

Hines/North Chicago Combined Research Program

Investigator's Manual

Guidelines for Conducting Research Studies That Involve Human Subjects

TABLE OF CONTENTS

Disclaimer	3
Background	3
Definitions	4
Purpose of the IRB	7
Principal Investigator Responsibilities	7
Vulnerable Populations	7
Protocol Submission:	9
Conflict of Interest	11
Investigational Drugs, Biologics, Devices	12
Privacy and Confidentiality of Participants	13
Use of VA Records for Research	13
HIPAA	14
Authorizations	14
Waiver of Authorization	14
Guidance on Informed Consent	16
Guidance on Informed Consent Forms	18
Recruitment of Subjects	18
Recruitment of Non-Veterans as research Participants	19
Progress Notes and Flagging of the Medical Record	19
Dual Enrollment	20
Amendments	20
Adverse Event Monitoring and Reporting	20
Tissue Banking	21
Continuing Review	22
Investigator Audits	23
Publication of Study Results	24
Study Check-list	25
Web-Links	28
OHRP Decision Charts	29

DISCLAIMER:

This document is an information guide. It is meant to supplement the official policies and procedures and offer guidance. It does not contain all of the information contained in the /IRB policies and procedures and the Human Research Protection Program (HRPP), VHA Research Handbook 1200.5 and applicable VA, FDA and DHHS regulations. For complete information, these documents can be accessed through the research website at <http://www.hines.va.gov/research/>

This document will be updated as policies and procedures are updated. Please contact the IRB with any questions.

BACKGROUND INFORMATION

ACCREDITATION:

The VA has mandated that facilities involved in human research must be accredited. The Human Research Protection Program(s) at Edward Hines Jr. VHA and North Chicago VAMC received full 3 year accreditation by NCQA (National Committee on Quality Assurance) on December 3, 2003.

In January, 2006, the accreditation contract was awarded to AAHRPP (Association for the Accreditation of Human Research Protection Programs, Inc). There are 5 domains under AAHRPP: Organization, Research Review Unit (IRB), Investigator, Sponsored Research and Participant Outreach.

All research personnel are encouraged to review the accreditation standards and principals, regulatory references and outcome criteria at www.aahrpp.org.

Committees:

The Research and Development Committee is responsible to the Hospital Director through the Chief of Staff for promoting research and development programs that will assist the hospital in providing quality patient care. The Committee advises the Hospital Director on professional and administrative aspects of the R&D program. All R&D activities within the hospital, whether funded or unfunded, are within its purview. Decisions on matters outside the committee's jurisdiction will be treated as recommendations to the Hospital Director.

The Committee is responsible for maintaining high standards throughout the Research and Development Program. These standards include: assuring the scientific quality of the R&D projects, protection of human rights, laboratory safety, and welfare of animals in research. Other responsibilities include but are not limited to: 1. Approving or disapproving the conduct of each research activity performed at Hines VA Hospital and/or North Chicago VA Medical Center. 2. Approving distribution of research funds, space, personnel, equipment, supplies and common-use facilities. 3. Determining the

extent to which the objectives of the research and development programs are being attained and their impact on maintaining and improving VA-Medical School relations. **No research project, regardless of the review category, may begin until R&D approval is obtained**

The IRB (Institutional Review Board formerly known as Human Studies Subcommittee) is a subcommittee of the Research and Development Committee. The IRB is entrusted with the responsibility of insuring that research at Hines VA Hospital/North Chicago VA Medical Center is conducted under the most rigorous ethical standards in order to assure the protection of the rights, welfare, and safety of the veteran patients. Following approval by the IRB, projects are forwarded to the R&D Committee for scientific and administrative review. The IRB Office forwards approvals to the R&D Coordinator for transmittal to the Principal Investigator once all subcommittee approvals are obtained.

The Research Safety Subcommittee (RSS) is a subcommittee of the Research and Development Committee (R&D) that includes staff with related safety expertise who are representative of the geographic makeup of the Research Service, the Administrative Officer for Research and Development Service, and the Hospital Radiation Safety Officer. The Research Safety Subcommittee (RSS) is responsible for coordinating the safety program in all research areas. All studies that are to be conducted at Hines VA Hospital or North Chicago VA Medical Center, regardless of funding source, must be reviewed and approved by the RSS before the proposal can be forwarded to the R&D Committee for approval or any funding source and prior to implementation of the study. Certain studies may be exempt from safety reviews.

DEFINITIONS as defined in VHA Research Handbook 1200.5,

Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes and are subject to IRB review [38 CFR §16.102(d)] [45 CFR §46.102(d)]

Research is defined as the testing of concepts by the scientific method of formulating a hypothesis or research question, systematically collecting and recording relevant data, and interpreting the results in terms of the hypothesis or question. [VHA Handbook 1200.5 3.v] **Note difference**

FDA Clinical investigation means any experiment that involves a test article and one or more *human participants* and that is one of the following: [21 CFR §50.3(c)] [21 CFR §56.102(c)]

- Subject to requirements for prior submission to the Food and Drug Administration under §505(i) or §520(g) of the *act*.
- Not subject to requirements for prior submission to the Food and Drug Administration under these sections of the *act*, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

- The term does not include experiments that are subject to the provisions of 21 CFR §58, regarding non-clinical laboratory studies.

Human Subject. A human subject is a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or through identifiable private information (38 CFR 16.102(f)). The definition provided in the Common Rule includes investigators, technicians, and others assisting investigators, when they serve in a "subject" role by being observed, manipulated, or sampled. As required by 38 CFR 16.102(f) an intervention includes all physical procedures by which data are gathered and all physical, psychological, or environmental manipulations that are performed for research purposes.

NOTE: *The FDA definition of human subject differs according to the applicable regulation. See 21 CFR 812.3(p), 21 CFR 50.3(g), 312.3(b,) and 56.102(e).*

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

- Private information must be individually identifiable (i.e., the identity of the participant is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human participants. [38 CFR §16.102(f) (2)] [45 CFR §46.102(f) (2)]

Adverse event (AE). An AE is defined as any untoward physical or psychological occurrence in a human subject participating in research. An AE can be any unfavorable or unintended event including abnormal laboratory finding, symptom or disease associated with the research or the use of a medical investigational test article. An AE does not necessarily have to have a causal relationship with the research, or any risk associated with the research or the research intervention, or the assessment. Loss of Confidentiality may be an adverse event.

(1) **Serious Adverse Event (SAE).** A SAE is defined as death; a life threatening experience; hospitalization (for a person not already hospitalized); prolongation of hospitalization (for a patient already hospitalized); persistent or significant disability or incapacity; congenital anomaly and/or birth defects; or an event that jeopardizes the subject and may require medical or surgical treatment to prevent one of the preceding outcomes.

