

APPENDIX C

VA Human Research Protection Accreditation Program Draft Accreditation Standards

BACKGROUND

The Department of Veterans Affairs has contracted with NCQA to develop and implement an accreditation program for Veterans Affairs Medical Center (VAMC) Human Research Protection Programs (HRPPs). The purpose of the program is to strengthen the protections afforded human subjects of research at VAMCs through an ongoing program of independent, external review. The public must be assured that research is performed ethically and in the best interests of study volunteers to ensure its continued support for, and participation in, research studies. The VA has long held a set of policies governing the conduct of research, and in particular, the protection of human study participants. This program is the first to provide a routine, independent evaluation of VAMCs' compliance with these policies.

These draft standards for the accreditation of Veterans Affairs Medical Center (VAMC) Human Research Protection Programs (HRPPs) are being published for public comment. In June 2001 program standards will be finalized after analysis of public comments and results of pilot tests to be conducted in April and May, 2001. The resultant standards will be revised annually to reflect changes in VA policy and other applicable federal regulation.

These standards apply to VAMCs that operate their own IRBs, those that operate an IRB jointly with an affiliated university and those that delegate IRB functions to the affiliated university's IRB. Standards include requirements for the oversight of affiliated IRBs. The VAMC retains responsibility for protecting human subjects of research even when it delegates the performance of some functions (e.g., IRB) to the affiliated university. All the standards for the performance

of the IRB apply to the IRB, whether operated by the VAMC, the affiliated university or jointly.

SOURCE OF STANDARDS

These draft standards were compiled from regulations and other applicable policies that apply to research conducted at VA medical facilities and by VA employees. The principal sources were:

- VA regulations at 38 CFR 16-17;
- DHHS regulations at 45 CFR 46;
- FDA regulations at 21 CFR 50, 56, 312 and 812;
- VA policy as documented in Chapter 9 of the M-3 manual;
- FDA Information Sheets;
- International Conference on Harmonization Good Clinical Practice Guidelines; and
- OHRP Compliance Activities: Common Findings and Guidance.

Accreditation standards may not necessarily match a specific regulation word-for-word. In general, if a regulation specifies an activity that must occur the standard reflects this fact, and focuses on measurable evidence that it occurred. Where allowed by a regulation, standards are flexible, for example, with respect to methods to be used to achieve a specified process or outcome. If a regulation has a specified intent, but does not specify how such intent shall be achieved, the required level of achievement, or other relevant details, standards were developed that are consistent with the expressed regulatory intent. Because these standards focus on VA research, they do not cover all regulations and policies pertaining to the conduct of international research, research involving children, fetuses, and prisoners, nor genetic research.

ORGANIZATION OF THE STANDARDS

In this document unless otherwise specified, the term “standards” encompasses the rationale, standards, requirements and elements, inclusively. The standards are organized into the following six domains:

1. Institutional Responsibilities;
2. IRB Structure and Operation;
3. Consideration of Risks and Benefits;
4. Subject Recruitment and Selection;
5. Privacy and Confidentiality; and
6. Informed Consent.

Each of the six domains of standards includes a statement of rationale. Following in hierarchical fashion, are standards, requirements and elements that

detail the performance expectations of the VAMC HRPP. The standards are organized to indicate a chain of activity, from policy and procedure (suggesting intent), through results (documented demonstration that the intent is being met and the desired outcome achieved). Each standard may be composed of one or several requirements.

Each requirement contains many specific elements that provide detail and dimension to the requirement. Standards pertain to the following areas:

- Policies and procedures;
- Implementation of required activities;
- Performance of activities to demonstrate the HRPP is achieving required results (quality assurance and improvement); and
- Required results.

Standards identify the allowable sources of evidence, and methods for the evaluation of evidence, to determine whether or not a particular standard has been met. While many data sources may be listed for a requirement, they are generally listed as alternative sources. That is, a VAMC need not demonstrate compliance with a requirement in each and every data source listed; rather, it must demonstrate compliance in at least one data source (and not contradict the finding in others). Interviews are the exception and will be used only to clarify and confirm information from other sources. Data sources listed are intended to provide information about different aspects of performance (generally reflected in the different elements). For example, a requirement may include data sources such as policies and procedures, as well as IRB protocol files. In this instance, the surveyor will look for evidence that the HRPP has a policy or procedure governing an issue, and will look in a sample of protocol files to assess whether the policy has been implemented effectively.

The accreditation survey will result in one of four outcomes, as documented in the draft Accreditation Outcome Table below. Depending on their performance, Human Research Protection Programs can achieve Full Accreditation, Conditional Accreditation, Probationary Accreditation or No Accreditation. Each accreditation outcome brings with it a set of actions by NCQA as well as VA offices. These actions include, for example, follow-up oversight by NCQA, VA Office of Research and Development requirements for, and restrictions on, starting new research or continuing research and VA Office of Research Compliance and Assurance follow-up, remedial action and training. Please note that NCQA can only address its own actions and policies related to each outcome.

TABLE C-1 Draft Accreditation Outcomes and Remedial Action

Outcome	Description	Criteria	Programmatic Outcome	Actions by ORCA	Actions by ORD	Actions by Accreditor
Full	Meets all standards at acceptable level.	Score above xx points on 100 point scale; <i>performance meets all threshold standards.</i>	Research continues. Resurvey in 3 years.	Reviews accreditation report. [Note: May independently comment or request additional information from the VAMC.]	Reviews accreditation report. [Note: May independently comment or request additional information from the VAMC.]	Resurvey in 3 years.
Conditional	Meets most standards at acceptable level.	Score between yy and xx points on 100 point scale; <i>performance meets all threshold standards.</i>	Research may proceed. Submit Remediation Action Plan (RAP) to accreditor, ORCA, and ORD within 30 days.	Reviews accreditation report. [Note: May independently comment or request additional information from the VAMC. Monitors performance against RAP via periodic VAMC reporting at least until Full Accreditation is achieved. May require education and development (TED) program.]	Reviews accreditation report. [Note: May independently comment or request additional information from the VAMC. Monitors performance against RAP via periodic VAMC reporting at least until Full Accreditation is achieved.]	Monitors performance against periodic VAMC reporting at least until Full Accreditation is achieved. Follow-up survey may advance to Full Accreditation when RAP is fully implemented. Resurvey in 3 years (from date of original accreditation determination).

Probational	Meets some standards at acceptable level, but inadequate performance on many others.	Score between zz and yy points on 100 point scale; <i>performance meets all threshold standards.</i>	No new projects may be initiated until all deficiencies are corrected. Submit RAP to accreditor, ORCA, and ORD within 30 days.	Reviews accreditation report [Note: May independently comment or request additional information from the VAMC. Monitors performance against RAP via periodic VAMC reporting at least until Full Accreditation is achieved. May require TED program. Consider ORCA site visit.]	Reviews accreditation report. [Note: May independently comment or request additional information from the VAMC. Monitors performance against RAP via periodic VAMC reporting at least until Full Accreditation is achieved. In addition, withhold funding for new projects and may withdraw funding for current projects until at least Conditional Accreditation is achieved.]	Follow-up survey required to advance to Conditional Accreditation. Resurvey in 1 year (from date of Accreditation upgrade to Conditional).
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TABLE C-1 *Continued*

Outcome	Description	Criteria	Programmatic Outcome	Actions by ORCA	Actions by ORD	Actions by Accreditor
Not Accredited	Fails to meet basic accreditation standards.	Score below zz points on 100 point scale; OR unacceptable performance on one or more threshold standards	All research must cease until corrections are made. A patient already enrolled in studies may continue only if that is in the subject's best interest. No new subjects may be enrolled and no new projects may be started. Submit RAP to accreditor, ORCA, and ORD within 30 days.	Reviews accreditation report [Note: May independently add comments or request additional information from VAMC. Monitors performance against RAP via periodic VAMC reporting at least until Full Accreditation is achieved. May require TED program. Consider ORCA site visit.]	Reviews accreditation report. [Note: May independently add comments or request additional information from the VAMC. Monitors performance against RAP periodic VAMC reporting at least until Full Accreditation is achieved. Withdraw funding for all research (except amounts required assuring patient safety) until at least Probationary Accreditation is achieved.]	Decides when to determine if site can advance to Probationary Accreditation. Resurvey in 1 (one) year (from date of Accreditation upgrade to Probationary).

NOTES: ^aAt the accreditor's discretion, a site may not need to have a follow-up survey to move out of Conditional status to Full Accreditation. Rev. 12/21/00

OPERATION OF ACCREDITATION PROGRAM

VAMCs to be accredited will submit documents to demonstrate their compliance with accreditation program standards. A team of certified surveyors will visit each VAMC to be accredited. Surveyors will verify the VAMC's compliance with each standard and record their assessments in a structured report. The VAMC will be allowed to comment on the report's accuracy. The Program Accreditation Committee will review the surveyors' report and any VAMC comments, and issue an accreditation decision.

PROGRAM COMPONENTS UNDER DEVELOPMENT

Work is still underway to finalize data collection methods and protocol sampling strategies. These will be formalized in guidelines for surveyors. Sampling issues under consideration include how many protocols to sample and how to stratify samples to provide meaningful information about issues that present infrequently in some institutions. In addition to work on the sampling strategies, work is underway to determine the scoring of elements and requirements, including those that are applicable only in some instances (e.g., requirements relating to planned emergency research). First-year scoring will be more lenient than scoring in future years, when it will be possible to provide more advance notice of standards. Finally, the threshold scores required to achieve each accreditation outcome will be determined after each element's and requirement's relative weight has been determined. Comments on sampling and scoring are invited along with comments on the standards, requirements, elements, data sources and review methods presented.

DEFINITIONS

ADVERSE EVENT (AE) Any untoward medical occurrence that does not necessarily have a causal relationship with treatment. An AE can be any unfavorable and unintended sign, symptom or disease.

AFFILIATE'S HUMAN RESEARCH PROTECTION PROGRAM The HRPP of a VAMC's academic affiliate. See HRPP.

CERTIFICATE OF CONFIDENTIALITY Where data are being collected from subjects about sensitive issues (such as illegal behavior, alcohol or drug use, or sexual practices or preferences), researchers can obtain an advance grant of confidentiality from the Public Health Service that will provide protection even against a subpoena for research data.

FDA FORM 3454 The financial disclosure form required by the FDA to reveal/identify any potential financial conflict of interest that an investigator(s), sub-investigator(s) or their spouse and children may have that is applicable to the submission of marketing applications for human drug, biological product, or device for each covered study.

