making capacity before proceeding with the consent process.

- Individuals, who because of a known condition, are at high risk to temporary or fluctuating lack of decision-making capacity must be evaluated by a qualified practitioner to determine the individual’s ability to provide consent. This evaluation must be performed as described in the IRB-approved protocol.

- If the individual is deemed to lack decision-making capacity at the time of their participation in the study, a legally authorized representative must provide consent.

- If the participant regains decision-making capacity, the researcher must repeat the consent process with the participant, and obtain the participant’s permission to continue with the study.

- Disclosures to be made to the participant must be made to the participant’s legally authorized representative.

- The participant’s legally authorized representative must be told that that his or her obligation is to try to determine what the participant would do if able to make an informed decision. If the prospective participant’s wishes cannot be determined, the legally authorized representative must be told that he or she is responsible for determining what is in the participant’s best interest.

- Have the researcher explain the proposed research to the prospective participant when feasible even when the participant’s legally authorized representative gives consent.

- Have the practitioner explain the proposed research to the prospective participant when feasible.

- Ensure the study includes appropriate procedures for respecting dissent. Prohibit participants from being forced or coerced to participate in a research study.

When following DoD requirements:

- 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.

When following ED requirements:

- Policies and procedures include a process to comply with the Protection of Pupil Rights Amendment. This process may occur outside the IRB or EC:

- For certain types of research projects directly funded by the U.S. Department of Education: 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).

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 not an emancipated minor.

For certain types of research projects not directly funded by the U.S. Department of Education and conducted in a school that receives funding from the U.S. Department of Education: Policies and procedures include a process to verify compliance with 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 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.
• 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).
• The right of a parent of a student to inspect, upon the request of the parent, any instructional material used as part of the educational curriculum for the student.
• Any applicable procedures for granting a request by a parent for reasonable access to 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 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.
• The right of a parent of a student to inspect, upon the request of the parent, 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 instrument within a reasonable period of time after the request is received.

**Common Types of Materials That May Be Used to Meet the Element**
- Application form
- Reviewer checklist
- Consent template

**Outcomes**
- IRB or EC members approve research involving participants with diminished decision-making capacity that includes additional safeguards for seeking their consent.
Element II.4.C. The IRB or EC has and follows written policies and procedures for making exceptions to consent requirements for planned emergency research and reviews such exceptions according to applicable laws, regulations, codes, and guidance.

Commentary
An IRB or EC should have policies and procedures to consider a request for a waiver of the requirement for consent for planned emergency research, unless the organization does not intend to conduct such research. Policies and procedures should account for the differences between various laws, regulations, codes, and guidance that govern such research, such as the FDA regulations and the DHHS regulations depending on whether the research is subject to FDA regulation.

See AAHRPP Tip Sheet 1.
See AAHRPP Tip Sheet 11.
See AAHRPP Tip Sheet 20.

Regulatory and Guidance References
- DHHS: 45 CFR 46 Waiver of Informed Consent Requirements in Certain Emergency Research (Federal Register, Vol. 61, No. 192, pp. 51531-51533, October 2, 1996), 45 CFR 46.116(f)
- FDA: IRB Information Sheets - Exception From Informed Consent for Studies Conducted in Emergency Settings
- DoD: Instruction 3216.2, para. 4.2; SECNAVINST 3900.39D, para. 6a(3)and 7a(l); 10 U.S.C. 980 (a,b); 10 USC 980
- VA: VHA Handbook 1200.05, 4, 41
- ICH-GCP: 3.1.7, 4.8.15

Required Written Materials

Essential requirements:
- Policies and procedures describe the criteria to waive the requirement to obtain consent for planned emergency research.

When following FDA regulations:
- Policies and procedures describe the criteria to approve planned emergency research. The research plan must be approved in advance by the FDA and the IRB or EC, and publicly disclosed to the community in which the research will be conducted.

When following VA requirements:
- Policies and procedures do not allow the IRB to waive the requirement to obtain consent for planned emergency research.
- Policies and procedures describe the criteria to waive the requirement to obtain consent for planned emergency research.

When following DoD requirements:
- Policies and procedures require that the participant or the participant’s legally authorized representative is informed about the clinical trial as soon as possible and provides consent if the participant wishes to continue.

When following the ICH-GCP (E6) guideline:
- Policies and procedures require that the participant or the participant’s legally authorized representative is informed about the clinical trial as soon as possible and provides consent if the participant wishes to continue.

Outcomes
- Waivers to the requirement to obtain consent for planned emergency research are granted in accordance with applicable laws, regulations, codes, and guidance.
Standard II-5: The IRB or EC maintains documentation of its activities.

Element II.5.A. The IRB or EC maintains a complete set of materials relevant to the review of the research protocol or plan for a period of time sufficient to comply with legal and regulatory requirements, sponsor requirements, and organizational policies and procedures.

Commentary
IRB or EC recordkeeping should follow legal and regulatory requirements, sponsor requirements, and organizational policies and procedures. IRB or EC records for a protocol or research plan should also be organized to allow a reconstruction of a complete history of all IRB or EC actions related to the review and approval of the protocol.

The IRB or EC should have a policy and procedure governing document retention that follows legal and regulatory requirements, sponsor requirements, and organizational policies and procedures. The method for record retention should allow access by authorized personnel and ensure that documents are kept safely and confidentially.