(2) **Unexpected Adverse Event (UAE).** An UAE is any adverse event and/or reaction, the specificity or severity of which is not consistent with the informed consent, current investigator brochure or product labeling. Further, it is not consistent with the risk information described in the general investigational plan or proposal.

(3) **Unanticipated problems involving risks to participants or others.**

Unanticipated problems refer to untoward events involving any aspect of the research study, are events involving anyone, including participants, research staff, or others not directly involved in the research, are always unanticipated by definition .

-clinical research.

Belmont Report: Document produced by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. This report identifies the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and establishes guidelines which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: (i) the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, (ii) the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects, (iii) appropriate guidelines for the selection of human subjects for participation in such research and (iv) the nature and definition of informed consent in various research settings. This report discusses the three basic ethical principles: Respect for persons, Beneficence, and Justice.

Human Research Protection Program (HRPP). An HRPP is a comprehensive system to ensure the protection of human subjects participating in research. The HRPP consists of a variety of individuals and committees such as: the Medical Center Director, Associate Chief of Staff (ACOS) for Research and Development (R&D), the Administrative Officer (AO) for R&D, compliance officers, etc., the R&D Committee, the IRB, other committees or subcommittees addressing human subjects protection (e.g., Biosafety, Radiation Safety, Radioactive Drug Research, Conflict of Interest), investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer) and research pharmacy staff. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

Institution. In the context of the VHA Handbook, an institution is a VA medical center or integrated VA health care system and its satellite facilities including community-based outpatient clinics.

Legally Authorized Representative. A legally authorized representative is an individual or body authorized under applicable law to provide permission on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. For the purposes of this Handbook, a legally authorized representative includes not only a person appointed as a health care agent under a Durable Power of Attorney for Health Care (DPAHC), a court appointed guardian of the person, but also next-of-kin in the following order of priority unless otherwise specified by federal law: spouse, adult child (18 years of age or older), parent, adult sibling (18 years of age or older), grandparent, or adult grandchild (18 years of age or older). NOTE: the VA follows the federal laws.

Office of Research and Development (ORD). ORD is the office within VA Central Office responsible for the overall policy, planning, coordination, and direction of research activities within VHA.

Office of Research Oversight (ORO). ORO is the primary VHA office for advising the

Under Secretary for Health on all matters regarding compliance and oversight of research in the protection of human subjects, animal welfare, and research safety. ORO also oversees investigations of allegations of research misconduct.

VA-approved Research. VA-approved research is research that has been approved by the VA R&D Committee.

PURPOSE OF INSTITUTIONAL REVIEW BOARD (IRB)

The purpose of the IRB [HSS] is to safeguard the rights and welfare of human subjects involved in research at Edward Hines, Jr. VA Hospital and North Chicago VA Medical Center. Research protocols are reviewed to determine if the rights and welfare of human subjects involved in research are adequately protected, to assure that the benefits to an individual outweigh the potential risks to him or her, to review the processes of recruitment and enrollment into the research protocol, to review the process and documentation of effective informed consent or assent, and to assure that consent/assent is obtained by methods that are adequate and appropriate. Additionally, the IRB must review the Investigator's plan to monitor adverse events and unanticipated problems and review any changes to the research. The Committee reviews the research at timely intervals appropriate to the degree of risk, but at least annually, and taking all other actions necessary for the protection of human subjects involved in research.

The functions of the IRB are guided by the federal regulations, FDA: 21 CFR 50, 56, 312 (drugs) and 812 (devices), DHHS: 45 CFR 46 and VA: 38 CFR 16, AAHRPP accreditation standards and by the ethical principals outlined in the Belmont Report.

PRINCIPAL INVESTIGATOR RESPONSIBILITIES:

If there are any questions regarding whether or not a proposed project is human subjects research, the Investigator should contact the IRB Chair for assistance.

The Principal Investigator is personally responsible for the conduct of the study and for all actions of study personnel under his/her supervision. The safety and welfare of the research subject ultimately rests with the Principal Investigator.

Responsibilities of the Principal Investigator are set forth in the HRPP. The investigator and the research team are required to comply with the policies and procedures in the IRB approval documents and to cooperate with members of the IRB charged with initial and continuing review of the project.

VULNERABLE POPLUATIONS:

Vulnerable populations as listed in the Federal regulations include:

- a. Pregnant women and fetuses;
- b. Prisoners;
- c. Mentally disabled and those with impaired decision-making capacity;

- d. Children; and
- e. Economically and educationally disadvantaged persons.

The federal regulations apply additional protections to these populations. No research involving children, prisoners or pregnant women will be conducted at the Hines and North Chicago facilities.

If a participant enrolled in a research protocol becomes incarcerated:

- The investigator will promptly notify the IRB.
- All interactions and interventions with, obtaining identifiable private information about the now incarcerated participant (prisoner) **must cease**

Protocols that may enroll individuals from “c” and “e” above, must address plans to address issues specific to the population. Part III (Appendix A) lists criteria that must be addressed.

IF the study involves vulnerable populations:

If the study involves vulnerable participants, or those who may become vulnerable or may be vulnerable to coercion or undue influence, the IRB evaluates safeguards and processes in place to protect the rights and welfare of these participants. Examples of these participants include: students, employees, homeless persons, the educationally disadvantaged, financially disadvantaged, or adults who lack the ability to consent, or may lose the ability to consent (psychiatric patients).

In order to evaluate the appropriateness of enrollment or continuing participation, the Investigator must provide a written explanation how these individuals will be protected, in addition to VA regulations 38 CFR 16, and 45 CFR 46

Examples of instances to think about are enrolling veterans with early dementia who may not remember agreeing to participate, or the enrollment of a veteran having an emergent health crisis such as a heart attack, or terminal illness. Another consideration is the enrollment of the educationally or economically challenged, and the possible coercion of these individuals. The Investigator must advise the IRB how research personnel will approach these individuals and evaluate their ability to consent.

The VHA Research Handbook also sets forth requirements for the consideration of including vulnerable populations in research, which the investigator must provide adequate justification:

- **Research involving persons with impaired decision-making capability may only be approved when the following conditions apply:**

(1) Only incompetent persons or persons with impaired decision making capacity are suitable as research subjects. Competent persons are not suitable for the proposed research. The investigator must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as

subjects. Incompetent persons or persons with impaired decision-making capacity must not be subjects in research simply because they are readily available.

(2) The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.