- FEDERALWIDE ASSURANCE (FWA)** An agreement or contract between the institution and OHRP, on behalf of the Secretary, HHS, stipulating the method(s) by which the organization will protect the welfare of research subjects in accordance with the regulations. The Assurance, approval of which is a condition of receipt of DHHS support for research involving human subjects, spells out the organization's responsibilities for meeting the requirements of 45 CFR 46. The FWA replaces all other previous forms of assurance (i.e., MPA, SPA, etc.).
- FOOD AND DRUG ADMINISTRATION (FDA)** The Federal agency responsible for the regulation of food, drugs and cosmetics, including the human subject research performed for FDA-regulated articles.
- HUMAN RESEARCH PROTECTION PROGRAM (HRPP)** The systematic and comprehensive approach by an organization to ensure human subject protection in all research. The implementation of any part of the program may be delegated to specific committees, individuals or entities (i.e., academic affiliate or another VAMC) by the organization.
- HUMAN SUBJECT** A living individual about whom a research investigator (whether professional or student conducting research) obtains data through intervention or interaction with the individual or identifiable information.
- INSTITUTION** The individual VAMC. The institution retains ultimate responsibility for human subject protection in research conducted at their facility and/or by their staff.
- INSTITUTIONAL REVIEW BOARD (IRB)** An independent committee comprised of scientific and non-scientific members established according to the requirements outlined in Title 38, part 16 (same as Title 45, part 46 and Title 21, part 56) of the U. S. Code of Federal Regulations.
- INVESTIGATIONAL DEVICE EXEMPTION (IDE)** The process by which the FDA permits a device that otherwise would be required to comply with a performance standard or to have premarket approval to be shipped lawfully for the purpose of conducting investigations of that device.
- INVESTIGATIONAL NEW DRUG APPLICATION (IND)** The process by which new drugs or biologics, including the new use of an approved drug, are registered with the FDA for administration to human subjects. An IND number is assigned by the FDA to the drug or biologic for use in tracking.
- INVESTIGATOR (Principal investigator)** An individual who conducts an investigation, i.e., under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.
- INVESTIGATOR/SPONSOR** A term defined in the FDA regulations as an individual with responsibility for initiating and conducting a research study.
- LEGALLY AUTHORIZED REPRESENTATIVE** An individual, judicial or other body authorized under applicable law to consent on behalf of a pro-

spective subject to the subject's participation in the procedure(s) involved in research.

MEDWATCH The FDA Medical Products Reporting Program, is an initiative designed both to educate all health professionals about the critical importance of being aware of, monitoring for, and reporting adverse events and problems to FDA and/or the manufacturer and to ensure that new safety information is rapidly communicated to the medical community, thereby improving patient care. The purpose of the MedWatch program is to enhance the effectiveness of postmarketing surveillance of medical products as they are used in clinical practice and to rapidly identify significant health hazards associated with these products.

MEMORANDUM OF UNDERSTANDING (MOU) A legal agreement outlining the details of the relationship between organizations, including the responsibilities of each. Such an agreement is used by the VAMC to delineate the terms and conditions under which it may utilize another entity's IRB.

MINIMAL RISK The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

MULTIPLE PROJECT ASSURANCE (MPA) An agreement or contract between the institution and OPRR, on behalf of the Secretary, HHS, stipulating the method(s) by which the organization will protect the welfare of research subjects in accordance with the regulations. The Assurance, approval of which is a condition of receipt of DHHS support for research involving human subjects, spells out the organization's responsibilities for meeting the requirements of 45 CFR 46. MPAs will be replaced by FWAs.

POLICY A principle or course of action to guide decision-making.

PROCEDURE See Standard Operating Procedure (SOP).

PROTOCOL A plan that includes, at minimum, the objectives, rationale, design, methods and other conditions for the conduct of a research study.

PROTOCOL FILE The documents maintained by the IRB administration containing the protocol, investigator's brochure, IRB/investigator communications and all other supporting materials.

QUALITY IMPROVEMENT (QI) The effort to assess and improve the level of performance of a program or institution. QI includes quality assessment and implementation of corrective actions to address any deficiencies identified.

RESEARCH A systematic investigation, including development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

SAFETY REPORTS (IND/IDE) Written reports from sponsors notifying the FDA and all participating investigators of any adverse experience associated with the use of a drug that is both serious and unexpected.

SERIOUS ADVERSE EVENT (SAE) Any event that results in death, a life threatening situation, hospitalization or prolonged hospitalization, persistent

or significant disability/incapacity or a congenital anomaly/birth defect. SAEs require reporting to the sponsor and the IRB.

SPONSOR Any person or entity who takes responsibility for and initiates a clinical study. The sponsor may be an individual, pharmaceutical company, device manufacturer, governmental agency, academic institution, private organization, or other organization.

STANDARD OPERATING PROCEDURE (SOP) A formalized established series of steps for the uniform performance of a function or activity.

UNEXPECTED ADVERSE EVENT Any adverse event that has not previously been observed (e. g., included in the investigator brochure).

VULNERABLE SUBJECTS Individuals whose willingness to volunteer in a research study may be unduly influenced or coerced and individuals with limited autonomy.

TABLE C-2 INSTITUTIONAL RESPONSIBILITIES

Rationale

Each institution engaged in research involving human subjects is responsible for ensuring the rights, safety, and well-being of those recruited to participate in research activities. It is also responsible for assuring that investigators and their staffs understand and comply with standards for the ethical conduct of research. These broad responsibilities can be met through three institutional actions: developing a Human Research Protections Program to monitor, evaluate, and improve the protection of human research subjects; establishing and/or designating an Institutional Review Board to review research following federal and institutional requirements; and educating staff involved in research about their ethical responsibility to protect research participants. This standard outlines the responsibilities of institutions that conduct human subjects research.

KEY for Regulatory Guidance

CFR = Code of Federal Regulations

M-3, Part 1 = The Veterans Affairs Manual, Chapter 9

VA MPA = Veterans Affairs Multiple Project Assurance Contract

IRB-GB = OPRR IRB Guidebook

FDA-IS = FDA Information Sheets

FDA-IS, (CL) = Appendix H: Self-Evaluation Checklist for IRBs

FDA-IS, (FAQ) = Frequently Asked Question

FDA-IS, (ICG) = The Guide to Informed Consent

FDA-IS, (CR) = Continuing Review After Study Approval

ICH-GCP = International Conference on Harmonization, Good Clinical Practice Guidelines

OHRP CFG = OHRP Compliance Activities: Common Findings and Guidance for 9/1/2000

IR 1 The institution has a systematic and comprehensive program, Human Research Protection Program (HRPP), with dedicated resources to ensure the rights, safety and well-being of human research subjects in relation to their participation in research activities.

Requirement	Element	Data Source	Method
<p>1.A. The institution has a written description of (or plan for) its human research protection program (HRPP) appropriate for the volume and nature of the human subject research conducted at the institution.</p> <p><i>Regulation/Source</i> 38 CFR 16.103 M-3, Part 1, 9.07 VA MPA 45 CFR 46.103 45 CFR 46.107(e) OHRP - CFG IRB-GB, (I)(B) IRB-GB, (II)(ii) FDA-IS, (FAQ)(I) 45 CFR 46.103(b)(2) M-3, Part 1, 9.07(b) IRB-GB, (I)(B) 45 CFR 46.103(b)(4) OHRP CFG (A) (1), (B), (C),(D), (E)</p>	<p>1.A.1. The description includes:</p> <p>1.A.1.1. A statement of principles concerning the protection of human research subjects.</p> <p>1.A.1.2. The institutional officer accountable for the HRPP.</p> <p>1.A.1.3. The organizational structure, process, roles and responsibilities for making policy to protect human research subjects.</p> <p>1.A.1.4. A process to identify and incorporate changes in VA and Federal regulations and policies into the HRPP.</p> <p>1.A.1.5. A description of the types of research to be undertaken and the classes of subjects to be regularly included.</p> <p>1.A.1.6. The description specifically addresses whether vulnerable persons will be regularly included in research and whether additional protections for vulnerable persons are needed in accordance with VA policy.</p> <p>1.A.1.7. The institution has one or more of the following arrangements for an IRB:</p> <p>1.A.1.7.1. The institution sponsors its own IRB.</p> <p>1.A.1.7.2. The institution has a written arrangement with a regional VA IRB or another VA IRB.</p> <p>1.A.1.7.3. The institution has a written arrangement with an affiliated medical or dental school or university.</p> <p>1.A.1.8. The HRPP description includes a resource plan or budget and a defined process for allocating resources.</p> <p>1.A.1.9. The HRPP description specifies the role, organizational structure and functions of the R&D Com-</p>	<p>HRPP plan HRPP employee list, including time allocation (i.e., FTE)</p> <p>FWA, MPA, or other assurance</p> <p>Relevant institutional or IRB policies and procedures</p> <p>IRB and other committee charters, organizational charts</p> <p>Current Memoranda of Understanding or current written agreements for designated IRB(s)</p> <p>HRPP budget, HRPP resource analysis</p>	<p>Review documents for presence of each requirement of the standard</p>

mittee, the IRB(s) and other committees and individuals with responsibilities for protecting human subjects in research.

1.A.1.10. The HRPP description specifies the education and training requirements for individuals with roles in the HRPP, including:

1.A.1.10.1. VA HQ education and training requirements.

1.A.1.10.2. Any additional institutional requirements.

1.A.1.11. The HRPP includes policies and procedures to address complaints, allegations and findings of non-compliance with institution policies.

1.A.1.12. The HRPP description includes a plan for monitoring program effectiveness and applicability, including monitoring compliance with applicable VA, Federal, state, and local policies and regulations.

1.B. The institution provides sufficient resources for the HRPP and its IRB(s).

Regulation/Source

38 CFR 16.103

M-3 Part 1, 9.07(b)

45 CFR 46.103(b)(2)

IRB-GB, (I)(B)

1.B.1. To ensure sufficient resources the institution does the following:

1.B.1.1. The institution has a mechanism for determining resource needs for the HRPP and its IRB(s) that includes staff, equipment, materials, and space.

1.B.1.2. The institution annually reviews those resource needs based on the type of research being conducted, the volume of research being reviewed, and feedback from IRB members and staff.

1.B.2. The institution has an information system, database, or log capable of tracking:

1.B.2.1. Research proposal status.

1.B.2.2. QI data.

HRPP and budget; interviews with HRPP staff (R&D and IRB staff); observation of equipment, materials, and document storage facilities.

Review of the mechanism used by the institution, annual review process, and the presence of an information system for tracking of IRB data

1.C. The Institution maintains and supports a current and approved Federalwide Assurance (FWA) with OHRP and/or an assurance in accordance with current VA regulations that includes its principles and guidelines for protecting human subjects.

Regulation/Source
 38 CFR 16.103
 VA MPA
 45 CFR 46.103(b-f)
 IRB-GB, (I)(B)
 FDA-IS, (FAQ)(I)
 OHRP Requirements

The institution demonstrates its maintenance and support of a Federalwide Assurance in the following ways:

- 1.C.1. The institution is operating under an approved assurance.
- 1.C.2. The institution has policies and procedures in place governing the conduct of the assurance.
- 1.C.3. The institution adheres to any conditions or restrictions to the approved assurance and communicates these to the IRB(s) and investigators.
- 1.C.4. The institution registers its IRB(s) as required under an OHRP Federalwide Assurance.
- 1.C.5. The institution holds MOUs with IRBs that it uses. These IRBs must be registered as required by Federal regulations.
- 1.C.6. The IRB(s) provides to the investigator a form indicating IRB approval. For VA protocols, it shall be the form VA 10-1223.
- 1.C.7. The institution updates its assurances and IRB registration as required by OHRP and in accordance with VA policies.
- 1.C.8. The institution identifies the responsible official for the assurance.
 - 1.C.8.1. In VA facilities, the Medical Center Director/CEO is the responsible official.