Regulatory and Guidance References
- DHHS: 45 CFR 115(a)-(b), OHRP Guidance on Written Institutional Review Board (IRB) Procedures
- DoD: Instruction 3216.02 15.d
- VA: VHA Handbook 1200.05, 26
- ICH-GCP: 3.4, 4.4, 4.9

Required Written Materials

Essential requirements:
- In order to allow a reconstruction of a complete history of IRB actions related to the review and approval of the protocol, policies and procedures have IRB or EC records include copies of:
  - Protocols or research plans.
  - Investigator brochure, if any.
  - Scientific evaluations, when provided by an entity other than the IRB or EC.
  - Recruitment materials.
  - Consent documents.
  - Progress reports submitted by researchers.
  - Reports of injuries to participants.
  - Records of continuing review activities.
  - Data and safety monitoring reports, if any.
  - Modifications to previously approved research.
  - Unanticipated problems involving risks to participants or others.
  - Documentation of non-compliance.
  - Significant new findings.
  - All correspondence between the IRB or EC and researchers.
  - Policies and procedures have IRB records for initial and continuing review of research by the expedited procedure include:
    - The justification for using the expedited procedure.
    - The rationale for conducting continuing review of research that otherwise would not require continuing review.
    - The rationale for a determination that research appearing on the list of eligible expedited review categories is greater than minimal risk.
    - Actions taken by the reviewer.
    - Any findings required by laws, regulations, codes, and guidance to be documented.
  - Policies and procedures have IRB or EC records document the justification for exempt determinations.
  - Policies and procedures have IRB or EC records document determinations required by laws, regulations, codes, and guidance.

When following VA requirements:
- Policies and procedures indicate that the required records, including the researcher’s research records, must be retained for a minimum of six years.
- 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 five years after cancellation.
- Policies and procedures have IRB records include:
  - Correspondence between the IRB and the Research and Development Committee.
• Correspondence between the IRB and researchers.
• A resume for each IRB member.
• All previous membership rosters.

*When following DoD requirements:*
- Records maintained that document compliance or non-compliance with DoD regulations must be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component.

**Outcomes**
- IRB or EC recordkeeping follows legal and regulatory requirements, sponsor requirements, and organizational policies and procedures.
- Records of a research protocol or plan are organized to allow a reconstruction of a complete history of IRB or EC actions related to the review and approval of the research protocol or plan.
- Records are retained for the required period of time.
- Records are stored in a way that maintains confidentiality.
Element II.5.B. The IRB or EC documents discussions and decisions on research studies and activities in accordance with legal and regulatory requirements, sponsor requirements (if any), and organizational policies and procedures.

Commentary
The IRB or EC must document discussions, decisions, and findings. This can be accomplished either through the minutes or, when the expedited procedure for review is used, through documentation in the protocol file or other records. Records may be maintained in printed form or electronically.

Minutes of IRB or EC meetings should be clear about the actions the IRB or EC takes and exactly what the IRB or EC approved. Minutes should specify the modifications required to secure approval and the reason the IRB or EC is requesting the modifications. Minutes should indicate proposals or motions voted upon by the IRB or EC, and the results of each vote. When conducting initial or continuing review, minutes should document the IRB’s determination of the approval period.

See AAHRPP Tip Sheet 3.

Regulatory and Guidance References
- DoD: Instruction 3216.02 15.d
- VA: 38 CFR 16.115(a)(2), 38 CFR 16.116(c)-(d), 38 CFR 16.117(c), VHA Handbook 1200.05, 24, 28

Required Written Materials
Essential requirements:
- Policies and procedures have IRB or EC minutes document:
  - Attendance at the meeting, including:
    - Each member’s full name.
    - Each member’s representative capacity (scientist, non-scientist, member who represents the general perspective of research participants, unaffiliated).
  - The names of members who participated in the convened meeting via an alternative mechanism, such as telephone or video conferencing.
  - If a consultant is present at the convened meeting, the name of the consultant, and a brief description of the consultant’s expertise, and documentation that the consultant did not vote with the IRB or EC on the study.
  - The names of non-members and guests, such as IRB or EC support staff, researchers, and study coordinators.
  - When an alternate member replaces a primary member, including the name of the alternate member.
  - The names of IRB or EC members who leave the meeting because of a conflict of interest along with the fact that a conflict of interest is the reason for the absence.
  - Actions taken by the IRB or EC with sufficient information to identify the research activities being reviewed and voted on by the IRB or EC at that meeting, including:
    - Initial review of a protocol.
    - Review of a request to modify a protocol.
    - Continuing review of a protocol.
    - Separate deliberations for each action.
  - Votes for each protocol as numbers for, against, or abstaining.
  - The basis for requiring changes in research.
  - The basis for disapproving research.
  - A written summary of the discussion of controverted issues and their resolution.
  - For initial and continuing review, the approval period.
• Required determinations and protocol-specific findings justifying those determinations for:
  • Waiver or alteration of the consent process.
  • Research involving pregnant women, fetuses, and neonates.
  • Research involving prisoners.
  • Research involving children.
  • Research involving participants with diminished capacity to consent.