(3) Procedures have been devised to ensure that participant's representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Health care agents (appointed under Durable Power of Attorney for Health Care (DPAHC)) and next-of-kin, or guardians, must be given descriptions of both proposed research studies and the obligations of the person's representatives. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest.

d. The IRB must make a determination in writing of each of the criteria listed in subparagraph 6c. If these criteria are met, the IRB may approve the inclusion of incompetent subjects or subjects with impaired decision-making capacity in research projects on the basis of informed consent from authorized representatives as defined in paragraph 11 of this VHA Handbook.

e. Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary.

f. Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

PROTOCOL SUBMISSION:

All research involving human subjects must first be reviewed and approved by the IRB. The research may not begin until all the appropriate subcommittees have reviewed and approved it. The final approval is determined by the R&D

Retrospective chart reviews are considered research and must obtain the appropriate approvals prior to initiating the project. The IRB does not have the authority to grant retroactive approval.

All research personnel must have current education and credential verification as required by VACO. Annual recertification is required. The education module is subject to change annually. Certificates of completion should be forwarded to the IRB to verify completion.

Review of applications will not go forward until all study personnel have completed the training.

The process begins by completing the project submission forms for review to the R&D, Research Safety Subcommittee and IRB. If applicable, the Radiation Safety Committee must also review and approve a study prior to initiation. Certain projects may be exempt from review by the Research Safety Committee (see Part I for additional information). Completed submission forms are submitted to the Research Office and distributed to the appropriate subcommittee. Applicable forms are Part I, the Request to Conduct; Part II, the Research Safety Subcommittee application; and Part III (Appendix A) for the Research Involving Human Subjects, or Part IV, the Radiation Safety Committee.

An investigator must complete and submit all applicable forms plus a protocol, applicable appendices, data collection sheets, informed consent document, HIPAA Authorization or Alteration request, and recruitment materials to begin the process for approval.

Forms are available on the research website: <http://www.hines.med.va.gov/research/>

The IRB application is Part III, (Appendix A). The form must be filled out completely for the IRB to be able to assess the project. At minimum, the following information should be included:

- 1) A relevant review of the literature (Rationale)
- 2) Proposed hypotheses (Purpose and Objective)
- 3) Subject sample with inclusion and exclusion criteria (*Note: Current Federal and VA regulations require that whenever possible and scientifically desirable, researchers should include women and minorities in their research, especially in population-based studies. If these populations are excluded or inadequately represented, the investigator must provide a compelling rationale for the exception. Attention must be paid to issues of research design and sample size related to the composition of the study population by gender and race/ethnic group*).
- 4) Methods, procedures, and the anticipated risks associated with participation
Participant recruitment and enrollment plans, data analysis plans, including adequate methods for maintaining the confidentiality of subjects. The research plan must make adequate provisions for monitoring the data collected to ensure the safety of subjects (38 CFR 16.111(a)(6)). The plan must include procedures for reporting adverse events and minimizing risks for unanticipated adverse events and problems. Additionally, plans for establishing a Data Safety and Monitoring Board (DSMB) or a Data Monitoring Committee (DMC) as required by DHHS or FDA policy, and a plan for reporting DSMB or DMC findings to the IRB may be required.

If the study involves an investigational drug, or is a new use of an approved drug, or a device, a full protocol (complete DHHS approved protocol if applicable), consent (and DHHS approved sample consent if applicable) official FDA documentation of the IND or IDE number, and an investigator's brochure or equivalent is required to be submitted. Additionally, all FDA requirements are expected to be met.

Complete applications received for full review by the deadline will be placed on the next agenda. Incomplete submissions will be returned to the Investigator and may result in a delay in review of the project.

PI must have a VA appointment (employee or WOC).

Students (fellows residents post-docs) cannot be PI's.

Projects must have either a co-PI or plan in the event that the PI is unable to continue to be responsible for the study.

To facilitate the review process, Investigators may be asked to attend the IRB meeting to provide information or to discuss potential issues. Investigators may also request to present the protocol to the IRB.

Applications received requesting expedited or exempt review will be reviewed by the Chair or authorized designee. If the application does not meet the criteria as stipulated in the applicable federal regulations for expedited or an exemption, the investigator will be notified and the project will be placed on the next available agenda for full board review.

Only the IRB may determine a study qualifies for an exemption. An application for review must be submitted. If the IRB determines a study meets the criteria for an exemption, the R&D must still review and approve the project prior to beginning the project. Annual progress reports are still required to be reviewed by the R&D Committee.

Investigators will receive written notification of approval, disapproval, tabling or conditional approval from the IRB. If the conditions for approval are minor, the investigator submits all required revisions to the IRB Office for review by the Chair, or other designated IRB member. If appropriate, the Chair will grant final approval and IRB staff will place the information on the next agenda and forward all final approval documents to the R&D Coordinator.

If the Investigator can not, or will not comply with the conditions as specified by the IRB, s/he must provide a written explanation. The response will be placed on the agenda for further discussion and determination at the next available convened IRB meeting.

CONFLICT OF INTEREST

Part 1 includes the Hines/North Chicago Conflict of Interest statement. Conflict of interest may occur when the Investigator(s) or his/her family member(s) (spouse or dependant children) have financial *or non-financial* conflict of interests. There are also conflicts when the investigator acts as both study investigator and primary physician, is listed on publications and/or has a conflict because of his/her position within the facility.

Investigators must review the policy and attest that they have no financial or non-financial conflicts of interest. If a Conflict of Interest exists, there are policies and procedures in place to review and manage Investigator conflict of interest.

Contact the ACOS or AO for questions regarding the Conflict of Interest Policy and the process for management.

Once the conflict has been resolved or a management plan put in place, the IRB will review the project, and management plan to determine if the project may be approved.

All research personnel are expected to provide complete and accurate information and comply with applicable requirements.

DHHS (NIH), FDA and VA and sponsors also have Conflict of Interest requirements and guidelines that must be adhered to.

If an IRB member or his/her family member has a conflict of interest, s/he must identify this conflict and absent themselves from the room during the discussion and vote.

All VA investigators must comply with VHA policies and procedures regarding conflict of interest. [VHA Handbook 1200.5 7.a (9)]

INVESTIGATIONAL DRUGS, BIOLOGICS AND DEVICES

Use of Investigational drugs, biologics and devices must be conducted according to applicable FDA regulations (21 CFR 312, 314, 812, 814).

All Investigational drugs and devices are dispensed through the Investigational Drug Pharmacy

Please refer to the facilities policies on Investigational Drugs, Biologics and Devices.