Assurance
 Certifications, review of approved grant applications, HRPP policies and procedures

Review for current, approved assurance and certifications (not expired or suspended, dated within three years of date of application)

1.D. If the institution uses the IRB(s) of a VA regional system, affiliated university or another VA facility, the arrangement is specified in writing and the institution conducts oversight activities.

Regulation/Source
38 CFR 16.103
M-3, Part 1, 9.07
VA MPA
45 CFR 46.103

1.D.1. For each such arrangement, there is a memorandum of Understanding (MOU). The MOU describes:

1.D.1.1. Specific requirements for the membership and operation of the IRB to review VA research in compliance with VA regulations.

1.D.1.2. The respective responsibilities of the institution and the designated IRB for human subject protection.

1.D.1.3. The scope of activities delegated to the IRB.

1.D.1.4. The method, frequency, and nature of reporting to the institution.

1.D.1.5. The process by which the institution evaluates the IRB's performance.

1.D.1.6. The remedies, including revocation of the designation, available to the institution if the designated IRB does not fulfill its obligations.

1.D.2. The institution conducts sufficient oversight of designated IRB(s). The institution:

1.D.2.1. Evaluates the designated IRB's capacity to perform the designated activities prior to designation.

1.D.2.2. Evaluates the designated IRB's charter, policies, procedures and membership annually.

1.D.2.3. Evaluates regular reports as specified in 1.4 above.

1.D.2.4. Evaluates annually whether the designated IRB is in compliance with current VA, Federal and other regulations and guidance.

Current Memorandum of Understanding

Minutes of R&D Committee, IRB minutes reviewed by R&D Committee and reports from designated IRB on performance (prior to MOU execution)

Designated IRB charter, policies, membership reviewed and approved annually

Reports on current performance reviewed

MOU for each arrangement has the requirements of the standard

Frequency of R&D review of IRB

QI Reports on the effectiveness of designated IRBs evaluate the requirements of the standard

Documentation of evaluation results

<p>1.F. The institution has policies and procedures to identify and manage institutional, IRB member, and investigator conflicts of interest with research conducted at the institution.</p>	<p>The institution's policies and procedures include:</p> <p>1.F.1. Identification and management of financial conflict of interest of the institution.</p> <p>1.F.2. Identification and management of financial conflict of interest of IRB members.</p> <p>1.F.3. Identification and management of financial conflict of interest of investigators.</p>	<p>Policies and procedures</p> <p>FDA Form 3454</p> <p>Disclosure documents</p> <p>IRB minutes</p>	<p>Review of policies and procedures on conflict of interest</p> <p>Review of disclosure documentation</p> <p>Review of IRB minutes for IRB member disclosure of conflict of interest</p>
<p><i>Regulation/Source</i> ICH-GCP 5.1 21 CFR 54</p> <p>1.G. The institution provides a system enabling research subjects to ask questions or to voice concerns or complaints.</p>	<p>The institution has the following procedures in place:</p> <p>1.G.1. The institution designates a specific individual with the responsibility to respond to questions, concerns, or complaints.</p> <p>1.G.1.1. The name and telephone number of the individual(s) is included in all consent forms.</p> <p>1.G.2. The institution ensures a response to each question, concern, or complaint and that action is taken, as needed.</p> <p>1.G.3. The institution implements its policies and procedures to address complaints, allegations and findings of noncompliance with HRPP and IRB policies.</p>	<p>Individual responsible and procedure description</p> <p>Complaints</p>	<p>Review the procedure description and reports or data on questions, concerns and complaints</p>
<p><i>Regulation/Source</i> 38 CFR 16.116(a)(7) M3, Part 1, Appendix – Procedures for Obtaining Informed Consent (10) 45 CFR 46.116(a)(7) 21 CFR 50.25(a)(7)</p>	<p>The use of investigational products or devices are subject to the following institutional processes:</p> <p>1.H.1. The institution's Pharmacy Service has policies and procedures for the storage, security, and dispensing of investigational test articles that follow Federal regulations and are in accordance with VA policy.</p> <p>1.H.2. The institution ensures that Pharmacy Service conducts audits of its compliance with policies and procedures regarding the use of investigational test articles and uses the</p>	<p>Pharmacy Service policies and procedures for investigational drugs.</p> <p>Results of audits or reports of compliance.</p> <p>Institutional</p>	<p>Review for policies and procedures that address the requirements of the standard</p> <p>Documentation of audit results and evidence of interventions when noncompliance is identified</p>
<p><i>Regulation/Source</i> M3, Part 1, 9.15</p>			

21 CFR 312
21 CFR 812

results for quality improvement purposes.
1.H.3. The institution has policies and procedures for the storage, security, and dispensing of investigational devices that follow Federal regulations and are in accordance with VA policy.
1.H.4. The institution ensures that audits of compliance with policies and procedures are conducted regarding the use of investigational devices and uses the results for quality improvement.

1.I. The institution's plan for monitoring program effectiveness and conducting quality improvement is implemented and includes measuring, assessing, and improving compliance with HRPP policies, assurances, and other requirements for the protection of human subjects in research.

Regulation/Source
38 CFR 16.103
M3, Part 1, 9.09(f)
VA MPA
45 CFR 46.103
IRB-GB, (I)(B)(D)
FDA-IS, (FAQ)(III)(24)

1.I.1. A designated committee or individual has responsibility for ensuring that the HRPP plan is operational. Specific responsibilities include:
1.I.1.1. The implementation of HRPP policy.
1.I.1.2. The review and evaluation of the reports and results of monitoring compliance assessment and quality improvement activities.
1.I.1.3. The implementation of needed actions and follow-up on actions, as appropriate.
1.I.1.4. The documentation of its decisions and actions through dated and signed contemporaneous committee minutes. Or in the case of an individual, written documentation to record and communicate the individual's decisions and actions.
1.I.2. The institution monitors its performance in protecting human subjects.
1.I.3. The institution monitors the performance of the VA or the affiliate IRB(s). Monitoring includes the following areas:
1.I.3.1. Evaluation of the informed consent process.
1.I.3.2. Evaluation of the content and accuracy of informed consent forms.
1.I.3.3. Evaluation of research proposal risk and benefit including designation of minimal risk when appropriate.

HRPP compliance plan

Job description (s)

HRPP policies and procedures

HRPP Committee minutes or individual correspondence

Review of compliance plan for evidence of requirements

Review of job descriptions for evidence of roles in HRPP

Review of policies and procedures for evidence of requirement to monitor HRPP plan

Review of minutes from the committee with designated responsibility for HRPP monitoring for review of monitoring in the areas required by the standards (or correspondence of designated individual)

- 1.I.3.4. Evaluation of special considerations and protections for vulnerable or potentially vulnerable populations.
- 1.I.3.5. Evaluation of privacy and confidentiality protections.
- 1.I.3.6. Evaluation of continuing review of approved research.
- 1.I.3.7. Use of expedited review, emergency review, or other procedures requiring review of less than the full IRB.
- 1.I.3.8. Granting exemption from Federal requirements for IRB review.
- 1.I.3.9. Granting waivers for documentation of informed consent.
- 1.I.3.10. Granting waivers of any informed consent requirements.
- 1.I.3.11. Continuing review of safety and monitoring.
- 1.I.4. The institution monitors the performance of investigators. Monitoring includes the following areas:
- 1.I.4.1. Use of approved consent forms and procedures.
- 1.I.4.2. Obtaining consent prior to initiating any research related procedures and documenting such in progress notes.
- 1.I.4.3. Reporting of all required safety issues and protocol deviations.
- 1.I.4.4. Adherence to HRPP policies and IRB approved protocols and conditions.
- 1.I.5. The institution monitors its responsiveness and reporting about subject questions, concerns, and complaints. Monitoring includes:
- 1.I.5.1. Review of data on questions, concerns, and complaints for reporting and quality improvement purposes.
- 1.I.6. The institution makes improvements to the HRPP based on performance monitoring results.

Monitoring or compliance reports

Review for the presence of a report or documentation of monitoring in the areas required by the standards

IR 2 The institution is responsible for educating institutional staff involved in research on their responsibility to protect the rights, safety, and well-being of human research subjects and holding them accountable for human subject protections.

Requirement	Elements	Data Source	Method
<p>2.A. The institution is responsible for ensuring that research investigators, research staff, IRB members, and other individuals with responsibility for human subject protection have completed required training in human subject protection.</p> <p><i>Regulation/Source</i> VA MPA OHRP Requirements IRB-GB, (I)(B)</p>	<p>The institution's responsibilities for training investigators and staff in human subject protection include the following:</p> <p>2.A.1. The institution has information on HRPP requirements and IRB requirements.</p> <p>2.A.2. The institution communicates information on HRPP and IRB requirements to investigators and other individuals with human subject protection responsibility and makes it readily available.</p> <p>2.A.3. The institution has a description of the type and scope of human subject protection education and training that meets VA and other regulatory requirements.</p> <p>2.A.4. The institution ensures that investigators and other individuals have received education and training appropriate to their roles.</p> <p>2.A.5. The institution periodically evaluates the training and certification status of research investigators, IRB members, and other individuals with responsibility for human subject protection.</p> <p>2.A.6. The institution has taken steps to train staff where identified gaps exist in education and training.</p>	<p>Policies, forms, checklists, and related HRPP and IRB materials.</p> <p>Training programs and materials</p> <p>Description of educational and training requirements</p> <p>Training log for the past year Database on training certification</p> <p>List of all investigators, IRB members, and HRPP staff from the past year</p>	<p>Review of materials requirements and the method of communication of HRPP and IRB</p> <p>Training log reflects training for all investigators. The Institution has taken steps to train staff where gaps exist</p>

2.B. The institution provides proper guidance to investigators regarding development of consent forms and conduct of the consent process.

Regulation/Source
IRB-GB, (D)(B)
FDA-IS, (ICG)
M-3
21 CFR 50.23(a)
21 CFR 50.24

The institution provides guidance in the following areas:

- 2.B.1. Model consent forms.
- 2.B.2. Memoranda or other communications to investigators concerning conduct of the consent process, documentation of consent and content of consent forms.
- 2.B.3. Provision of mandatory training on the consent process.
- 2.B.4. IRB policies and procedures.
- 2.B.5. New VA, Federal, and local regulations, when appropriate.

Communications to investigators, training logs, model consent forms, guidance materials, etc.
HRPP and IRB policies and procedures

Surveyors assess the completeness of materials.