When following the revised Common Rule when it goes into effect:
• 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. (See Element II.2.F.)
• Records must include documentation specifying the responsibilities that a relying organization and an organization operating an IRB or EC each will undertake to ensure compliance with the requirements of the Common Rule. (See Standard I-9)

When following VA requirements:
• 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.
• Minutes must communicate the decision and expedited review category in the minutes of the next available meeting, and in written notification to the researcher and research and development committee.

When following DoD requirements:
• Records maintained that document compliance or non-compliance with DoD regulations must be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD component.

Common Types of Materials That May Be Used to Meet the Element
• Minutes
• Other records, including documentations

Outcomes
• IRB or EC records reflect the actions of IRB or EC members.
Domain III: Researcher and research staff

Commentary
The environment in which researchers and research staff conduct research and the type of research they conduct influence their roles and responsibilities. Competent, informed, conscientious, compassionate, and responsible researchers and research staff provide the best possible protection for human research participants. This Domain of Standards sets forth requirements for researchers and research staff involved in research using human participants. As part of its Human Research Protection Program, an organization can improve its protection of research participants if it has arrangements ascertaining and enhancing the competence of researchers and research staff.

Standard III-1: In addition to following applicable laws and regulations, Researchers and research staff adhere to ethical principles and standards appropriate for their discipline. In designing and conducting research studies, researchers and research staff have the protection of the rights and welfare of research participants as a primary concern.

Element III.1.A. Researchers and research staff know which of the activities they conduct are overseen by the Human Research Protection Program, and they seek guidance when appropriate.

Commentary
Researchers and research staff should understand which activities are overseen by the HRPP or seek guidance. They should have an understanding of the definitions of what constitutes research involving human participants according to legal and regulatory definitions and the organization’s policies and procedures. When necessary, they should be aware of the process to obtain an opinion from the HRPP and whom to contact.

See AAHRPP Tip Sheet 2.
See AAHRPP Tip Sheet 18.

Regulatory and Guidance References
- DHH: 45 CFR 46.102(d), 45 CFR 46.102(f)
- FDA: 21 CFR 50.3(a), 21 CFR 50.3(c), 21 CFR 50.3(g), 21 CFR 50.3(j), 21 CFR 56.102(c), 21 CFR 56.102(l)

Required Written Materials
Essential requirements:
- Policies and procedures pertaining to Element I.1.A. that address essential requirements.

When following DHHS regulations:
- Policies and procedures pertaining to Element I.1.A. that address DHHS-specific requirements.

When following FDA regulations:
- Policies and procedures pertaining to Element I.1.A. that address FDA-specific requirements.

In the cases above, the policies and procedures pertaining to Element I.1.A also address the written material requirements for this Element. If the same policies and procedures are provided to researchers and research staff, simply reference those documents in the application for this Element. If there are additional materials, such as an Investigator Handbook or Web pages for researchers, that are not included in the materials used to support Element I.1.A, but are in support of Element III.1.A, include them here.

Outcomes
- Researchers and research staff understand which activities are overseen by the HRPP and when to seek guidance.
Element III.1.B. Researchers and research staff identify and disclose financial interests according to organizational policies and regulatory requirements and, with the organization, manage, minimize, or eliminate financial conflicts of interest.

Commentary
Researchers and research staff should understand the organization’s financial conflict of interest policy in order to follow it. For example, researchers and research staff should know which interests the organization requires to be disclosed. Researchers and research staff should know how, when, and to whom to disclose financial interests.

Researchers and research staff should understand how financial conflicts of interest can influence the protection of research participants. Researchers and research staff should also work collaboratively with the organization in the management of financial conflicts of interest.

Independent researchers and research staff who work with independent IRBs should understand legal and regulatory requirements for disclosing, managing, minimizing, or eliminating financial conflicts of interest. Such researchers and research staff should know how, when, and to whom to disclose financial interests and work collaboratively with independent IRBs in the management of financial conflicts of interest.

See AAHRPP Tip Sheet 10.

Regulatory and Guidance References
- DHHS: 42 CFR 50.603, 42 CFR 50.606(a), 45 CFR 690
- FDA: 21 CFR 54.1, 21 CFR 54.2, 21 CFR 54.4, 21 CFR 312.64(d), 21 CFR 812.110(d)
- VA: VHA Handbook 1200.05, 9

Required Written Materials

Essential requirements:
- Policies and procedures pertaining to Element I.6.B. that address essential requirements.

When following DHHS regulations:
- Policies and procedures pertaining to Element I.6.B. that address DHHS-specific requirements.

When following FDA regulations:
- Policies and procedures pertaining to Element I.6.B. that address FDA-specific requirements. In the cases above, the policies and procedures pertaining to Element I.6.B. also address the written material requirements for this Element. If the same policies and procedures are provided to researchers and research staff, simply reference those documents in the application for this Element. If there are additional materials, such as an Investigator Handbook or Web pages for researchers, that are not included in the materials used to support Element I.6.A., but are in support of Element III.1.B., include them here.

When following VA requirements:
- Researchers must disclose conflicts of interest. This means disclosing to the IRB any potential, actual, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and complying with all applicable VA and other federal requirements regarding conflict of interest.