North Chicago: MCM-151-2003-09

Hines: 578-02-119-054 (drugs)

Hines: 578-03-119-057 (devices)

For studies utilizing investigational drugs, a completed Investigational Drug Form, VA Form 10-9012, for each drug used in the study protocol, is required to be submitted. All authorized prescribers should be listed on this form in Section 19. Copies of Approved 10-9012 forms will be sent to the Investigator. It is the Investigator's responsibility to provide the Investigational Drug Pharmacy with copies of the protocol, Investigator's Brochure, 10-1223 and 10-9012. In addition, the investigator is responsible to make sure copies are filed in the participant's medical record.

Additionally, the Investigator must submit verification of the FDA's IND number to the IRB.

For studies involving devices:

For Significant Risk Devices: the IDE number and copy of the FDA's approval to go forward with the study must be submitted. The IRB will not review SR device studies without verification of the IDE number and FDA status.

For NSR device studies: adequate information and justification must be provided for the IRB to evaluate both the risk of the device, and to determine if the study can be carried out at the facility. If the IRB determines the device does not fit the criteria for NSR, written notification will be provided. The study must be resubmitted with appropriate IDE number and FDA letter, revised protocol and other appropriate information.

PRIVACY AND CONFIDENTIALITY OF PARTICIPANTS

The privacy and confidentiality of the research participant must be protected. Privacy and confidentiality are not the same. For the purposes of human subject research, privacy related to the *person*, confidentiality relates to the *data*.

The Investigator will submit their plan to maintain the privacy and confidentiality in the initial submission. This will be re-evaluated at continuing review.

The VA Privacy Act and VA Privacy Handbook 1605.1 provides more complete explanation of the regulations covering veteran's data. Section 13 refers to research uses. <http://www1.va.gov/vhapublications/publications.cfm?pub=2>

USE OF VA RECORDS FOR RESEARCH AND DEVELOPMENT

As described in 1200.5 13

- a. VA personnel are bound by all legal and ethical requirements to protect the rights of human subjects, including the confidentiality of information that can be identified with a person.
- b. Obtaining and using medical, technical, and administrative records from other VA facilities or VA databases (national, regional, or subject specific) for R&D purposes must be in compliance with all VHA regulations and with the Standards for Privacy of Individually-Identifiable Health Information (45 CFR Parts 160 and 164). Obtaining and disclosing individually-identifiable patient records must be in compliance with all applicable and confidential statues and regulations including those discussed in 1200.5 subparagraph 7a (7).
- c. Persons not employed by VA can be given access to medical and other VA records for R&D purposes only within the legal restrictions imposed by such laws as the Privacy Act of 1974 and 38 U.S.C. Requests for such use must be submitted to the CRADO in VA Central Office at least 60 days before access is desired. Requests for information filed pursuant to the Freedom of Information Act ordinarily requires a response within 10 working days. VA guidelines and policy must be followed when making such requests to allow for a timely reply.

This does not apply to those individuals having access for the purpose of monitoring the research. Obtaining and using the records must be in compliance with all VHA regulations and with the Standards for Privacy of Individually-Identifiable Health Information (45 CFR Parts 160 and 164).

Please note that the VA Privacy Act and HIPAA are two separate and distinct sets of regulations and, at times, the VA Privacy policy is more restrictive.

This information is contained in the required, annual VA Privacy Training Module

The IRB must report, or require the Investigator to report:

- Reporting to the Privacy Officer any unauthorized use, loss, or disclosure of individually-identifiable patient information to the Privacy Officer
- Reporting violations of VA information security requirements to the appropriate VHA Information Security Officer.

HIPAA

For information used and/or disclosed that is not related to the treatment, health care operations or billing, either written patient authorization or an approved request for an alteration or waiver of the HIPAA requirements is necessary.

Basic HIPAA information is contained in the annual VA Privacy Training module.

Adequate provisions must be taken to protect the privacy of subjects and to maintain the confidentiality of individually-identifiable data. Such provisions must consider the requirements of Standards for Privacy of Individually-Identifiable Health Information (HIPAA Privacy Rule), 45 CFR Parts 160 and 164, and other laws regarding protection and use of veterans' information, including Privacy Act of 1974, 5 U.S.C. 552a; VA Claims Confidentiality Statute, 38 U.S.C. 5701; Confidentiality of Drug Abuse, Alcoholism and Alcohol Abuse, Infection with Human Immunodeficiency Virus (HIV), and Sickle Cell Anemia Medical Records, 38 USC 7332; and Confidentiality of Healthcare Quality Assurance Review Records, 38 USC 5705

The HIPAA Privacy Rule requires that a written authorization from the veteran, containing elements detailed in the Privacy Rule, be obtained from research subjects, unless the researcher has obtained a waiver of authorization from an IRB.

NOTE: The IRB and researchers must continue to adhere to the mandates of the Common Rule 38 CFR 16 (45 CFR 46) while implementing the requirements of the HIPAA Privacy Rule.

Authorizations

Authorization forms: To ensure that a research program can continue recruiting subjects, researchers must use the official VA approved authorization template in conjunction with the approved informed consent. This form contains language that the VHA Office of

General Counsel has determined is necessary for compliance with several privacy laws to which the VHA is subject. *Please note that sponsors can not add their language to the form because they are not the covered entity.*

A written authorization is signed by the research participant to whom the information or record pertains to. An authorization is required when Hines or North Chicago Investigators:

- need to utilize individually identifiable health information for a purpose other than treatment, payment, and/or health care operations and other authority does not exist;
- disclose information for any purpose where other legal authority does not exist; and
- to conduct marketing.

The VACO approved template for an authorization is located on the website.

**Waivers of Authorization
(Title 45 Code of Federal Regulations (CFR) 164.512(i)(2))**

The second critical element that must be addressed to ensure uninterrupted research within VHA is a procedure for the IRB to grant waivers or alterations to the HIPAA Law.

To use or disclose a patient's identifiable health information for research based on a waiver, a VHA researcher must have documentation of a waiver from the IRB. To obtain the waiver, the researcher must provide adequate justification to the IRB to allow the IRB to make its determination.