TABLE C-3 INDIVIDUAL IRB STRUCTURE AND OPERATIONS

Rationale

Institutional Review Boards (IRB) are the administrative bodies established to protect the rights and welfare of human research subjects through prospective and concurrent review of research. IRB structure, composition and function must be sufficient to allow for thorough and expert review of research to assure that subjects are adequately protected. This standard contains the requirements for IRB membership and processes to provide adequate supervision of research.

KEY:

CFR = Code of Federal Regulations

M-3, Part 1 = The Veterans Affairs Manual, Chapter 9

IRB-GB = OPRR IRB Guidebook

FDA-IS = FDA Information Sheets

FDA-IS, (CL) = Appendix H: A Self-Evaluation Checklist for IRBs

FDA-IS, (FAQ) = Frequently Asked Question

FDA-IS, (ICG) = The Guide to Informed Consent

FDA-IS, (CR) = Continuing Review After Study Approval

FDA-IS, (SR/NSR) = Significant Risk and Nonsignificant Risk Medical Device Studies

ICH-GCP = International Conference on Harmonization, Good Clinical Practice Guidelines

OHRP-CFG = Office of Human Research Protection Compliance Activities: Common Findings and Guidance 9/1/2000

HHSIGR = HHS Inspector General's Report

IRB 1 The IRB's structure and composition are appropriate to the amount and nature of research reviewed and meet regulatory requirements.

Requirement	Element	Data Source	Method
<p>1.A. The IRB maintains, or has access to, information about each IRB member.</p> <p><i>Regulation/Source</i> 38 CFR 16.103(b)(3) 38 CFR 16.115 (a)(5) M-3, Part 1, 9.09 (g)(1)(e) 45 CFR 46.103(b)(3) 45 CFR 46.115(a)(5) 21 CFR 56.115(a)(5) IRB-GB, (I)(B) FDA-IS, (CL)(VI) ICH-GCP, (3.21)</p>	<p>Information about each IRB member includes the following:</p> <p>1.A.1. Name and address.</p> <p>1.A.2. Earned degrees.</p> <p>1.A.3. Representative capacity (e.g., physician, non-scientist, ethicist, community member, etc.).</p> <p>1.A.4. Indications of experience, such as board certifications, licensures, certifications, etc.</p> <p>1.A.5. For community members, past or present association with the VA (including academic affiliates) or its employees.</p> <p>1.A.6. Statement of financial and other interests which may constitute a conflict of interest.</p> <p>1.A.7. Documentation of training in human subject protection.</p> <p>1.A.8. Documentation of the voting status of each member.</p> <p>1.A.9. Documentation of alternate status.</p>	<p>Files maintained by the institution on each IRB member including but not limited to: curriculum vitae; disclosure documentation; copies of training certificates</p>	<p>Review of IRB files shows compliance with requirements for current and past IRB members for the past one year</p>

<p>1.B. The IRB consists of the appropriate number, type and diversity of members.</p> <p><i>Regulation/Source</i> 38 CFR 16.107 (a)(b)(c)(d) M-3, Part 1, 9.08(a) 45 CFR 46.107 (a)(b)(c)(d)(f) 21 CFR 56.107 (a)(b)(c)(d) IRB-GB, (I)(B) FDA-IS, (FAQ)(II) FDA-IS, (CL)(VI) ICH-GCP, (3.2.1)</p>	<p>The IRB includes:</p> <p>1.B.1. At least five members.</p> <p>1.B.2. At least one member whose primary area of interest is non-scientific (e.g., lawyer, clergy and ethicist).</p> <p>1.B.3. At least one member whose primary area of interest is scientific.</p> <p>1.B.4. At least one member who does not have any past or present association with the VA or university affiliate that would negate the status of a community, non-affiliated member.</p> <p>1.B.5. Diversity of membership based on gender, cultural background and sensitivity to community issues and/or community attitudes.</p> <p>1.B.6. Members of more than one profession.</p> <p>1.B.7. Affiliate IRBs have at least one member that is a VA representative.</p> <p>1.B.8. Officials with responsibility for development and oversight of the HRPP are non-voting, ex-officio members.</p>	<p>Policies and procedures</p> <p>IRB membership lists, from the past year</p>	<p>Review of policies and procedures reflect compliance with regulations</p> <p>Review of IRB files shows compliance with requirements for current and past IRB members</p>
<p>1.C. The IRB meets regularly and with sufficient frequency, and members have sufficient time to review the materials prior to the meeting. Materials include the full protocol, a proposed informed consent form, any relevant</p>	<p>1.C.1. IRB meetings have the following arrangements:</p> <p>1.C.1.1. The IRB has a set meeting schedule.</p> <p>1.C.1.2. Except under specified “emergency” conditions, IRB members receive meeting materials</p>	<p>Policies and procedures</p> <p>IRB meeting schedule</p>	<p>Review of policies and procedures shows evidence of requirements</p> <p>Confirm existence of meeting schedule or regularly scheduled meeting date and time</p>

<p>merit review or grant applications, the investigator's brochure (if one exists), and any advertising intended to be seen or heard by potential subjects.</p>	<p>far enough in advance of the scheduled meeting to allow for sufficient review.</p> <p>1.C.1.3. The IRB has established timelines for receipt by the IRB office and distribution of materials to members.</p> <p>1.C.2. The IRB follows its established timelines.</p> <p>1.C.3. The IRB periodically evaluates established timelines and it updates timelines to ensure effective participation of IRB members.</p>	<p>Distribution schedule</p> <p>IRB submission deadline schedule</p> <p>IRB member interview</p> <p>IRB minutes</p> <p>QI results</p>	<p>(e.g., first Monday of the month at 8:00 a.m.)</p> <p>Ask IRB member how soon before scheduled meetings, they typically receive materials. Ask them whether they believe this is enough time to allow for sufficient review.</p> <p>Review of IRB minutes for evidence of actual meeting dates conforming to scheduled dates</p> <p>Review of QI results for evidence of compliance with meeting schedules</p>
<p><i>Regulation/Source</i> 38 CFR 16.108(a)(1) 45 CFR 46.108(a)(1) 21 CFR 56.108(a)(1)</p>	<p>1.D. The IRB has a system for assigning reviewers to protocols prior to initial review (e.g., primary/secondary reviewer system), if applicable.</p>	<p>Policies and procedures</p> <p>IRB member interview</p> <p>QI results</p>	<p>Review of policies and procedures for evidence of primary reviewer system, if applicable</p> <p>IRB member is able to articulate the process for assigning protocols</p> <p>Review of QI results for evidence of compliance with, and appropriateness of, outlined protocol review system</p>

IRB 2 The IRB systematically evaluates each research protocol to ensure adequate protection of human subjects in research.

Requirement	Element	Data Source	Method
<p>2.A. There are written policies and procedures that describe IRB operations and functions.</p> <p><i>Regulation/Source</i> 38 CFR 16.103(b)(4)(5) 38 CFR 16.108(a)(e) 38 CFR 6.115(a)(b)(6) 45 CFR 46.103(b)(4)(5) 45 CFR 46.115(a)(b) 21 CFR 56.108(a)(b)(c) 21 CFR 50.24 M-3, Part I, 9.09(c)(a) IRB-GB, (I)(B) FDA-IS, (CL) ICH-GCP, (3.3) MPA VA Handbook</p>	<p>2.A.1. These polices and procedures shall be consistent with all applicable VA and Federal requirements and include the following:</p> <p>2.A.1.1. Procedures and required information for conducting initial review and continuing review activities.</p> <p>2.A.1.1.1. Procedures for reporting findings and actions to the investigator the R&D Committee, and institutional officials as required.</p> <p>2.A.1.1.2. Procedures for determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.</p> <p>2.A.1.2. Procedures and criteria for making the following determinations for a research protocol: approval; require modifications in (to secure approval); or disapproval.</p> <p>2.A.1.3. Procedures and criteria for suspension or termination of IRB approval of research protocols.</p> <p>2.A.1.4. Criteria for when research protocols should include a Data Safety Monitoring Board (DSMB) as required by VA, DHHS, and FDA.</p> <p>2.A.1.5. Review of protocol amendments,</p>	Policies and procedures	Review of policies and procedures shows evidence of requirements for IRB operations and functions

including procedures for determining criteria for what type of changes require full IRB review versus expedited review.

2.A.1.6. Procedures and criteria for determining if an expedited review process can be used.

2.A.1.7. Investigator reporting requirements, including:

2.A.1.7.1. Providing IRB required data for continuing review.

2.A.1.7.2. Submitting proposed changes in research protocol and/or consent forms for approval.

2.A.1.7.3. Reporting deviations from approved protocol or other regulations and policies.

2.A.1.7.4. Reporting adverse events.

2.A.1.7.5. Reporting unanticipated problems involving risks to subjects.

2.A.1.7.6. Submitting termination/completion reports.

2.A.1.8. Continuing review occurs at the specified time interval.

2.B. The IRB reviews required and relevant information to make evaluations on research proposals during initial review.

Regulation/Source
38 CFR 16.115(a)
45 CFR 46.115(a)
21 CFR 56.115(a)
FDA-IS, (FDA)(IV)
FDA-IS, (CL)(XI)

2.B.1. The IRB considers the following at initial review:

2.B.1.1. Attestation, when required, by the investigator as to whether the proposal, or one substantially similar to it, has been disapproved by another IRB.

2.B.1.2. Scientific evaluations (if any) that accompany the proposal.

2.B.1.3. Research design.

2.B.1.4. Scientific rationale.

2.B.1.5. Statement of known and suspected

Initial review submission forms and checklists used by the IRB

Sample of IRB initial review files

IRB communications to investigators

Review of submission form and checklists for requirements

Review of protocols for evidence of content of requirements

Review of IRB communications or other guidance for notice of submission

ICH-GCP, (3.1.2)(4.9.4)(8.0)
OHRP-CFG
HHS-IGR

risks and benefits.
2.B.1.6. Procedures to minimize risks.
2.B.1.7. Recruitment and enrollment procedures, including payment to subjects.
2.B.1.8. Subject selection criteria.
2.B.1.9. Procedures to protect subject privacy and confidentiality.
2.B.1.10. Where appropriate, additional safeguards planned to protect the rights and welfare of potentially vulnerable subjects.
2.B.1.11. Process for monitoring and reporting adverse events.
2.B.1.12. Presence of a Data Safety Monitoring Board (DSMB) if applicable.
2.B.1.13. Other information to be used for recruitment or to inform subjects or potential subjects about the nature of the research.
2.B.1.14. Scientific training and qualifications of investigator and research staff.
2.B.1.15. Human subject protection training of investigators and research staff.
2.B.1.16. Investigator potential financial conflicts.
2.B.1.17. Proposed informed consent documents.
2.B.2. Based on its review of the information above, the IRB approves, requires modifications or disapproves proposed research.
2.B.3. The IRB conducts audits of the adequacy of information at initial review. Results are used for QI purposes and actions taken, as needed

2.C. The IRB uses required and relevant information to conduct

2.C.1. In addition to copies of the documents required for the initial review, the IRB consid-

IRB minutes

QI results

Policy and procedures

requirements

Review of IRB minutes shows IRB consideration of requirements as appropriate, and decisions to approve are not proforma
Review of QI results shows evidence of assessment of requirements for initial submission

Review of policies and procedures shows evidence

continuing review of research proposals and makes recommended changes.