Outcomes
- Researchers and research staff understand the concept of conflict of interest.
- Researchers and research staff disclose required financial interests.
- Researchers and research staff work collaboratively with the organization or independent IRB to manage financial conflicts of interest.
Element III.1.C. Researchers employ sound study design in accordance with the standards of the discipline. Researchers design studies in a manner that minimizes risks to participants.

Commentary
Researchers should design research studies so that the research will most likely develop or contribute to generalizable knowledge. Studies should be designed according to standards and ethical practices of the discipline. Researchers should design research to be sound enough to meet the study’s objectives before agreeing to enroll participants.

As part of their obligation to protect participants, researchers should understand the concept of minimizing risks. When researchers design research, they should consider designs that minimize risks. In protocols, researchers should describe the rationale for the chosen procedures and provide a risk-potential benefit analysis of the research.

When appropriate, researchers who design research should incorporate plans to monitor the data for the safety of participants. For example, research studies involving more than minimal risk are expected to have a plan for monitoring the data for the safety of participants. Researchers should understand that monitoring might occur at specific points in time, after a specific number of participants have been recruited, or upon recognition of harms. Monitoring might be conducted by a third party (e.g., the sponsor, medical monitor, data monitoring committee, or another researcher).

See AAHRPP Tip Sheet 11.

Regulatory and Guidance References
- ICH-GCP: 4.7,4.5.1

Required Written Materials

Essential requirements:
- Policies and procedures pertaining to Elements II.3.A., II.3.B., and II.4.A. that address essential requirements are consistent with educational materials or Web site information for researchers, or the Investigator Handbook.

In the case above, the policies and procedures pertaining to Elements II.3.A., II.3.B., and II.4.A. also address the written material requirements for this Element. If the same policies and procedures are provided to researchers and research staff, simply reference those documents in the application for this Element. If there are additional materials, such as an Investigator Handbook or Web pages for researchers, that are not included in the materials used to support Elements II.3.A., II.3.B., and II.4.A., but are in support of Element III.1.C., include them here.

When following DOJ requirements:
- Policies and procedures indicate that for research conducted within the Bureau of Prisons, the researcher must have academic preparation or experience in the area of study of the proposed research.
- Policies and procedures indicate that for research conducted within the Bureau of Prisons, when submitting a research protocol, the applicant must provide the following information:
  - A summary statement, which includes:
    - Names and current affiliations of the researchers.
    - Title of the study.
    - Purpose of the study.
    - Location of the study.
    - Methods to be employed.
    - Anticipated results.
    - Duration of the study.
    - Number of participants (staff or inmates) required and amount of time required from each.
    - Indication of risk or discomfort involved as a result of participation.
  - A comprehensive statement, which includes:
    - Review of related literature.
    - Detailed description of the research method.
    - Significance of anticipated results and their contribution to the advancement of knowledge.
• Specific resources required from the Bureau of Prisons.
• Description of all possible risks, discomforts, and benefits to individual participants or a class of participants, and a discussion of the likelihood that the risks and discomforts will actually occur.
• Description of steps taken to minimize any risks.
• Description of physical or administrative procedures to be followed to:
  • Ensure the security of any individually identifiable data that are being collected for the study.
  • Destroy research records or remove individual identifiers from those records when the research has been completed.
• Description of any anticipated effects of the research study on organizational programs and operations.
• Relevant research materials such as vitae, endorsements, sample consent statements, questionnaires, and interview schedules.
• A statement regarding assurances and certification required by federal regulations, if applicable.

*When following the ICH-GCP (E6) guideline:*
• Policies and procedures describe that researcher and research staff are knowledgeable about the following responsibilities:
  • During and following a participant’s participation in a clinical trial, the researcher ensures that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the clinical trial. Researchers inform participants when medical care is needed for other illnesses of which the researchers become aware (not applicable to independent IRBs or ECs).
• The researcher follows the clinical trial’s randomization procedures, if any, and ensures that the code is broken only in accordance with the protocol. If the clinical trial is blinded, the researcher promptly documents and explains to the sponsor any premature unblinding.

**Outcomes**
• Researchers use sound scientific designs in the conduct of research.
• Researchers design studies using methodologies and ethical standards consistent with the standards of the discipline.
• Researchers understand the concept of minimizing risk.
• Researchers consider whether other procedures involving less risk are appropriate when designing a research study.
• Researchers design studies that use procedures already being conducted on the participants for non-research reasons.
• Researchers modify research designs to mitigate potential injuries in on-going research.
• Researchers design studies to monitor data to ensure the safety and well-being of participants.
Element III.1.D. Researchers determine that the resources necessary to protect participants are present before conducting each research study.

Commentary
Researchers should have the resources required to conduct research in a way that will protect the rights and welfare of participants and ensure the integrity of the research. These resources might include personnel, time, and access to a study population. Researchers should not commence a research study without adequate resources to protect participants and should stop a research study if resources become unavailable. 

See AAHRPP Tip Sheet 11.

Regulatory and Guidance References
- VA: VHA Handbook 1200.05, 9
- ICH-GCP: 4.2.1, 4.2.2, 4.2.4, 4.3.2

Required Written Materials

Essential requirements:
- Policies and procedures pertaining to Element II.3.A. that address essential elements. The policies and procedures pertaining to Element II.3.A also address the written material requirements for this Element. If the same policies and procedures are provided to researchers and research staff, simply reference those documents in the application for this Element. If there are additional materials, such as an Investigator Handbook or Web pages for researchers, that are not included in the materials used to support Element II.3.A, but are in support of Element III.1.D, include them here.