The IRB may receive a request for waiver of authorization for new studies that are submitted after April 14, 2003 or for an existing study that does not meet the transition provisions (i.e., is not "grandfathered" under the Privacy Rule). In either case, the board may use either normal review procedures (38 CFR 16.108(b)) or expedited review procedures (38 CFR 16.110) as defined in the Common Rule. In any circumstance, the criteria for granting the waiver remain the same. The IRB must determine that a request for a waiver of authorization satisfies **all** the following criteria:

1. The use or disclosure of the requested information involves no more than a minimal risk to the privacy of individuals based on, at least, the presence of the following elements:
 - a. An adequate plan to protect the identifiers from improper use and disclosure
 - b. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
 - c. Adequate written assurances that the requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the requested information would be permitted by the Privacy Rule;

2. The research could not practicably be conducted without the waiver or alteration; and
 3. The research could not practicably be conducted without access to and use of the requested information.
- If research personnel intend to screen for potential participants through a database search, or IRM, or clinic files, or by referral, you must request a waiver of the HIPAA requirements. A waiver or alternate request must be completed for a partial waiver of the requirements for screening/recruitment purposes. The waiver request form is available on the website.
 - Retrospective chart reviews also require a request for waiver of the HIPAA requirements.
 - At Hines and North Chicago, HIPAA language is in a separate Authorization form and not imbedded in the consent form. Please note that sponsor requested (required) language in an authorization is generally not appropriate, as the VA facility is the covered entity, NOT the sponsor.
 - The IRB reviews the Authorization, but does not stamp the Authorization
 - The Authorization form should reference a *reasonable* expiration time or event.
 - Please be sure to provide adequate information so the IRB can evaluate the request properly, according to the law.
 - The VA Privacy Act must be adhered to, in addition to HIPAA

INFORMED CONSENT:

- Respect for persons is the underlying concept for obtaining informed consent. The informed consent **is an ongoing process** that begins with the initial presentation of the research to the prospective participant by the investigator or his/her appropriate designee. (refer to the Belmont Report)
- The project must be presented to the participant or his/her legally authorized representative, in a language that is understandable to the participant or representative.
- The research participant must give consent without coercion or undue influence.
- Adequate time should be given for the participant to ask questions and give his/her participation careful consideration. It is not unreasonable for the participant to take the unsigned consent document home to review and discuss with family members.
- Informed consent must be obtained prior to entering a subject into a study and/or conducting any procedures required by the protocol.
- The consent process is documented by signing the consent form, unless some elements of informed consent have been waived by the IRB.
- The IRB has the authority to require an IRB staff or Committee member to observe the consent process.
- Investigators and research team should be sensitive and responsive to questions, concerns and complaints of participants.

It is expected that an assessment will be made by the investigator or designee of the participant's capacity to consent to a research protocol.

If surrogate consent is sought, there are specific criteria that must be met and documented. Please refer to the SOPs and the VHA Handbook 1200.5 for specific information.

The Principal Investigator may delegate the duty of obtaining informed consent to other study personnel provided: 1) Those duties fall within the scope of practice for which the individual is licensed or certified, and has been awarded clinical privileges by the institution. 2) The individual is familiar with the purposes, methods, and procedures of the protocol, 3) The individual has been so designated within the project and approval for the individual's responsibilities have been obtained from the IRB.

Delegation of duties to other individuals does not release the Principal Investigator from responsibilities for the safe and proper conduct of the protocol.

REQUEST FOR WAIVER OR ALTERATION OF CONSENT:

If a waiver of consent is sought, the request must be indicated in the initial submission with a completed waiver request.

If an alteration of informed consent is sought (i.e. written documentation, waiver of some of the elements), the request must be completed and submitted with the application with appropriate justification provided based on:

- (1) An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects, if it finds either:
 - (a) That the only record linking the subject and the research would be the consent document and the principal risk to the subject would be potential harm resulting from a breach of confidentiality. Each subject must be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or
 - (b) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.
- (2) In cases in which the documentation requirement is waived, the IRB must document the reason for the waiver and may require the investigator to provide subjects with a written statement regarding the research.

If the study is FDA regulated, there are only 2 instances in the regulations where the IRB may consider a waiver of the informed consent requirements. Please refer to the SOPs for specific information

Please note that a waiver of consent is not the same as waiver or alteration of HIPAA requirements.

INFORMED CONSENT FORMS

The informed consent document must be the VA Form 10-1086, approved by the IRB as evidenced by a stamped approval and expiration date on each page, and signed by the subject or the subject's legally authorized representative, except in cases where the documentation of informed consent is waived by the IRB. Prior approval must be obtained by the IRB to allow the participant's legally authorized representative to give permission to participate in a research study (surrogate consent).

The consent form must include all basic elements of information as set forth in VA and other Federal regulations, and not include exculpatory language, waive any of the patient's legal rights, or release, or appear to release the investigator, sponsor or institution for liability from negligence. Depending on the study, there are additional elements of information that may be required.

If there is payment to the participant, all information concerning payment, including the amount and payment schedule, must be included in the consent form.

Please refer to the consent check-list and the consent template for additional guidance.

- **The form must be dated and signed by a witness who is unrelated to the study. If the participant is not able to sign for him/herself, or can not write their name, two witnesses are required to be present during the entire explanation of the study and sign the form.**
- The original signed consent form must be retained in the Investigator's research file under conditions of confidentiality. A copy is sent to Medical Records for scanning into the electronic medical record and another copy sent to the IRB which will review and file them under conditions of confidentiality. The subject or legally authorized representative must receive a copy of the signed and dated consent form.
- **For studies utilizing photography, digital imaging or voice recordings, the VA form 10-3203 is also required.**

Under certain circumstances, oral informed consent may be used. Refer to the SOPs for specific requirements

RECRUITMENT OF PARTICIPANTS

The protocol submission must include the plan for how participants will be selected and recruited (from where, by whom, referral practice, etc). Investigators should use fair and equitable recruitment practices and be sensitive to the participant's sense of privacy and reduce risks of coercion or undue influence.

If students, residents or employees are anticipated to be enrolled, approval must be given by the IRB and specific language incorporated into the consent form reiterating that participation is voluntary and performance appraisals or recommendations will not be affected.

All final advertisements, written, audio or video, are required to be reviewed and approved by the IRB, and should be submitted at the time of initial and continuing review.

Payments to investigators or other health care professionals for recruitment, identifying or enrolling participants are not allowed.

Refer to the Institutions Recruitment Policy

Recruitment of Non-Veterans as research Participants

Non-veterans may be entered into VA-approved research studies only when there are insufficient veterans available to complete the study in accordance with 38 CFR 17.45 and 38 CFR 17.92.

All regulations pertaining to the participation of veterans as research subjects including requirements for indemnification in case of research-related injury pertain to non-veteran subjects enrolled in VA-approved research.

A letter of request (sample available on website), with justification and copies of the research protocol and IRB approval documents and consent are routed through the research office to the Hospital Director. The Investigator should identify the source of funds to treat the non-veteran in the event of a research related injury. If the Director approves the request, a non-veteran may be enrolled in the project.

