Department of Veterans Affairs

Memorandum

Date: SEP 23 2004

From: Acting Chief Research and Development Officer (12)

Subj: Institutional Review Board (IRB) Arrangements: Serving as the IRB of Another Facility or Institution

To: Associate Chief of Staff for Research and Development, VA Medical Centers (151)
Thru: Medical Center Director (00)
Thru: Chief of Staff (11)

1. The purpose of this memorandum is to clarify VHA policy on appropriate IRB arrangements and to request that each VA facility conducting research involving human subjects review its IRB arrangements for compliance with current policy. Paragraph 4 describes actions that must be taken if your facility is not in compliance.

2. VHA Handbook 1200.5 "Requirements for the Protection of Human Subjects in Research," sets forth VHA policy on this issue. VHA policy requires that every VHA facility that conducts research involving human subjects have an established or designated IRB of record. The VHA facility may secure the services of an Office for Human Research Protections (OHRP) registered IRB(s) associated with another VA facility or a VA regional IRB. It may also secure the services of an IRB(s) that is established by its affiliated university with a medical or dental school. Under exceptional circumstances a VA facility may request a waiver from the Chief Research and Development Officer to utilize the services of an IRB within another Federal agency that is signatory to the Federal Policy for the Protection of Human Subjects (the Common Rule). All IRB arrangements must be formalized by a written agreement such as a memorandum of understanding (MOU) that outlines each institution's responsibility.

3. A VHA IRB may only serve as the IRB of record for another VA facility, or for a VA nonprofit research and education foundation. The VA IRB may not review research that is conducted at non-VA facilities by non-VA investigators.

4. It is the responsibility of the VHA IRB(s) of record to review all VHA human subject research prior to its initiation either through full or expedited review, unless the research has been exempted from IRB review in compliance with Handbook 1200.5. This responsibility cannot be fulfilled through the use of Cooperative agreements described in 38 CFR 116.114 or joint review arrangements.

4. If you find that your facility is not in compliance contact the Office of Research Oversight for assistance in developing appropriate arrangements and, if needed, in formalizing your

current arrangements through a written agreement such as an MOU. Specifically, areas of non-compliance that must be addressed include:

a) Your IRB's serving as the IRB of record for a non-VA institution,

b) Your facility's utilizing an IRB as your IRB of record that is not allowed by VHA policy, or

c) Your IRB arrangements have not been formalized by a written agreement such as an MOU. *Note: If they have not contact the Office of Research Oversight.*

5. If you have any questions concerning this issue please contact K. Lynn Cates, M.D. (phone: (202) 254-0282, e-mail: lynn.cates@hq.med.va.gov) or Brenda Cuccherini, Ph.D. (phone: (202) 254-0277, e-mail: Brenda.cuccherini@hq.med.va.gov) within the Office of Research and Development.

Stephan D. Fihn, M.D.,MPH.

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U. S. Department of Health and Human Services (DHHS)
Office for Human Research Protections (OHRP)

FEDERALWIDE ASSURANCE OF PROTECTION FOR HUMAN SUBJECTS

A. TERMS OF THE FEDERALWIDE ASSURANCE FOR INSTITUTIONS WITHIN THE UNITED STATES

1. Human Subject Research Must be Guided by Ethical Principles

All of the Institution's human subject activities and all activities of the Institutional Review Boards (IRBs) designated under the Assurance, regardless of funding source, will be guided by the ethical principles in: (a) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, or (b) other appropriate ethical standards recognized by Federal Departments and Agencies that have adopted the Federal Policy for the Protection of Human Subjects.

2. Applicability

These terms apply whenever the Institution becomes engaged in federally-supported* (i.e., conducted or supported) human subject research, which is not otherwise exempt from the Federal Policy for the Protection of Human Subjects. The Institution becomes so engaged whenever (a) the Institution's employees or agents intervene or interact with human subjects for purposes of federally-supported research; (b) the Institution's employees or agents obtain individually identifiable private information about human subjects for purposes of federally-supported research; or (c) the Institution receives a direct federal award to conduct human subject research, even where all activities involving human subjects are carried out by a subcontractor or collaborator.