- Researchers are responsible to:
  - Ensure that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.
  - Ensure that research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials and, when relevant, privileges) to perform procedures assigned to them during the study.

Outcomes
- When conducting a research study, researchers have the resources necessary to protect human participants, including:
  - Adequate time for the researchers to conduct and complete the research.
  - Adequate number of qualified staff.
  - Adequate facilities.
  - Access to a population that will allow recruitment of the necessary number of participants.
  - Availability of medical or psychosocial resources that participants may need as a consequence of the research.
  - A process to ensure that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions.
Element III.1.E. Researchers and research staff recruit participants in a fair and equitable manner.

Commentary

Researchers should use fair and equitable recruitment practices in research and avoid practices that place participants at risk for coercion or undue influence. See AAHRPP Tip Sheet 11.

Regulatory and Guidance References

- DHHS: 45 CFR 46.111(a)(3), 45 CFR 46.116
- FDA: 21 CFR 56.111(a)(3), 21 CFR 56.20, FDA Information Sheets: Recruiting Study Subjects, Payment to Research Subjects
- ICH-GCP 4.3.3, 4.3.4, 4.8.3

Required Written Materials

Essential requirements:
- Policies and procedures pertaining to Element II.3.C. that address essential requirements.

When following FDA regulations:
- Policies and procedures pertaining to Element II.3.C. that address specific FDA regulations.

When following VA requirements:
- Policies and procedures pertaining to Element II.3.C. that address specific VA regulations.

When following DoD requirements:
- Policies and procedures pertaining to Element II.3.C. that address specific DoD requirements.

In the cases above, the policies and procedures pertaining to Element II.3.C. also address the written material requirements for this Element. If the same policies and procedures are provided to researchers and research staff, simply reference those documents in the application for this Element. If there are additional materials, such as an Investigator Handbook or Web pages for researchers, that are not included in the materials used to support Element II.3.C., but are in support of Element III.1.E., include them here.

When following VA requirements:
- 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.

Outcomes

- Researchers and research staff develop and implement appropriate recruitment techniques.
- During the recruitment process, 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). The 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.
- Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.
- Researchers are knowledgeable about the following responsibilities:
  - The researcher informs the participant’s primary physician about the participant’s participation in the clinical trial if the participant has a primary physician and if the participant agrees to the primary physician being informed (not applicable to independent IRBs or ECs).
  - Although a participant is not obliged to give his or her reasons for withdrawing prematurely from a clinical trial, the researcher makes a reasonable effort to ascertain the reason, while fully respecting the participant’s rights.
- Researchers and research staff understand the importance of equitable selection of participants.
- Researchers and research staff use recruitment processes that are fair and equitable.
Element III.1.F. Researchers employ consent processes and methods of documentation appropriate to the type of research and the study population, emphasizing the importance of comprehension and voluntary participation to foster informed decision-making by participants.

**Commentary**
Researchers and research staff should understand the concept of respect for persons and the obligation to obtain the consent of participants or their legally authorized representatives. Researchers and research staff should understand that consent is a continual process, and conduct the consent process in a way that meets the criteria for legally effective consent. Researchers and research staff should understand the difference between the consent process, itself, and documentation of the consent process. Researchers and research staff should know how to document the consent of a participant or a legally authorized representative. See AAHRPP Tip Sheet 11.

**Regulatory and Guidance References**
- DHHS: 45 CFR 46.116, 45 CFR 46.116(a)(7), 45 CFR 46.117(a)
- ICH-GCP 4.6.6, 4.8.1, 4.8.2, 4.8.4 - 4.8.15

**Required Written Materials**

**Essential requirements:**
- Policies and procedures pertaining to Elements II.3.F., II.3.G., and II.4.B.

**When following DHHS or FDA regulations**
- When the long form of consent documentation is used, researchers or research staff follow regulatory and IRB or EC requirements.
- When the short form of consent documentation is used, researchers or research staff follow regulatory and IRB or EC requirements.

**When following DHHS regulations:**
- Policies and procedures pertaining to Elements II.3.F., II.3.G., and II.4.B.

**When following FDA regulations:**
- Policies and procedures pertaining to Elements II.3.F., II.3.G., and II.4.B. that address essential requirements.

**When following VA requirements:**
- Policies and procedures pertaining to Elements II.3.F., II.3.G., and II.4.B. that address specific VA requirements.

**When following DoD requirements:**
- Policies and procedures pertaining to Elements II.3.F., II.3.G., and II.4.B. that address specific DoD requirements.

**When following the ICH-GCP (E6) guideline:**
- Policies and procedures describe that researchers and research staff provide all the disclosures and follow the requirements pertaining to consent covered by ICH-GCP.

In the cases above, the policies and procedures pertaining to Elements II.3.F., II.3.G., and II.4.B. also address the written material requirements for this Element. If the same policies and procedures are provided to researchers and research staff, simply reference those documents in the application for this Element. If there are additional materials, such as an Investigator Handbook or Web pages for researchers, that are not included in the materials used to support Elements II.3.F., II.3.G., and II.4.B., but are in support of Element III.1.F., include them here.