PROGRESS NOTES and FLAGGING of MEDICAL RECORD

Pursuant to 1200.5, must be entered into electronic be completed in a timely manner, so the participant is identified as being in a research study.

- (1) At a minimum, the progress note must include:
 - (a) The name of the study,
 - (b) The person obtaining the subject's consent,
 - (c) A statement that the subject or the subject's legally-authorized representative was capable of understanding the consent process,
 - (d) A statement that the study was explained to the subject, and
 - (e) A statement that the subject was given the opportunity to ask questions.
 - (2) An entry must also be placed in the progress note when the human subject is actually entered into the study and when the human subject's participation is terminated. **NOTE:** *Consent and entry notes can be combined when both occur at the same visit.*
- This process may decrease potential for being prescribed a contraindicated medication or enrollment into more than one interventional research study. The entry of research progress notes is still required.

DUAL ENROLLMENT

In general, subjects may not be enrolled in more than one interventional or long-term observational study at a time.

For some studies with long-term follow-up, this may limit a subject's ability to enroll in other research. Thus, investigators may petition the IRB for permission to dual enroll. Both principal investigators must sign a letter of agreement for dual enrollment. These letters may be specific to a patient or a study (blanket dual enrollment).

CHANGES TO THE APPROVED RESEARCH - AMENDMENTS:

An amendment is any change to the project or consent form as originally approved by the IRB. All amendments require approval prior to implementation, unless the change is to eliminate an immediate hazard to participants. Any changes made prior to approval to eliminate an immediate hazard to participants are to be promptly reported to the IRB.

Prior approval is required before changes to the approved protocol procedures, consent forms or, recruitment materials are implemented.

To request an amendment, the Investigator completes the amendment form, including a summary and justification of the change. Any documents supporting the change such as revised consent, protocol, Investigator's brochure, advertisement or other documents must be attached to the request.

If the amendment addresses an issue related to biosafety or radiation safety, the appropriate committee or subcommittee must first approve the change and a copy of the approval should be submitted to the IRB with the amendment form.

ADVERSE EVENT MONITORING and REPORTING

Regulations (38 CFR 16.103(b)5, 21 CFR 312.64(b) and 21 CFR 812.150(a)(1), require prompt reporting of adverse events and unanticipated events involving risks to subjects.

Reporting Requirements:

- All local serious adverse events (SAE) events must be reported to the IRB within 48 hours of the investigator or staff becoming aware of the event.
- Any unexpected death must be reported to the IRB within 24 hours. IRB has the responsibility to report such deaths within 24 hours to ORO pursuant to the requirements set forth in VHA Handbook 1058.1.
- A summary of all local unanticipated related adverse events that are not serious, must be reported to the IRB will be reported at the time of continuing review. Any local AE directly or indirectly related to the study, such as loss of confidentiality or emotional trauma are reportable.
- All local Unanticipated events

- Any emergency actions taken to eliminate immediate hazards to subjects must be reported in writing within 24 hours to the IRB Chair.
- Non-Local adverse events are to be reported immediately if there are recommendations for changes to the protocol, investigator brochure, consent, or halts enrollment for safety considerations. Otherwise non-local adverse event reports may be reported at the time of continuing review.
- Protocol violation and serious protocol deviations.
- All unanticipated problems involving risk to participants or others are to be reported within 24 hours to the IRB.
- Reports of serious protocol deviation that impact on risks to the research subject or integrity of the protocol.
- **DSMB/C (Data Safety Monitoring Board / Committee):** The reports from these committees may be quarterly, semi-annually or annually.

If the non-local SAE was unexpected and related, the Investigator must promptly report this to the IRB to be considered at a convened meeting prior to continuing review.

The Investigator must also report non-local SAE's prior to continuing review if:

- Risks to subjects are increased
- There is a modification to the protocol required to reduce risks
- A change in the consent form is required.

SERIOUS PROTOCOL DEVIATIONS

A serious protocol deviation may be non-compliance (by being omitted or committed) of a procedure outlined by the study protocol, standard operating procedures of the medical center, HRPP or IRB. This type of protocol deviation may expose participants to increased risk or compromise the integrity of the study.

The investigator must notify the IRB in writing using the Adverse Event reporting form within 48 hours of such deviations.

TISSUE BANKING:

VA Directive 2000-043 prohibits veteran biological samples, defined as any material derived from human subjects, such as blood, urine, tissues, organs, hair, nail clippings, or any other cells or fluids, whether collected for research purposes or as residual specimens, be forwarded to a sponsor, or non-VA sponsored or non-VA Approved tissue bank for future research purposes unless there is specific approval from the CRADO.

For VA approved, or VA sponsored tissue bank, the consent form must clearly state:

- (1) if the specimen will be used for future research, and allow the participant the choice of how the specimen will be used (i.e. any research, research by specific PI, genetic analysis, research related to a specific area)
- (2) If the research results of reuse of the specimen will be conveyed to the participant
- (3) If the participant will be re-contacted after the original study is completed

- (4) If the participant requests, the specimen and all links to the clinical data will be destroyed

If an investigator wishes to establish a tissue bank at Hines or North Chicago, the request must be submitted to the R&D, IRB and ACOS, and include at least the following information:

1. Investigator:
2. Address (location) of tissue bank
3. Person responsible for maintaining bank
4. Are samples from one specific study or more?
5. Title of study(ies) and :
6. Is this bank associated with an approved Protocol?
7. Study start date:
8. Study end date:
9. For what purpose(s) have the samples been agreed to? (specific to one study, open ended, genetic?) Attach approved consent form.
10. What information is on the samples (i.e. Study ID, SSN, initials etc)
11. Are the samples linked to the subject's identity? If yes, describe and what precautions are in place to protect confidentiality.
12. How are the samples secured? (i.e. locked room, locked freezer etc)
13. Who has access to samples?
14. What will happen to the samples if the PI leaves the facility, or has an unexpected, extended leave of absence?
15. Are the samples infectious?
16. Will samples be analyzed off VA facility? Describe procedure, personnel, plan for return of remaining specimen, etc. (*Note, there should be a MOU in place specifying analysis/use as defined in protocol*)
17. Do you plan on sharing samples with other investigators? If yes, how do you determine appropriateness of sharing, IRB approval etc?

CONTINUING REVIEW

All studies are reviewed at least annually relative to the degree of risk. Some projects will be reviewed more frequently because of the degree of risk to subjects or other reasons as determined by the IRB.