Regulation/Source
 38 CFR 16.1.09 (e)
 M-3, Part 1, 9.09 (f)
 45 CFR 46 1.09 (e)
 21 CFR 56 1.09 (f)

ers the following information, where applicable, for continuing review:

- 2.C.1.1. Currently approved informed consent documents.
- 2.C.1.2. Approved or proposed amendments, including minor changes, (if any) and the IRB action on each amendment.
- 2.C.1.3. Research findings to date.
- 2.C.1.4. Reports of injuries to subjects.
- 2.C.1.5. All serious adverse events or unanticipated problems involving risks to subjects.
- 2.C.1.6. Recent published medical or scientific studies applicable to the protocol.
- 2.C.1.7. Review of information that may change risk/benefit ratio, including adverse events or unanticipated problems.
- 2.C.1.8. Documentation of protocol violations and/or deviations.
- 2.C.1.9. Documentation of non-compliance with applicable regulations.
- 2.C.1.10. Number of subjects enrolled and entered into the study.
 - 2.C.1.10.1. Gender and minority status of subjects entered into the protocol.
 - 2.C.1.10.2. Number of subjects in each of the following categories: children, prisoners, pregnant women, economically disadvantaged, decisionally impaired, or homeless.
- 2.C.1.11. Number of subjects withdrawn by self and by investigator, and reasons for withdrawal.
- 2.C.1.12. Review of a summary of the DSMB meetings (if applicable) or findings

Continuing review submission forms

Checklists and forms used by IRB

Sample of IRB continuing review files

IRB communications to investigators

IRB minutes

of requirements for submission of continuing review

Forms have requirements listed

IRB checklists show evidence of IRB consideration of required information

Protocols reviewed show evidence of IRB consideration of required information and that continuing review was submitted and considered within the required timeframe for the protocol

IRB communications list requirements for continuing review submission

IRB minutes reflect consideration of requirements

based on information collected on AEs, UAEs and SAEs as required by the approved data and safety monitoring plan.

- 2.C.1.12.1. An assurance that all SAEs and UAEs have been reported as required.
- 2.C.1.12.2. Review of IND/IDE safety reports and MedWatch reports.
- 2.C.1.13. Any new recruitment documents.

2.C.2. Based on its review of the above information, the IRB decides that the research can be continued, continued with modifications, suspended or terminated.

2.C.3. Based on its continuing review, the IRB requires appropriate changes to the following:

- 2.C.3.1. Informed consent form content.
- 2.C.3.2. Frequency of continuing review.
- 2.C.3.3. Level of safety monitoring.

2.C.4. The IRB conducts audits of the adequacy of information considered at continuing review.

- 2.C.4.1. Results are used for QI purposes and actions taken, as needed.

2.D. The IRB has policies and procedures for the conduct of expedited review (if applicable) and appropriately utilizes such review.

Regulation/Source
 38 CFR 16.110
 M-3, Part I, 9.10
 45 CFR 46.110

2.D.1. The IRB's policies and procedures for expedited review conform to VA and Federal regulations and include:

- 2.D.1.1 The IRB identifies categories of research for which expedited review is allowed.
- 2.D.1.2. There are established qualifications and experience criteria for those IRB members who serve as Chairperson's designee(s) in conducting expedited review.

Policies and procedures

IRB submission forms and checklists used by the IRB

Sample of IRB expedited review

Review of policies and procedures for evidence of requirements for expedited review

Review of IRB submission forms for requirements for expedited review

Review of protocols ap-

21 CFR 56.110
FDA-IS, (FAQ)(20)
FDA-IS, (CL)(IX)(C)
OHRP-CFG (B)

2.D.1.3. The IRB must have criteria for establishing that research involves no more than minimal risk.

files

proved through expedited review shows that the protocols met criteria

2.D.1.4. The IRB must have criteria for establishing that changes in previously approved research are "minor."

IRB minutes

IRB minutes show that protocols reviewed through expedited review were presented to full committee for consideration

2.D.1.5. The IRB has methods to keep IRB members advised of research proposals approved under expedited review that include documentation of specific permissible categories justifying expedited review.

2.D.2. The IRB conducts expedited review of protocols in conformance with its policies and procedures.

2.D.2.1. Expedited review shall be conducted by IRB Chairperson or by one or more experienced IRB members designated by the IRB Chairperson.

2.D.2.2. Expedited reviews comply with the IRB policies and procedures and applicable VA and Federal regulations.

2.D.3. The IRB conducts audits or self-assessments of compliance with VA and Federal regulations and its policies and procedures on expedited review.

2.D.3.1. Results are used for QI purposes and actions taken, as needed.

2.E. The IRB has policies and procedures for determining whether research involving human subjects is exempt from IRB review and correctly makes such determinations.

2.E.1. The IRB policies and procedures for determining exempt status conform to VA and Federal regulations and include:

Policies and procedures

Review of policies and procedures for presence of requirements for exempt status

2.E.1.1. Definition of all categories of research that are exempt from IRB review.

2.E.1.2. Process for determining exempt

IRB minutes

IRB minutes show evi-

<p><i>Regulation/Source</i> 38 CFR 16.101(b) M-3, Part I, 9.06 45 CFR 46.101(b) IRB-GB, (I)(A)</p>	<p>status. 2.E.2. The IRB makes determination of exempt status in accordance with federal regulations. 2.E.3. The IRB conducts audits or self-assessments of compliance with VA and Federal regulations and its policies and procedures on exempt status. 2.E.3.1. Results are used for QI and actions taken, as needed.</p>	<p>IRB Chair interview IRB coordinator interview QI results</p>	<p>dence of evaluation of protocols for exempt status IRB Chair is able to discuss application of exempt status at the institution IRB coordinator is able to discuss process for determining exempt status QI results show evidence of compliance with VA and Federal regulations and IRB policies and procedures on the determination of exempt status</p>
<p>2.F. The IRB has policies and procedures for determination of risk level of investigational devices, appropriately makes such determinations, and implements any resulting actions. <i>Regulation/Source</i> 21 CFR 812.62, 66 FDA-IS, (SR/NSR)</p>	<p>2.F.1. The IRB's policies and procedures for the review of investigational devices address the following: 2.F.1.1. The IRB decision is based on proposed use of the device and not the device alone. 2.F.1.2. The IRB may agree or disagree with the sponsor's assessment of significant risk or nonsignificant risk. 2.F.1.3. The IRB notifies the sponsor and investigator when it determines the device is a significant risk device and proceeds to review the study only after an IDE is obtained by the sponsor. 2.F.1.4. The IRB proceeds to review the study under requisite criteria for any study when the device is determined to be non-</p>	<p>Policies and procedures IRB minutes Sample of device protocols QI results</p>	<p>Review of policies and procedures for determination of risk level of devices IRB minutes reflect evaluation of risk level of device Review of device protocols contains evidence of risk level of device QI results show evidence of compliance with VA and Federal regulations and IRB policies and procedures on the determina-</p>

significant risk.
2.F.2. The IRB conducts audits or self-assessments of compliance with VA and Federal regulations for assessing whether the investigational devices are significant or non-significant risk.
2.F.2.1. Results are used for QI and actions taken, as needed.

tion of risk level of devices

IRB 3 The IRB maintains documentation of its activities.

Requirement	Element	Data Source	Method
3.A. The IRB documents discussions and decisions on research proposals and activities. <i>Regulation/Source</i> 38 CFR 16.115(a)(2) M-3, Part 1, 9.09(g)(1)(b) 45 CFR 46.115(a)(2) 21 CFR 56.115(a)(2) IRB-GB, (I)(B) FDA-IS, (CL)(X) ICH-GCP, (3.4) OHRP-CFG (G64)	3.A.1. Minutes of IRB meetings contain sufficient detail to show:	Policies and procedures	Review of policies and procedures shows evidence of evaluation of requirements for content of IRB minutes
	3.A.1.1. Attendance.	IRB minutes	IRB minutes contain required information
	3.A.1.2. Approval of previous meeting minutes.	IRB minutes	IRB minutes contain required information
	3.A.1.3. Actions taken by the IRB at the meeting.	IRB communications	IRB communications to investigators, R&D Committee or other institutional officials document decisions made by the IRB
	3.A.1.4. The vote on actions, including the number of members voting for, against, and abstaining.	IRB communications	IRB communications to investigators, R&D Committee or other institutional officials document decisions made by the IRB
	3.A.1.4.1. Names of members abstaining.	R&D Committee minutes	R&D Committee minutes document acknowledgement of IRB decisions
	3.A.1.4.2. Quorum requirements were met at each recorded vote or for the entire meeting, including circumstances in which members recused themselves due to conflicts of interest.	R&D Committee minutes	R&D Committee minutes document acknowledgement of IRB decisions
	3.A.1.4.3. A non-scientific member of the IRB was present during the entire meeting.	R&D Committee minutes	R&D Committee minutes document acknowledgement of IRB decisions
	3.A.2. When an IRB member has a real or potential conflict of interest relative to the proposal under consideration, the minutes will document that the IRB member did not participate in the deliberations or voting on the proposal and that the quorum was maintained.		
	3.A.3. Minutes document the basis for requiring changes in or disapproving research and documentation of resolution of these		

issues when resolution occurs.

3.A.4. Minutes document required IRB findings where needed to approve exceptions, waivers or use of vulnerable populations.

3.A.5. Minutes include a written summary of the discussion of:

3.A.5.1. Controverted issues and their resolution.

3.A.5.2. Risk/benefit analysis.

3.A.5.3. Informed consent.

3.A.5.4. Risk level of investigational devices.

3.A.5.5. Additional safeguards to protect vulnerable populations if entered as study subjects.

3.A.6. Minutes reflect results of expedited reviews and the eligibility category serving as justification for meeting expedited review criteria.

3.A.7. Minutes include items approved as exempt from review and documentation of the eligibility category serving as justification for the exemption.

3.A.8. Minutes document the frequency of continuing review of each research project, based upon the degree of risk, as determined by the IRB.

3.A.9. IRB decisions are reported promptly and in writing to the investigator and appropriate institutional officials. In addition, suspensions and terminations are reported to the Department or Agency head.

3.A.10. IRB minutes are completed in a timely manner and forwarded to the R&D

3.B. The IRB retains required records for at least three years from study completion.

Regulation/Source
38 CFR 16,115(b)
M-3, Part 1, 9.09(g)(2)
45 CFR 46,115(b)
21 CFR 56.115(b)
IRB-GB, (I)(B)
FDA-IS, (CL)(X)(I)
ICH-GCP (3.4)

Committee.