[*Federally-supported is defined throughout the FWA and the Terms of Assurance as the U.S. Government providing any funding or other support (including, but not limited to, providing supplies, products, drugs, and identifiable private information collected for research purposes) and/or the conduct of the research involves U.S. Government employees.]

3. Compliance with the Federal Policy for the Protection of Human Subjects

Institutions conducting federally-supported human subject research and the IRB(s) designated under the Institution's Assurance will comply with the Federal Policy for the Protection of Human Subjects, known as the Common Rule. All federally-supported human subject research will also comply with any additional human subject regulations and policies of the supporting Department or Agency. All human subject research conducted or supported by the Department of Health and Human Services (DHHS) will comply with all Subparts of DHHS regulations at Title 45 Code of

Federal Regulations Part 46 (45 CFR 46 and its Subparts A, B, C, and D).

The reference in the Code of Federal Regulations is shown below for each Agency which has adopted the Common Rule:

7CFR 1c	Department of Agriculture
10 CFR 745	Department of Energy
14 CFR 123	National Aeronautics and Space Administration
15 CFR 27	Department of Commerce
16 CFR 1028	Consumer Product Safety Commission
22 CFR 225	Agency for International Development
24 CFR 60	Department of Housing and Urban Development
28 CFR 46	Department of Justice
32 CFR 219	Department of Defense
34 CFR 97	Department of Education
38 CFR 16	Department of Veterans Affairs
40 CFR 26	Environmental Protection Agency
45 CFR 46	Department of Health & Human Services
45 CFR 690	National Science Foundation
49 CFR 11	Department of Energy
By Executive Order	Central Intelligence Agency
By Statue	Social Security Administration

4. Written Procedures

a) The Institution should establish, and should provide a copy to OHRP upon request, written procedures for:

1) ensuring prompt reporting to the IRB, appropriate institutional officials, the relevant Department or Agency Head, any applicable regulatory body, and OHRP of any: (i) unanticipated problems involving risks to subjects or others, (ii) serious or continuing noncompliance with the Federal Regulations or IRB requirements, and (iii) suspension or termination of IRB approval.

2) Verifying, by a qualified person or persons other than the investigator or research team, whether proposed human subject research activities qualify for exemption from the requirements of the Common Rule;

b) The designated IRB(s) has established, and will provide a copy to OHRP upon request, written procedures for:

1) Conducting IRB initial and continuing review (not less than once per year), approving research, and reporting IRB findings to the investigator and the Institution;

2) Determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred

since the previous IRB review;

3) Ensuring that changes in approved research protocols are reported promptly and are not initiated without IRB review and approval, except when necessary to eliminate apparent immediate hazards to the subject.

5. Responsibilities and Scope of IRB(s)

Except for research exempted or waived in accordance with Sections 101(b) or 101(i) of the Common Rule, all human subject research will be reviewed, prospectively approved, and subject to continuing oversight and review at least annually by the designated IRB(s). The IRB(s) will have authority to approve, require modifications in, or disapprove the covered human subject research.

6. Informed Consent Requirements

Except for research exempted or waived in accordance with Sections 101(b) or 101(i) of the Common Rule, informed consent will be:

a) sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by Section 116 of the Common Rule;

b) appropriately documented, in accordance with, and to the extent required by Section 117 of the Common Rule.

7. Requirement for Assurances for Collaborating Institutions/Investigators

The Institution is responsible for ensuring that all institutions and investigators engaged in its U.S. federally-supported human subject research operate under an appropriate OHRP or other federally-approved Assurance for the protection of human subjects. In some cases, one institution may operate under an Assurance issued to another institution with the approval of the supporting Department or Agency and the institution holding the Assurance.

8. Written Agreements with Non-Affiliated Investigators

The engagement in human research activities of each independent investigators who is not an employee or agent of the Institution may be covered under the FWA only in accordance with a formal, written agreement of commitment to relevant human subject protection policies and IRB oversight. OHRP's sample Unaffiliated Investigator Agreement may be used or adapted for this purpose, or the Institution may develop its own commitment agreement. Institutions must maintain commitment agreements on file and provide copies to OHRP upon request.