**Outcomes**
- Researchers and research staff understand the difference between the consent process and the documentation of the consent process.
- Researchers and research staff understand consent to be an ongoing process throughout the participant’s involvement in the research.
- Researchers and research staff:
  - Obtain the legally effective consent of the participant or the participant’s legally authorized representative.
• Provide the prospective participant or the legally authorized representative sufficient opportunity to consider whether to participate.
• Minimize the possibility of coercion or undue influence.
• Communicate with the participant or the legally authorized representative in language understandable to the participant or the legally authorized representative. Do not use exculpatory language when communicating with a prospective participant or the legally authorized representative.
• Document the consent process as required.
Element III.1.G. Researchers and research staff have a process to address participants’ concerns, complaints, or requests for information.

Commentary
Researchers and research staff should be open to participants’ complaints or requests for information. Researchers and research staff should respond appropriately to such complaints or questions. Researchers should explain to research participants how to contact the research staff to ask questions about the research or express concerns or complaints about the research.

A common, although not exclusive, mechanism for providing contact information is language in the consent document.

Regulatory and Guidance References
- DHHS: 45 CFR 46.116(a)(6), 45 CFR 46.116(a)(7)
- FDA: 21 CFR 50.25(a)(6), 21 CFR 50.25(a)(7)

Required Written Materials
Essential requirements:
- Policies and procedures describe the way in which the organization provides research participants with information on how to contact the researchers or research staff in regards to:
  - Concerns, complaints, or questions about the research study.
  - Requests for information.

Outcomes
- Researchers and research staff provide information and processes for participants to submit concerns, complaints or requests for information.
- Researcher and research staff respond to complaints and requests for information from participants.
- Researchers and research staff involve the IRB or EC and other components of the HRPP in response to complaints or request for information.
Standard III-2: Researchers meet requirements for conducting research with participants and comply with all applicable laws, regulations, codes, and guidance; the organization’s policies and procedures for protecting research participants; and the IRB’s or EC’s determinations.

Element III.2.A. Researchers and research staff are qualified by training and experience for their research roles, including knowledge of applicable laws, regulations, codes, and guidance; relevant professional standards; and the organization’s policies and procedures regarding the protection of research participants.

Commentary
Researchers and research staff should be qualified by training and experience for their roles and responsibilities in conducting research so that they follow the protocol and abide by the organization’s policies and procedures. Researchers and research staff should have the knowledge to follow laws, regulations, codes, and guidance such as those concerning IRB or EC review, consent requirements, reporting requirements, maintenance of records, retention of records, and supervision of research conduct. When appropriate, Researchers and research staff should understand and apply relevant professional standards that are applicable to their research.

See AAHRPP Tip Sheet 11.
See AAHRPP Tip Sheet 18.

Regulatory and Guidance References
- DHHS: 45 CFR 46.102(d), 45 CFR 46.102 (f)
- FDA: 21 CFR 50.3(a), 21 CFR 50.3(c), 21 CFR 50.3(g), 21 CFR 50.3(j), 21 CFR 56.102(c), 21 CFR 56.102(l)
- VA: 38 CFR 16.102(d), 38 CFR 16.102 (f), ICH-GCP: 2.7, 2.8, 4.1.1 – 4.1.4, 4.3.1, 4.3.2, 4.4.1 – 4.4.3, 4.5.1 – 4.5.4, 4.6.1 – 4.6.6, 4.7, 4.9.1-4.9.5
- DOJ: 28 CFR 512.11 (a)( 6)

Required Written Materials

Essential requirements:
- Policies and procedures pertaining to Element I.I.D. that address essential requirements.
- The policies and procedures pertaining to Element I.I.D. also address the written material requirements for this Element. If the same policies and procedures are provided to researchers and research staff, simply reference those documents in the application for this Element. If there are additional materials, such as an Investigator Handbook or Web pages for researchers, that are not included in the materials used to support Element I.I.D. but are in support of Element III.2.A., include them here.

When following the ICH-GCP (E6) guideline:
- Policies and procedures describe that the researcher and research staff are knowledgeable about the following responsibilities:
- The researcher provides evidence of his or her qualifications through up-to-date curriculum vitae or other relevant documentation requested by the sponsor, the IRB or EC, or the regulatory authority.
- The researcher is familiar with the appropriate use of the investigational product, as described in the protocol, in the current investigator brochure, in the product information, and in other information sources provided by the sponsor.
- A qualified physician (or dentist, when appropriate), who is a researcher or a co-researcher for the clinical trial, is responsible for all clinical trial-related medical (or dental) decisions (not applicable to independent IRBs or ECs).
- During and following a participant’s participation in a clinical trial, the researcher ensures that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the clinical trial (not applicable to independent IRBs or ECs).
- The researcher ensures the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor.
Outcomes

- Researchers and research staff are qualified by training and experience for their roles and responsibilities in conducting research.
- Researchers and research staff know which laws, regulations, codes, and guidance govern their research studies and are knowledgeable about requirements pertaining to specific research studies.
- Researchers and research staff are knowledgeable about the organization’s policies and procedures.
Researchers maintain appropriate oversight of each research study, as well as research staff and trainees, and appropriately delegate research responsibilities and functions.