3.B.1. Required records are retained for a minimum of three years following the completion of the study, in accordance with VHA's Records Control Schedule, applicable FDA and DHHS regulations, or as required by sponsors.

3.B.2. All records shall be accessible for inspection and copying by authorized representatives of VA, including accreditors and appropriate federal departments or agencies, at reasonable times and in a reasonable manner.

3.B.3. IRB records are the property and the responsibility of the local research office and are maintained and/or stored as required to protect the privacy and confidentiality of subjects. Records must be stored in a secure environment (e.g., locking file cabinets).

3.B.4. There must be limited access to the files.

3.B.4.1. There must be logs or records of access to restricted files, including:

3.B.4.1.1 Who accessed the files with the exception of IRB and research office staff;

3.B.4.1.2. What files were accessed;

3.B.4.1.3. When the files were accessed;

3.B.4.1.4. For what purpose the files were accessed.

Policies and procedures

IRB files

IRB coordinator interview

IRB file access log

Review of policies and procedures shows evidence of requirements for record retention and access

IRB files are kept in a secure location

Staff demonstrates filing system to show that files are kept in an organized fashion in a secure location.

Review of access log reflects access by appropriate individuals or groups

Additionally, all research proposals and IRB minutes requested for the survey process were available.



TABLE C-4 CONSIDERATIONS OF RISKS AND BENEFITS

Rationale

All research should be designed to maximize possible benefits and minimize possible harms to participants. When a research proposal does not have the proper balance of risks and benefits, it should not be approved. One of the major responsibilities of the IRB is to assess the risks and benefits of the proposed research and to put in place safeguards that require investigators to act in ways that minimize harms to subjects. This standard contains the requirements for IRB actions related to assessment and balancing of risks and benefits.

KEY:

CFR = Code of Federal Regulations

M-3, Part 1 = The Veterans Affairs Manual, Chapter 9

IRB-GB = OPRR IRB Guidebook

FDA-IS = FDA Information Sheets

FDA-IS, (CL) = Appendix H: A Self-Evaluation Checklist for IRBs

FDA-IS, (FAQ) = Frequently Asked Question

FDA-IS, (ICG) = The Guide to Informed Consent

FDA-IS, (CR) = Continuing Review After Study Approval

ICH-GCP = International Conference on Harmonization, Good Clinical Practice Guidelines

OHRP-CFG = Office of Human Research Protections Compliance Activities: Common Findings and Guidance 9/1/2000

RB 1 The IRB systematically evaluates risks and anticipated benefits as part of the initial review and ongoing review of research.

Requirement	Element	Data Source	Method
1.A. The IRB has procedures (e.g., evaluation tools to be completed by reviewers) for initial review of the risks and benefits of research. <i>Regulation/Source</i> 38 CFR 16.111(a)(1)(2) M-3, Part 1, 9.09(a)(1) 45 CFR 46.103(b)(4) 45 CFR 46.111(a)(1)(2) 21CFR 56.111(a)(1)(2) IRB-GB, (III)(A)	1.A.1. Procedures for the initial review of the risks and benefits of research include:	Procedures for the evaluation of risks and benefits	Review of procedures for the presence of each element
	1.A.1.1. Identification of the risks associated with research. 1.A.1.2. Assessment of whether risks have been minimized. 1.A.1.3. Determination of the level of risk of the research (e.g., minimal, greater than minimal). 1.A.1.4. Identification of the probable individual and societal benefits of the research. 1.A.1.5. Determination that risks are reasonable in relation to the benefits to subjects and the knowledge to be gained. 1.A.1.6. Determination of intervals for continuing review based on the level of risk.	IRB member interview	IRB member describes processes for the evaluation of risks associated with research proposals

<p>1.C. The IRB evaluates each research proposal to identify the probable benefits of the research.</p>	<p>1.C.1. The IRB identifies the limit of anticipated benefits research subjects may derive from participation in the research.</p> <p>1.C.2. The IRB determines the importance of the knowledge that may be reasonably expected to result from the research. (The IRB should consider only the specific risks and benefits that may result from the research.)</p>	<p>IRB minutes</p> <p>IRB evaluation tools (or checklists)</p> <p>IRB member interview</p> <p>QI reports</p>	<p>Review of IRB minutes or completed protocol evaluation tools document assessment of anticipated benefits</p> <p>IRB members identify methods for determining anticipated benefits of research proposals</p> <p>Review QI reports for evidence of IRB compliance with procedures for assessing anticipated benefits of research proposals</p>
<p><i>Regulation/Source</i> 38 CFR 16.111(a)(1)(2) M-3, Part 1, 9.09(a)(2)(a) 45 CFR 46.111(a)(1)(2) 21 CFR 6.111(a)(1)(2) IRB-GB, (III)(A)</p>			

RB 1 The IRB systematically evaluates risks and anticipated benefits as part of the initial review and ongoing review of research.

Requirement	Element	Data Source	Method
1.D. The IRB determines that risks to subjects are reasonable in relation to anticipated benefits. <i>Regulation/Source</i> 38 CFR 16.111(a)(1)(2) M-3, Part 1, 9.09(a)(2)(a) 45 CFR 46.111(a)(1)(2) 21 CFR 56.111(a)(1)(2) IRB-GB, (III)(A)	1.D.1. The IRB determines the risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result.	IRB minutes	Review of IRB minutes or completed protocol evaluation tools document assessment of risk/benefit ratio
		IRB evaluation tools (or checklists)	
		IRB member interview	IRB members identify methods for determining risk/benefit ratio of research proposals
1.E. The IRB continually evaluates the risks and benefits of ongoing protocols. <i>Regulation/Source</i> 38 CFR 16.109(e) 38 CFR 16.111(a)(6) M-3, Part 1, 9.09(f) 45 CFR 46.109(e) 45 CFR 46.111(a)(6) 21 CFR 56.109(f) 21 CFR 56.111(a)(6)	1.E.1. The IRB determines for each approved research protocol, the specific interval for periodic review of risks and determines the need for monitoring safety. 1.E.2. The IRB demonstrates ongoing review of the following sources of risks and benefits: 1.E.2.1 Evaluation of adverse event reports from investigators. 1.E.2.2. Evaluation of sponsor safety reports (e.g., IND or IDE). 1.E.2.3. Evaluation of MedWatch reports. 1.E.2.4. Evaluation of amended or updated Investigator Brochures. 1.E.2.5. Evaluation of amendments to protocols. 1.E.2.6. Evaluation of any new information	QI reports	Review QI reports for evidence of IRB compliance with procedures for assessing risk/benefit ratio of research proposals
		IRB minutes	Minutes show review and discussion about whether there is a change in risk or action required
		IRB communications	Communications to investigators document decision about changes in risk or actions required
		Completed IRB continuing review tools	Sample of approved protocol files show documentation of consideration of risks and benefits at continuing reviews
		IRB serious adverse event reporting	Sample of approved protocol

available regarding the research project.

forms, safety reports, MedWatch reports

files show documentation of consideration of risks and benefits at review of SAE, safety reports and MedWatch reports

TABLE C-5 RECRUITMENT AND SUBJECT SELECTION

Rationale

Because research frequently poses risks of harm and the possibility of benefit, it is necessary to fairly distribute potential risks and benefits. It is also necessary to protect groups that have been discriminated against in the past, who are vulnerable to manipulation, or unable to freely consent, from the risks of research. IRBs must assure that procedures for selecting research subjects are fair. This standard outlines the expected processes that IRBs must use to ensure that research participants are identified and recruited properly.

KEY:

CFR = Code of Federal Regulations

M-3, Part 1 = The Veterans Affairs Manual, Chapter 9

IRB-GB = OPRR IRB Guidebook

FDA-IS = FDA Information Sheets

FDA-IS, (CL) = Appendix H: A Self-Evaluation Checklist for IRBs

FDA-IS, (FAQ) = Frequently Asked Question

FDA-IS, (ICG) = The Guide to Informed Consent

FDA-IS, (CR) = Continuing Review After Study Approval

FDA-IS, (RSS) = Recruiting Study Subjects

FDA-IS, (PRS) = Payment to Research Subjects

ICH-GCP = International Conference on Harmonization, Good Clinical Practice Guidelines

HHS IGR = HHS Inspector General's Report

RSS 1 The IRB systematically evaluates recruitment and subject selection practices.

Requirement	Element	Data Source	Method
<p>1.A. The IRB defines acceptable recruitment practices for proposed research.</p> <p><i>Regulation/Source</i> HHS-IGR M-3 Part I, 9.13 FDA-IS, (RSS) FDA-IS, (PRS)</p>	<p>The IRB's policies and procedures define acceptable recruitment practices as applied to the following:</p> <p>1.A.1. Payment to subjects. 1.A.2. Advertisements. 1.A.3. Compensation to investigators, physicians and other health care providers for identifying and/or enrolling subjects.</p>	<p>Policies and procedures</p>	<p>Review of policies and procedures for the presence of each element of the requirement</p>
<p>1.B. The IRB reviews subject recruitment methods, advertising materials and subject payment arrangements proposed, and determines that they are fair and appropriate.</p> <p><i>Regulation/Source</i> HHS-IGR M-3 Part I, 9.13 FDA-IS, (RSS) FDA-IS, (PRS)</p>	<p>The IRB demonstrates that it has considered the following recruitment practices as part of its review:</p> <p>1.B.1. The nature or amount of the compensation offered to subjects for participation in research does not create undue influence, particularly for economically disadvantaged subjects. 1.B.2. Claims made in advertisements appropriately reflect the study protocol.</p>	<p>IRB minutes</p> <p>Completed IRB protocol evaluation tools</p> <p>Sample of reviewed protocol advertisements (both approved and disapproved)</p> <p>Sample of protocols for subject information materials</p>	<p>IRB minutes document discussion of recruitment practices for protocols</p> <p>Completed evaluation tools demonstrate evaluation of recruitment practices</p> <p>Approved advertisements contain appropriate information and are consistent with protocol content</p> <p>Approved subject information materials contain appropriate information and are consistent with protocol content</p>