- A letter and Continuing Review Form are sent to the Investigator approximately 45 days prior to the renewal date of the project.
- It is the Principal Investigator's responsibility to ensure timely continuing review.
- It is expected that the continuing review for will be completed in it's entirety and returned to the IRB by the requested date. If the completed forms have not been returned by the designated date, approval of the project may expire and all research activity must cease.
- Pay close attention to completion of the form. Common errors include: incomplete or missing: Adverse events, Unanticipated Problems involving Risks to participants and others, Participant Benefits, interim findings, a current risk-benefit ratio assessment

based on study results, An assurance that all serious or unexpected adverse events had been reported as required

- Continued non-compliance to continuing review requests (late or continued lapses) may result in an internal audit.
- **All expirations are reported to the ACOS and Chief of Staff.**

Upon completion of a project, a request for closure must be submitted. The continuing review packet must be completed with the appropriate information and an updated progress report submitted.

STUDY CLOSURES/TERMINATIONS

Reports of study closures are submitted to the IRB using the Continuing Review Form. A progress report is required when closing a study.

If the study is being terminated, an explanation is also required (i.e study not feasible, sponsor closed site).

Once a study is closed, no additional identifiable data may be accessed.

Investigators are required to keep study records for a minimum of 5 years, unless the sponsor has separate requirements.

INVESTIGATOR AUDITS:

Outside Monitors/Audits

The ACOS/Research or AO/Research must be notified of the scheduled visits from the pharmaceutical or device sponsor, or CRO as soon as possible. The sponsor or CRO monitor must sign in at that Research Office as a visitor.

Any potential or serious findings conveyed to the study staff (investigator, coordinator), must be reported to the ACOS and/or AO. All findings of serious non-compliance must also be reported to the IRB. If there were no serious findings, this information will also be communicated to the ACOS or AO.

Investigators must send copies of external review/audit reports from external sources (i.e. CSP audits, FDA, sponsor) to the IRB.

Internal Audits

Authorized representatives from the IRB will conduct routine audits of Principal Investigator's research files to assure compliance to local and federal regulations.

An exit interview will be conducted with the study coordinator and principal investigator. This interview will provide a verbal summary of audit findings. A written summary report will follow.

The convened IRB will be notified of the results of the audit at the next scheduled meeting.

Investigator audits will include but are not limited to: 1) Inclusion and exclusion criteria are met; 2) All subjects are consented fully prior to entering the study; 3) The informed consent process is observed; 4) Investigator records are properly maintained. 5) **Reporting of serious adverse events and unanticipated problems.**

At NORTH CHICAGO:

In addition to possible IRB audits, the PIRF Committee will review and audit studies conducted at North Chicago. These audits will be placed on the agenda for IRB review and, if applicable, follow-up action.

PUBLICATION OF STUDY RESULTS (overseen by Research and Development Committee)

- 1) The VA must be given appropriate recognition in publications, presentations and press releases.
- 2) Where no direct VA research funding was provided by the VA, but the research involved the use of other VA resources, e.g. facilities, patients, investigator salary, an appropriate form of acknowledgement must be included.
"This work was conducted at, and supported by Hines Veteran's Administration Hospital, Hines, IL"
- 3) Authors of research publications shall acknowledge their VA employment in a format based on this example: "title – XXXX Service, Department of Veterans Affairs, Edward Hines, Jr., Hospital, Hines, IL 60141" (or North Chicago VA Medical Center, North Chicago, IL)
 - If the author holds an academic appointment, the academic title and name of the institution should be given as well.
 - The VA shall be listed first when the VA pays the major salary support (5/8th or greater)
- 4) Failure to acknowledge VA support as stipulated is likely to result in the discontinuation of current VA research funding, research space or the privilege to conduct research at this hospital.
- 5) The VA requires that research records and raw data be retained by the investigator for at least five years after publication or completion of the project
- 6) Please send a copy of the publication to the Research Office. This information is forwarded to VACO and is presented at the Research and Development Committee meeting

Study Check-list

Forms and links to information can be found on the following website:

<http://www.research.hines.med.va.gov/hss/title.htm>

	All study personnel current with mandatory education – Overview of Good Clinical Practice and Human Subjects Protection.
	PRIOR to initiating the research project, the Investigator is responsible for obtaining HSS review and approval. This includes: preparing the research protocol and submitting the necessary documentation for HSS review; the full protocol, investigator’s brochure, risk/benefit analysis, recruitment plan and any recruitment materials, data collection tools, surveys and/or questionnaires.
	All research committee approvals received: IRB (HSS), Safety, R&D
	Clinical Trial Agreement fully signed, if applicable (contact CARES)
	Reference: VA Research Handbook 1200.5 (available by link on website)
	Reference: Hines/North Chicago Investigator Handbook (available on website)
	All study drug or devices delivered to and dispensed through Investigational Pharmacy
	VA Form 10-9012 Investigational Drug(s) (completed with each prescriber identified on form)
	Current approved, stamped consent form in file (if applicable)
	Current approved, stamped information letter in file (if applicable)
	Documentation of approval for waiver of informed consent in file (if applicable)
	HIPAA authorization obtained
	Approval for Waiver HIPAA authorization obtained and filed (if applicable)
	Obtain Signed Consent and HIPAA authorization prior to ANY research procedures begun [Note, only an approved, Human Studies stamped consent is to be used. A stamped consent has a start date and an expiration date on each page. Do not obtain consent on an outdated consent. Contact the Human Studies Office if there are any questions.]
	Witness to subject signing consent document is not to be a member of the research team NOTE: if person is unable to write his/her own name, or signs with an “X”, 2 witnesses for the entire consent discussion is required
	Copies of signed consent form to: Participant, Pharmacy (if applicable), Medical Records, IRB Office. Keep original in Investigator files
	If pictures, video or audio – separate VA Consent form
	Copies of 10-9012 form (if applicable) filed in medical record