**Commentary**
Researchers are ultimately responsible for the conduct of research. Although researchers may delegate certain responsibilities and functions of the research, they must maintain oversight and retain ultimate responsibility for the conduct of those to whom they delegate responsibility.

When researchers delegate responsibilities or functions, they should ensure that research staff are trained and able to perform the function and assume the responsibility for the delegated function.

See AAHRPP Tip Sheet 11.
See AAHRPP Tip Sheet 18.

**Regulatory and Guidance References**
- FDA: 21 CFR 312.53(c) (1), 21 CFR 312.60, 21 CFR 312.61, 21 CFR 312.62, 21 CFR 812.43(c) (4), 21 CFR 812.100, 21 CFR 812.140
- VA: VHA Handbook 1200.05, 9, 63
- DOJ: 28 CFR 512.11(a)(7)
- ICH-GCP: 4.2.3, 4.2.4

**Required Written Materials**
*When following VA requirements:*
- Policies and procedures indicate that if the principal researcher or the local site researcher does not personally obtain consent, the researcher must formally and prospectively designate to another research team member in writing the protocol or the application for IRB approval the responsibility for obtaining consent, whether a waiver of documentation of the consent process has been approved by the IRB.
- If the researcher contracts with a firm to obtain consent, the firm must have its own IRB.
- Students and other trainees (including residents and fellows), 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, or use data, or human biological specimens that have been collected within VA for clinical, administrative, or research purposes.
- A researcher sufficiently experienced in the area of the trainee’s research interest must serve as principal researcher or co-principal researcher and is responsible for oversight of the research and the trainee.

*When following DOJ requirements:*
- Policies and procedures indicate that for research conducted within the Bureau of Prisons, the researcher must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor to the researcher.

*When following the ICH-GCP (E6) guideline:*
- Policies and procedures describe that the researcher maintains a list of appropriately qualified persons to whom they have delegated significant clinical trial-related duties.

**Outcomes**
- Researchers are involved in the conduct of the research, including recruitment and obtaining consent, and maintain oversight of recruitment, consent, and protocol procedures.
- Researchers hire qualified staff.
- Research Staff indicate that the researcher delegates responsibility to them commensurate with their training and qualifications.
- Researchers are available to research staff when needed.
Element III.2.C. Researchers and research staff follow the requirements of the research protocol or plan and adhere to the policies and procedures of the organization and to the requirements or determinations of the IRB or EC.

**Commentary**

Researchers and research staff should be knowledgeable about and follow all legal and regulatory requirements and the organization’s policies and procedures that pertain to their research. This includes adherence to the determinations and requirements of the IRB or EC. Once a research study is approved by the IRB or EC, researchers and research staff should follow the research plan or protocol as approved by the IRB or EC, and not implement changes until they are approved by the IRB or EC.

**Regulatory and Guidance References**

- FDA: FDA-Good Clinical Practice
- VA: VHA Handbook 1200.05, 9
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)
- ED: 34 CFR 98.3
- ICH-GCP: 4.1.3, 4.4.1, 4.5.1

**Required Written Materials**

*When following VA requirements:*

- Policies and procedures indicate:
  - The principal researcher, local site researcher, and researcher must uphold professional and ethical standards and practices and adhere to all applicable VA and other federal requirements, including the local VA facility’s standard operating procedures, regarding the conduct of research and the protection of human participants. The responsibilities of the researcher may be defined in the protocol or IRB application.

*When following DOE requirements:*

- Policies and procedures indicate researchers are required to follow DOE requirements for the protection of personally identifiable information by completing and complying with the requirements of the “Checklist for IRBs to Use in Verifying That HS Research Protocols Are in Compliance with DOE Requirements”, as outlined at: [https://science.energy.gov/ber/human-subjects/](https://science.energy.gov/ber/human-subjects/)

*When following ED requirements:*

- Policies and procedures indicate that for research funded by the U.S. Department of Education:
- All instructional material—including teachers' manuals, films, tapes, or other supplementary instructional material—which will be used in connection with any research or experimentation program or project must be available for inspection by the parents or guardians of the children engaged in such research.
- Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.
- Children are 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.

**Outcomes**

- Researchers and research staff are knowledgeable about and follow all legal and regulatory requirements and the organization’s policies and procedures that pertain to their research.
- Researchers and research staff adhere to the requirements of the IRB or EC.
- Researchers and research staff follow the requirements of the research plan or protocol.
Element III.2.D. Researchers and research staff follow reporting requirements during a research study in accordance with applicable laws, regulations, codes, and guidance; the organization’s policies and procedures; and the IRB’s or EC’s requirements.

Commentary
Researchers and research staff should understand the organization’s reporting requirements for events related to their research. This includes information related to unanticipated problems involving risks to participants or others or non-compliance. While Researchers or research staff do not make determinations of whether an event is an unanticipated problem involving risks to participants or others, they should know the type of events to report to allow the IRB or EC to make determinations. Likewise, researchers and research staff should submit information related to possible non-compliance in order for the IRB or EC to make final determinations. In addition to reporting to the IRB or EC, regulations and organizational policies and procedures may require reporting to other people or entities within the organization as well as to regulatory agencies. Researchers and research staff should also report suspensions or termination of the research, complaints, and data safety and monitoring reports when they occur or become available.