<p>1.C. The IRB has policies and procedures to evaluate the equitable selection of subjects in proposed research and considers subject selection in its review of research.</p>	<p>The IRB has policies and procedures for, and implements the following: 1.C.1. Purposes of research. 1.C.2. Setting in which research occurs. 1.C.3. Plan for soliciting subjects. 1.C.4. The scientific and ethical justification for including vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons (e.g., the homeless).</p>	<p>Policies and procedures</p> <p>IRB application forms</p>	<p>Review of policies and procedures for the presence of required elements</p> <p>Review of IRB application for evidence of collection of recruitment plans</p>
<p><i>Regulation/Source</i> 38 CFR 16.111(a)(3) M-3 Part I, 9.09 (a)(3) 45 CFR 46.111(a)(3) 21 CFR 56.111(a)(3) IRB-GB, (III)(C)</p>			
<p>1.D. The IRB determines that proposed subject selection (inclusion and exclusion criteria and recruitment procedures) is equitable with respect to the distribution of the burdens and benefits of the proposed research.</p>	<p>The IRB considers the following criteria: 1.D.1. The purpose of the research requires or justifies using the proposed subject population. 1.D.2. The burdens and benefits of research are fairly distributed. 1.D.3. Where specific populations are over or under-represented in the proposed subject population, the rationale for such over or under-representation is justified. 1.D.4. Subject selection is consistent with VA and DHHS policies on the participation of women, children and minorities in medical research involving human subjects.</p>	<p>IRB minutes</p> <p>Sample of reviewed research proposals.</p>	<p>IRB minutes show evidence of IRB consideration of equitable selection</p> <p>Protocols show evidence of subject selection considerations</p> <p>Protocols show evidence consideration of VA and DHHS policies on participation of women, children and minorities</p>

<i>Regulation/Source</i> 38 CFR 16.111(a)(3) M-3 Part I, 9.09 (a)(3) 45 CFR 46.111(a)(3) 21 CFR 56.111(a)(3) IRB-GB, (III)(C) HHS IGR	1.D.5. Where the purpose and nature of the research justifies the inclusion of vulnerable populations as subjects (e.g., children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons), the IRB determines that additional safeguards have been included in the study to protect the rights and welfare of these subjects and specifically documents those safeguards.	Protocols show evidence of additional safeguards for subject selection in vulnerable populations
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TABLE C-6 PRIVACY AND CONFIDENTIALITY

Rationale

Violation of a research subject's privacy may lead to significant harm from loss of work, embarrassment, loss of benefits, and loss of dignity. IRBs must ensure that proposed research protects human subjects from loss of privacy and breach of confidentiality. This requires that IRBs understand the risks of harm from loss of confidentiality, and methods, such as de-identifying data, that may reduce the risk of breach of confidentiality. This standard outlines requirements for the protection of privacy and confidentiality.

KEY:

CFR = Code of Federal Regulations

M-3, Part 1 = The Veterans Affairs Manual, Chapter 9

IRB-GB = OPRR IRB Guidebook

FDA-IS = FDA Information Sheets

FDA-IS, (CL) = Appendix H: A Self-Evaluation Checklist for IRBs

FDA-IS, (FAQ) = Frequently Asked Question

FDA-IS, (ICG) = The Guide to Informed Consent

FDA-IS, (CR) = Continuing Review After Study Approval

ICH-GCP = International Conference on Harmonization, Good Clinical Practice Guidelines

PC 1 The IRB systematically evaluates the protection of privacy and confidentiality in proposed research.

Requirement	Element	Data Source	Method
<p>1.A. The IRB has policies and procedures to evaluate provisions for the protection of privacy and confidentiality which conform to VA, Federal, and local requirements.</p> <p><i>Regulation/Source</i> 38 CFR 16.111(a)(7) 38 CFR 17.33(a)(1) 38 CFR 17.33(b)(1)(v) 38 CFR 17.33(f) M-3, Part I, 909 (a)(7) 45 CFR 46.111(a)(7) 21 CFR 56.111(a)(7) IRB-GB, (III)(D)</p>	<p>The IRB has policies and procedures which set forth, for investigators, the requirements for preserving privacy and confidentiality. Consideration must be given to:</p> <p>1.A.1. Methods used to obtain information about participants and potential participants. 1.A.2. Nature of information being sought. 1.A.3. Use of personally identifiable records. 1.A.4. Plan to protect the confidentiality of research data that may include coding, removal of identifying information, limiting access to data, use of Certificates of Confidentiality or other effective methods. 1.A.5. The investigator's disclosures to participants about confidentiality. 1.A.6. Determination of whether a Federal Certificate of Confidentiality should be obtained.</p>	<p>Policy and procedures</p>	<p>Review of policies and procedures for the presence of each element</p>
		<p>Guidance to Investigators</p>	<p>Guidance materials provided to investigators contain specifications for disclosure to participants in consent forms or other patient information</p>
<p>1.B. The IRB systematically assesses research proposals for provisions to protect privacy and confidentiality.</p>	<p>1.B.1. The IRB evaluates the following: 1.B.1.1. Methods used to</p>	<p>Sample of completed IRB protocol evaluation forms or IRB minutes</p>	<p>IRB evaluation forms or minutes demonstrate assessment of privacy and confidentiality issues associ-</p>

Regulation/Source
38 CFR 16.111(a)(7)
38 CFR 17.33(a)(1)
38 CFR 17.33(b)(1)(v)
38 CFR 17.33(f)
M-3, Part I, 909 (a)(7)
45 CFR 46.111(a)(7)
21 CFR 56.111(a)(7)
IRB-GB, (III)(D)

identify and recruit participants protect patient privacy and confidentiality.
1.B.1.2. Methods to obtain information about participants are reasonable and protect privacy.
1.B.1.3. There are adequate provisions for protecting the confidentiality of research data, including, where appropriate, Certificates of Confidentiality.
1.B.1.4. The informed consent form and other information presented to potential research participants adequately discloses the risks to privacy and confidentiality.
1.B.2. The IRB conducts audits or self-assessments of compliance with privacy and confidentiality requirements.
1.B.2.1. Results of audits or self-assessments are used for QI and actions are taken, as needed.

IRB application forms

QI reports

ated with the protocol

Review of IRB application for presence of each element

Review of QI reports for evidence of compliance with policies and procedures

TABLE C-7 INFORMED CONSENT

Rationale

Informed consent is critical to the protection of human research subjects. It permits participants to determine whether they are willing to accept the risks of the research in order to gain the potential benefits. Requirements for informed consent are met when potential participants are: 1) capable of deciding whether to participate; 2) adequately informed about the risks and benefits of participation; 3) able to understand the information; and 4) voluntarily decide to participate. This standard outlines the requirements for processes that research programs and IRBs must follow in assessing whether informed consent is adequate.

KEY:

CFR = Code of Federal Regulations

M-3, Part 1 = The Veterans Affairs Manual, Chapter 9

IRB-GB = OPRR IRB Guidebook

FDA-IS = FDA Information Sheets

FDA-IS, (CL) = Appendix H: A Self-Evaluation Checklist for IRBs

FDA-IS, (FAQ) = Frequently Asked Question

FDA-IS, (ICG) = The Guide to Informed Consent

FDA-IS, (CR) = Continuing Review After Study Approval

FDA-IS, (PRS) = Payment to Research Subjects

ICH-GCP = International Conference on Harmonization, Good Clinical Practice Guidelines NBAC = National Bioethics Advisory Commission Report

IC 1 The IRB assures that prospective human subjects give valid informed consent.

Requirement	Element	Data Source	Method
<p>1.A. The IRB has policies and procedures for the process of obtaining informed consent from subjects or their legally authorized representatives and ensures compliance with policies and procedures.</p> <p><i>Regulation/Source</i> 38 CFR 16.116 38 CFR 16.111(a)(4) M-3, Part 1, 9.09(a)(4) 45 CFR 46.111(a)(4) 45 CFR 46.116 21 CFR 50.20 21 CFR 50.25 ICH-GCP 4.8.5 FDA-IS, (ICG)</p>	<p>1.A.1. IRB policies and procedures describe the following:</p>	<p>Policies and procedures for the process of obtaining consent</p>	<p>Review of policies and procedures for evidence of elements of consent process</p>
	<p>1.A.1.1. The IRB has the authority to observe the consent process.</p>	<p>IRB communications to investigators regarding the consent process including Investigator Handbooks/Guidelines</p>	<p>Review of IRB communications for instructions to investigators on the IRB's requirements for the consent process</p>
	<p>1.A.1.2. Who, under VA policy, state and local law, may serve as a legally authorized representative for subjects determined to be incapable of making an autonomous decision. (There is a distinction between treatment authorization and research authorization).</p>	<p>IRB documentation of observation of consent process</p>	<p>Review of IRB documentation of consent process observations shows critical evaluation of the process with recommendations for improvement</p>
	<p>1.A.1.3. Who is eligible to inform the prospective subject about all aspects of the trial and conduct the informed consent process.</p>	<p>IRB minutes</p>	<p>Review of IRB minutes for evidence of consideration of proposed consent processes</p>
	<p>1.A.1.4. Consent is obtained prior to the conduct of any procedures required by the protocol.</p>	<p>QI results</p>	<p>QI results show evidence of investigator compliance with consent process guidelines</p>
	<p>1.A.2. In its review of research proposals, the IRB assures that the investigative staff conducts the informed consent process with the following considerations:</p>		
	<p>1.A.2.1 Assessing the subject's capacity to consent to a research protocol.</p>		
	<p>1.A.2.2. Ensuring that information is given to the subject, or their legally authorized representative, in</p>		

	<p>language that is understandable to the subject or representative.</p> <p>1.A.2.3. Providing the prospective subject or the legally authorized representative sufficient opportunity to consider whether or not to participate.</p> <p>1.A.2.4. Ensuring that subjects give consent without coercion or undue influence.</p> <p>1.A.3. The IRB conducts audits or self-assessments to assess investigator compliance with regulatory requirements.</p> <p>1.A.3.1 The IRB uses the results for QI purposes and takes action, as needed.</p>		
<p>1.B. The IRB has policies and procedures that define the required content for informed consent forms and ensures compliance with these policies and procedures.</p> <p><i>Regulation/Source</i> 38 CFR 16.116 M-3, Part 1, 9.09(4)(5) and Appendix 9C Procedures for Obtaining Informed Consent 45 CFR 46.116 21 CFR 50.20-27 FDA-IS, (FAQ)(V)(VI) IRB-GB, (III)(B) FDA-IS, (PRS)</p>	<p>1.B.1. The IRB requires that consent forms include all the basic elements of information as set forth in VA and other Federal regulations.</p> <p>1.B.2. The IRB requires the consent form to contain information in language understandable to the subject or the representative.</p> <p>1.B.2.1. Based on the potential population, the appropriate reading level of consent forms is defined.</p> <p>1.B.2.2. Validated translations of consent forms are required for non-English-speaking subjects.</p> <p>1.B.3. The IRB identifies those circumstances when the investigator must provide any of the additional</p>	<p>Policies and procedures outlining consent content requirements</p> <p>IRB template consent</p> <p>Sample of IRB approved informed consent forms</p> <p>IRB minutes documenting consent analysis</p> <p>QI results</p>	<p>Review of Policies and Procedures for consistency with regulations and all elements of the requirement</p> <p>Review of IRB template consent for consistency with regulations (Checklist contains all 8 required elements)</p> <p>Review of sample of IRB approved consent forms for evidence of consistency with regulations</p> <p>Review of IRB minutes for evidence of evaluation, documentation of requested changes to consent forms to comply with regulations, and investigator compliance.</p>

elements of information as set forth in VA and other Federal regulations.

1.B.4. The IRB requires all information concerning payment to subjects, including the amount and schedule of payments, to be included in the informed consent document.