Study Check-list – Page 2

	<p>An Enrollment Progress Note entered in CPRS, except for database studies, using a progress note titled "Research" Progress Note (<i>In order to enter, author must obtain authorization and access to research flag menu system</i>). Note has specific requirements per VHA handbook 1200.5:</p> <p>1) At a minimum, the progress note must include:</p> <p>(a) The name of the study,</p> <p>(b) The person obtaining the subject’s consent,</p> <p>(c) A statement that the subject or the subject’s legally-authorized representative was capable of understanding the consent process,</p> <p>(d) A statement that the study was explained to the subject, and</p> <p>(e) A statement that the subject was given the opportunity to ask questions.</p> <p>(2) An entry must also be placed in the progress note when the human subject is actually entered into the study and when the human subject’s participation is terminated. NOTE: <i>Consent and entry notes can be combined when both occur at the same visit.</i></p>
	<p>A Research Flag is entered for any subject enrolled in a study that has more than 1 visit [Also n/a for studies involving only the use of a questionnaire or the use of previously collected biological specimens] Contact Human Studies Office for additional information about when flagging is required.</p>
	<p>Participant can only participate in 1 study at a time. Contact IRB Office for additional information</p>
	<p>For database studies, enrollment relates to the number of individual subject records reviewed and must be reported at the time of continuing review.</p>
	<p>Adverse events are monitored and All Adverse Events and Serious Study Deviations/Violations are reported to the IRB.</p> <p>Any serious AE must be reported within 48 hours of PI identification. Contact IRB Office if AE occurs with a device trial, as AE reporting requirements are different.</p>
	<p>Any changes in the approved research has prior approval from the IRB Use Amendment form and provide any supporting documentation Changes to reduce risk to participants may be done immediately</p>
	<p>Has new information, significant changes and increased risks been reported to participants and affirmation of continuing in the study obtained?</p>
	<p>If a sponsored study, was a regulatory binder provided?</p>
	<p>If no: Collect and keep in organized fashion:</p> <ul style="list-style-type: none"> • Initial Approval letters from IRB & R&D • 10-1223 forms (VA approval form) • Stamped consent forms • HIPAA Authorization • Any HIPAA Waiver approvals • Correspondence with Sponsor and/or IRB • Copies of amendment requests and response from IRB • Copies of adverse event or deviation reports and response from IRB • Continuing review submissions and approvals

	<ul style="list-style-type: none"> • Any subsequent approved stamped revised consent forms (always use most current) • Signed Pharmacy cost agreement • Signed 10-1092 Form (if applicable) • Original of signed consent forms • Research Records of individuals who do not meet screening criteria, who drop out or are withdrawn. DO NOT GET RID OF DATA
	Privacy and Confidentiality continuously monitored and protected
	Questions and concerns of participants continuously addressed

Web-Links

- Research home page: <http://www.hines.med.va.gov/research/>
- **AAHRPP standards:** <http://www.aahrpp.org>
- **Belmont Report:** Ethical Principles and Guidelines for the Protection of Human Subjects of Research <http://ohsr.od.nih.gov/guidelines/belmont.html>
- **Conflict Of Interest:**
 - NIH: **Guidance for Preventing Conflict of Interest January 4, 2005:**
http://www.nihtraining.com/ohsr/site/new/COI-CR_1-4-2005FIN.pdf**OHRP:**
<http://www.hhs.gov/ohrp/humansubjects/finreltn/fguid.pdf>
 - **FDA:** <http://www.fda.gov/oc/guidance/financialdis.html>

Federal Regulations

- [45CFR46 The Common Rule \(HHS - Protection of Human Subjects\)](#)
- [38CFR16 \(VA - Protection of Human Subjects\)](#)
- [21CFR11 \(FDA - Electronic Records and Signatures\)](#)
- [21CFR50 \(FDA - Protection of Human Subjects\)](#)
- [21CFR56 \(FDA - Institutional Review Boards\)](#)
- [21CFR312 \(FDA - Investigational New Drug Application\)](#)
- [21CFR812 \(FDA - Investigational Device Exemptions\)](#)
- FDA: <http://www.fda.gov>
- FDA Regulations Relating to Good Clinical Practice and Clinical Trials:
<http://www.fda.gov/oc/gcp/regulations.html>
- FDA: Guidance for Institutional Review Boards and Clinical Investigators:
<http://www.fda.gov/oc/ohrt/irbs/default.htm>
- HIPAA Guidance:
<http://www.va.gov/resdev/fr/hipaa.cfm>
- OHRP: <http://www.hhs.gov/ohrp/>
- OHRP: Policy Guidance: <http://www.hhs.gov/ohrp/policy/index.html>
- OHRP: decision charts:
<http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm#c8>
- ORO (VA's Office of Research Oversight): <http://www1.va.gov/oro/>
 - What to report to ORO
- VA Publications for Handbooks, Forms, Directives:
<http://www1.va.gov/vhapublications>
- VA Research and Development Home page: <http://www1.va.gov/resdev/>
- **VHA Privacy Handbook 1605.1:**
- **VHA Handbook Research Misconduct 1058.2**
http://www1.va.gov/vhapublications/ViewPublication.asp?pub_ID=1259

Human Subject Regulations Decision Charts

<http://www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm>

September 24, 2004

The Office for Human Research Protections (OHRP) provides the following graphic aids as a guide for institutional review boards (IRBs), investigators, and others who decide if an activity is research involving human subjects that must be reviewed by an IRB under the requirements of the U.S. Department of Health and Human Services (HHS) regulations at 45 CFR part 46. OHRP welcomes comment on these decision charts. The charts address decisions on the following:

- whether an activity **is research** that must be reviewed by an IRB
- whether the review may be performed by **expedited procedures**, and
- whether **informed consent** or its documentation may be waived.

Considerations

The charts are intended to assist IRBs, institutions, and investigators in their decision-making process and should not be used as substitutes for consulting the regulations. OHRP cautions that the full text of applicable regulatory provisions should be considered in making final decisions.

These charts are necessarily generalizations and may not be specific enough for particular situations. Other guidance documents are available related to specific topics, at [OHRP Policy Guidance by Topic](#). OHRP invites inquiries for additional information.

The charts do not address requirements that may be imposed by other organizations, such as the Food and Drug Administration, National Institutes of Health, other sponsors, or state or local governments.

Chart 1: Is an Activity Research Involving Human Subjects?

Chart 2: Is the Human Subjects Research Eligible for Exemption?

Chart 3: Does Exemption 45 CFR 46.101(b)(1) (for Educational Settings) Apply?

Chart 4: Does exemption 45 CFR 46.101(b)(2) or (b)(3) (for Tests, Surveys, Interviews, Public Behavior Observation) Apply?

Chart 5: Does Exemption 45 CFR 46.101(b)(4) (for Existing Data, Documents, Records and Specimens) Apply?

Chart 6: Does Exemption 45 CFR 46.101(b)(5) (for Public Benefit or Service Programs) Apply?

Chart 7: Does Exemption 45 CFR 46.101(b)(6) (for Food Taste and Acceptance Studies) Apply?

Chart 8: May the IRB Review Be Done by Expedited Procedures?

Chart 9: May the IRB Continuing Review Be Done by Expedited Procedures?

Chart 10: May Informed Consent Be Waived or Consent Elements Be Altered under 45 CFR 46.116(d)?

Chart 11: May Documentation of Informed Consent Be Waived Under 45 CFR 46.117(c)?