See AAHRPP Tip Sheet 14.
See AAHRPP Tip Sheet 15.
See AAHRPP Tip Sheet 18.
See AAHRPP Tip Sheet 23.

Required Written Materials

Essential requirements:
- Policies and procedures pertaining to Elements I.5.D., II.2.G., II.2.H., and II.2.I. that address essential requirements.

When following DHHS regulations:
- Policies and procedures pertaining to Elements I.5.D., II.2.G., II.2.H., and II.2.I. that address specific DHHS regulations.

When following FDA regulations:
- Policies and procedures pertaining to Elements I.5.D., II.2.G., II.2.H., and II.2.I. that address specific FDA regulations.

When following VA requirements:
- Policies and procedures pertaining to Elements I.5.D., II.2.G., II.2.H., and II.2.I. that address specific VA requirements.

When following DoD regulations:
- Policies and procedures pertaining to Elements I.5.D., II.2.G., II.2.H., and II.2.I. that address specific DoD requirements.

In the cases above, the policies and procedures pertaining to Elements I.5.D., II.2.G., II.2.H., and II.2.I. also address the written material requirements for this Element. If the same policies and procedures are provided to researchers and research staff, simply reference those documents in the application for this Element. If there are additional materials, such as an Investigator Handbook or Web pages for researchers, that are not included in the materials used to support Elements I.5.D., II.2.G., II.2.H., and II.2.I., but are in support of Element III.2.D., include them here.

When following VA requirements:
- Policies and procedures require the following of researchers and research staff:
  - Within five business days of becoming aware of any local (i.e., occurring in the reporting individual’s own facility) unanticipated serious adverse event in VA research, members of the VA research community are required to ensure

Regulatory and Guidance References
- DHHS: 45 CFR 46.103(b)(5)(i), OHRP Guidance on Reporting Incidents to OHRP, OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events
- VA: 38 CFR 16.103(b)(5)(i), VHA Handbook 1200.05, 9, VHA Handbook 1058.01
- DOE: 10 CFR 745, DOE Order 443.1B, Chg. 1 (April 21, 2016), DOE Notice 443.1 (January 21, 2016), and their accompanying Contractor Requirements Documents (CRDs)
- DOJ: 28 CFR 512.19,20
that the serious adverse event has been reported in writing to the IRB.

- This requirement is in addition to other applicable reporting requirements (e.g., reporting to the sponsor under FDA regulations).
- The unfounded classification of a serious adverse event as “anticipated” constitutes serious non-compliance.
- Researchers are required to report deviations from the protocol to the IRB in a time frame specified in local standard operating procedures.
- Researchers are required to report complaints to the IRB in a time frame specified in local standard operating procedures.

When following DOE requirements:

- Policies and procedures indicate:
  - Researchers must promptly report the following to the human subject research program manager:
    - Any significant adverse events, unanticipated risks; and complaints about the research, with a description of any corrective actions taken or to be taken.
    - Any suspension or termination of IRB approval of research.
    - Any significant non-compliance with HRPP procedures or other requirements.
  - Events must be reported within 48 hours.
  - Any compromise of personally identifiable information must be reported immediately.
  - The time frame for immediately is defined as upon discovery.

When following DOJ requirements:

- Policies and procedures require that for National Institute of Justice-funded research, a copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.
- Policies and procedures require that for research conducted with the Bureau of Prisons:
  - At least once a year, the researcher must provide the Chief, Office of Research and Evaluation, with a report on the progress of the research.
  - At least 12 working days before any report of findings is to be released, the researcher must distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance. The researcher must include an abstract in the report of findings.
- In any publication of results, the researcher must acknowledge the Bureau's participation in the research project.
- The researcher must expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau.
- Prior to submitting for publication the results of a research project conducted under this subpart, the researcher must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons.

When following the ICH-GCP (E6) guideline:

- Policies and procedures describe that researcher and research staff are knowledgeable about the following responsibilities:
  - The researcher reports all serious adverse events (SAEs) to the sponsor except for those SAEs that the protocol or other document (e.g., investigator’s brochure) identifies as not needing immediate reporting. The researcher follows regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB or EC.
  - The researcher reports adverse events or laboratory abnormalities identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.
  - For reported deaths, the researcher supplies the sponsor and the IRB or EC with any additional requested information (e.g., autopsy reports and terminal medical reports).
  - The researcher provides written reports to the sponsor, the IRB or EC, and, where applicable, the organization on any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.
  - If the researcher terminates or suspends a clinical trial without prior agreement of the sponsor, the researcher informs the organization, sponsor, and the IRB or EC.
• If the IRB or EC terminates or suspends approval of the clinical trial, the researcher promptly notifies the sponsor.

• Upon completion of the clinical trial, the researcher informs the organization; the IRB or EC with a summary of the trial’s outcome; and the regulatory authority with any reports required.

Outcomes

• Researchers and research staff follow reporting requirements for research studies, including reporting:

• Events, incidents, and problems according to the organization’s policy on unanticipated problems involving risks to participants or others.

• Non-compliance.

• Suspensions or terminations of research.

• Complaints.

• Protocol deviations and violations.

• Data and safety monitoring reports.

• Other required information.
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