1.B.5. The IRB requires the content of consent forms to be consistent with state laws regarding content (if applicable).

1.B.6. The IRB prohibits any informed consent, whether oral or written, from including any exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

1.B.7. The IRB conducts audits or self-assessments to determine that only approved consent forms are used and have the required content.

1.B.7.1. The IRB uses the results for QI purposes and takes action, as needed.

QI results show evidence of compliance in evaluating consents for VA, Federal, local, and institutional requirements and that only approved consent forms are used by investigative staff.

1.C. The IRB has policies and procedures regarding documentation of informed consent and ensures that investigators and staff conform

1.C.1. The IRB requires informed consent to be documented by the use of a written consent form, VA Form 10-1086, approved by the IRB and signed by the subject or the subject's

Policies and procedures for documentation of informed consent
IRB template consent

Review of policies and procedures for evidence of requirements for consent documentation
Review of template consent for re-

to these policies and procedures.	legally authorized representative.	Sample of approved consents	quired signature and date lines
<i>Regulation/Source</i> 38 CFR 16.117(c) M-3, Part 1, 9.11 45 CFR 46.117(c) 21 CFR 50.23(a) 21 CFR 50.27(b)(2) IRB-GB, (III)(B)	1.C.1.1. Consent forms contain the required signature lines.		Review of sample of IRB approved consents for evidence of required signature lines
	1.C.1.1.1. Subject signature and date of signature.	IRB minutes	Review of IRB minutes for documentation of evaluation for use of short form consent
	1.C.1.1.2. Signature of person conducting the informed consent process.	Sample of protocols where short form consent is used	Review of sample of protocols with short form consents for evidence of requirements for appropriateness of use
	1.C.1.1.3. Witness to the signature.	IRB communications	Review of communications to investigators regarding the requirements for documentation of consent
	1.C.1.1.4. Investigator, if an investigator did not conduct the consent process.	Sample of signed consent forms	Review of sample of signed consent forms for presence of required signatures
	1.C.1.1.5. Witness signature on “short form.”	QI results	Review of QI results for evidence of IRB evaluation of consents and compliance of investigators with requirements for documentation of consent.
	1.C.2. Policies describe situations where the signature of a witness is required.		
	1.C.3. Policies describe conditions under which a “short form” informed consent may be used.		
	1.C.4. The IRB conducts audits to determine that investigators have documented informed consent through the use of the approved consent form, dated and signed, with a copy given to the subject or legally authorized representative, and the original is kept in the medical record.		
	1.C.4.1. In conjunction with the use of an IRB approved “short form,” the IRB approved written summary of what was said to the subject or legally authorized representative, is signed by the witness.		

1.C.4.2. The IRB uses the results for QI purposes and takes action, as needed.

1.D. The IRB has policies and procedures for approving waiver or alteration of the informed consent form and complies with these policies and procedures.

Regulation/Source
38 CFR 16.116
38 CFR 16.117
M-3, part 1, 9.11
45 CFR 46.116
45 CFR 46.117
21 CFR 50.109(c)
IRB-GB, (III)(B)
FDA-IS, (ICG)

1.D.1. The IRB defines the conditions under which it will permit waiver or alteration of any element of informed consent to include:

- 1.D.1.1. The research involves no more than minimal risk.
- 1.D.1.2. The waiver or alteration will not adversely affect the rights of the subjects.
- 1.D.1.3. The research could not be practically done without such waiver or alteration.
- 1.D.1.4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
- 1.D.1.5. The research or demonstration project is to be conducted by, or subject to the approval of, state or local government officials and is designed to study, evaluate, or otherwise examine public benefit of service programs, procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or possible changes in methods or levels of payment for benefits or services under those programs.

1.D.2. The IRB does not allow waiver

Policies and procedures for waiving or altering consent

Sample of protocols

IRB minutes

QI results

Review of policies and procedures for conditions for waiving or altering consent, content

Review of protocols where consent was waived or altered for assurance that conditions were met

IRB minutes show evidence of evaluation of conditions for waiver or alterations of consent content consistent with policies and procedures

QI results show evaluation of and compliance with conditions for waiving or altering consent content

or alteration of informed consent forms when FDA-regulated test articles are involved.

1.D.3. In its approval of waiver or alteration, the IRB documents its specific findings that conditions permitting waiver or alteration are met.

1.D.4. In its decision to waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects, the IRB documents the regulatory basis for such waiver, providing either that:

1.D.4.1. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from breach of confidentiality or

1.D.4.2. The research presents no more than minimal risk and involves no procedures for which written consent is normally required outside of the research context.

1.D.5. The IRB conducts audits to determine that waivers or alterations of informed consent are only made when permitted by regulation.

1.D.5.1. The IRB uses the results for QI purposes and takes action, as needed.

IC 2 The IRB protects human subject participating in research conducted with exceptions from the informed consent requirements.

Requirement	Element	Data Source	Method
<p>2.A. The IRB has policies and procedures for exceptions from the general requirements for obtaining informed consent before the use of a test article and appropriately reviews such exceptions.</p> <p><i>Regulation/Source</i> 21 CFR 50.23 IRB-GB, (III)(B) FDA-IS, (CL)(XIII) FDA-IS, (ICG)</p>	<p>For each individual situation in which a test article is to be administered and informed consent may not feasibly be obtained:</p> <p>2.A.1.The IRB requires that the investigator and a physician who is not otherwise participating in the clinical investigation must certify in writing all of the following:</p> <p>2.A.1.1. The subject is confronted by a life-threatening situation necessitating the use of the test article.</p> <p>2.A.1.2. Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.</p> <p>2.A.1.3. Time is not sufficient to obtain consent from the subject's legal representative.</p> <p>2.A.1.4. There is no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.</p> <p>2.A.2. The IRB requires that if the immediate use of the test article is, in the investigator's opinion, required to</p>	<p>Policies and procedures for exceptions from the general requirements for obtaining informed consent before the use of a test article</p> <p>IRB minutes</p> <p>Sample of protocols</p> <p>IRB Chair interview</p> <p>QI results</p>	<p>Review of policies and procedures for evidence of requirements for obtaining informed consent before the use of a test article.</p> <p>IRB minutes document evaluation of each exception to the general requirements for obtaining informed consent.</p> <p>Exceptions to the general requirements to informed consent met all required conditions.</p> <p>Ask the IRB Chair to express conditions for exceptions to the general requirements for obtaining informed consent.</p> <p>QI results show evidence that exceptions to general requirements for obtaining informed consent met required conditions.</p>

preserve the life of the subject, and time is not sufficient to obtain the independent determination by a physician not otherwise participating in the study, in advance, the use of the test article shall be reviewed and evaluated within 5 working days in writing by a physician not participating in the investigation.

2.A.3. The IRB requires documentation of emergency situations where exceptions to the general requirements to informed consent have occurred to be submitted to the IRB within 5 working days.

2.A.4. In its review of requests for exceptions, the IRB documents the regulatory basis for the exception and the timely receipt of written certification.

2.A.5. The IRB conducts audits to determine that exceptions from the general requirements for obtaining informed consent before use of a test article are made appropriately.

2.A.5.1. The IRB uses the results for QI purposes and takes action, as needed.

2.B. The IRB has policies and procedures for exceptions from informed consent requirements in planned emergency research and appropriately reviews such

2.B.1. The IRB requires planned emergency research proposals include documentation of all of the following:

2.B.1.1. The human subjects are in a life-threatening situation, available treatments are unproven

Policies and Procedures

IRB minutes

Review of policies and procedures for requirements for emergency research exceptions from informed consent requirements.

IRB minutes reflect evaluation of

exceptions.
Regulation/Source
 21 CFR 50.24
 IRB-GB, (II)(B)
 FDA-IS, (CL)(XIII)
 FDA-IS, (ICG)

or unsatisfactory, and the collection of valid scientific evidence is necessary to determine the safety and effectiveness of particular interventions.
 2.B.1.2. Obtaining informed consent is not feasible.
 2.B.1.3. Participation in the research holds out the prospect of direct benefit to subjects.
 2.B.1.4. The clinical investigation could not practically be carried out without the waiver.
 2.B.1.5. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence and the investigator has committed to attempting to contact a legally authorized representative within that window of time.
 2.B.1.6. The IRB has reviewed and approved informed consent procedures and an informed consent document as set forth in VA and other Federal regulations to be used in situations where the use of such procedures and documents is feasible.
 2.B.1.7. Additional protections of the rights and welfare of the subjects will be provided through, at least,
 2.B.1.7.1. Consultation with representatives of the

Sample of protocols

IRB communications

QI results

exceptions from informed consent in planned emergency research.

Review of protocols for planned emergency research show evidence of meeting requirements (i.e., public disclosure, plan for subject and family notification, etc.).

IRB communications provide evidence of meeting requirements (i.e., public disclosure, plan for subject and family notification, etc.).

QI results show evidence of compliance in evaluating and implementing planned emergency research.

community.

2.B.1.7.2. Public disclosure to the community prior to the study.

2.B.1.7.3. Public disclosure of the results of the investigation following completion.

2.B.1.7.4. Establishment of an independent data monitoring committee.

2.B.1.7.5. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

2.B.1.8. Procedures are in place to inform, at the earliest feasible opportunity, each subject or legally authorized representative or family member, of the subject's inclusion in the clinical investigation.

2.B.1.9. There is a procedure to inform the subject, legally authorized representative or family member that the subject's participation may be discontinued at any time without penalty or loss of benefits to which the subject is otherwise entitled.

2.B.1.10. There must be a separate IND or IDE for the study for any FDA regulated

product.

2.B.1.11. If the study does not involve an FDA-regulated product, there is concurrence by the Agency Secretary that the waiver is appropriate.

2.B.2. In its review of requests for exceptions in planned emergency research, the IRB documents its evaluation and the regulatory basis for approving the exception.

2.B.3. The IRB conducts audits that include a review of requests for exceptions from informed consent in planned emergency research.

2.B.3.3.1 The IRB uses the results for QI purposes and takes action, as needed.

Process for Submitting Comments
(due by May 15, 2001)

Please address all comments to VAHRP:

- **E-mail (preferred method)** to vahrpap@ncqa.org. You will receive an e-mail confirmation of receipt.
- **Mail** to VAHRPAP, NCQA, 2000 L. Street, Suite 500, Washington, D.C. 20036
- **Fax** to 202-955-3599, Attention – VAHRPAP.

Please provide the following information:

- Name
- Position
- Organization

Please organize comments as described below.

- **Word document (preferred method)** formatted as below.

Domain	Issue*	Comment
<i>Privacy and Confidentiality</i>	Requirement 1.B Data source/method	Should the IRB minutes be included as a possible data source/method for evaluating IRB assessment of provisions to protect privacy in individual proposals?
All	Data Source/method	Is a one year look-back period an appropriate time-frame for adequate evaluation of an HRPP?

* Issue may address a global comment, a specific requirement or element, the data sources or methods