9. Institutional Support for the IRB(s)

The Institution will provide the IRB(s) that it operates with resources and professional and support staff sufficient to carry out their responsibilities under the Assurance effectively.

10. Compliance with the Terms of Assurance

The Institution accepts and will follow items 1-9 above and is responsible for ensuring that (a) the IRB(s) designated under the Assurance agree to comply with these terms; and (b) the IRB(s)

possesses appropriate knowledge of the local research context for all research covered under the Assurance (please refer to the OHRP guidance on IRB Knowledge of Local Research Context on the OHRP website).

Any designation under this Assurance of another Institution's IRB or an independent IRB must be documented by a written agreement between the Institution and the IRB organization outlining their relationship and include a commitment that the designated IRB will adhere to the requirements of this Assurance. OHRP's sample IRB Authorization Agreement may be used for such purpose or the two organizations may develop their own agreement. This agreement should be kept on file at both organizations and made available to OHRP upon request.

11. Assurance Training

The OHRP Assurance Training Modules describe the major responsibilities of the Institutional Signatory Official, the Human Protection Administrator, and the IRB Chair(s) that must be fulfilled under the Assurance. OHRP strongly recommends that the Institutional Signatory Official, the Human Protections Administrator (e.g., Human Subjects Administrator or Human Subjects Contact Person), and the IRB Chair(s) personally complete the relevant OHRP Assurance Training Modules, or comparable training that includes the content of these modules, prior to submitting the Assurance.

12. Educational Training

OHRP strongly recommends that the Institution and the designated IRB(s) establish educational training and oversight mechanisms (appropriate to the nature and volume of its research) to ensure that research investigators, IRB members and staff, and other appropriate personnel maintain continuing knowledge of, and comply with, relevant ethical principles, relevant Federal Regulations, OHRP guidance, other applicable guidance, state and local laws, and institutional policies for the protection of human subjects. Furthermore, OHRP recommends that a) IRB members and staff complete relevant educational training before reviewing human subject research; and b) research investigators complete appropriate institutional educational training before conducting human subject research.

13. Renewal of Assurance

All information provided under this Assurance must be updated at least every 36 months (3 years), even if no changes have occurred, in order to maintain an active Assurance. Failure to update this information may result in restriction, suspension, or termination of the Institution's FWA for the protection of human subjects.

DOMESTIC INSTITUTIONS ACCEPTING THESE TERMS MAY PROCEED WITH THE ASSURANCE FILING PROCESS

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B. TERMS OF THE FEDERALWIDE ASSURANCE (FWA) FOR INTERNATIONAL (NON-U.S.) INSTITUTIONS

January 26, 1999

TO: Division of Human Subject Protections, OPRR

FROM: Director, Division of Human Subject Protections, OPRR

SUBJECT: Engagement of Institutions in Research

Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(a) require that each institution "engaged" in human subjects research provide OPRR with a satisfactory Assurance to comply with the regulations, unless the research is exempt under 45 CFR 46.101(b).

An institution becomes "engaged" in human subjects research when its employees or agents[1] (i) intervene or interact with living individuals for research purposes; or (ii) obtain individually identifiable private information for research purposes [45 CFR 46.102(d),(f)].

An institution is automatically considered to be "engaged" in human subjects research whenever it receives a direct HHS award to support such research. In such cases, the awardee institution bears ultimate responsibility for protecting human subjects under the award.

Examples

(A) Institutions would be considered "engaged" in human subjects research (and would need an Assurance) if their nonexempt involvement includes the following:

(1) Institutions whose employees or agents intervene with living individuals by performing invasive or noninvasive procedures for research purposes (e.g., drawing blood; collecting other biological samples; dispensing drugs; administering other treatments; employing medical technologies; utilizing physical sensors; utilizing other measurement procedures).

[1] Agents include all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility.

(2) Institutions whose employees or agents intervene with living individuals by manipulating the environment for research purposes (e.g., controlling environmental light, sound, or temperature; presenting sensory stimuli; orchestrating environmental events or social interactions; making voice, digital, or image recordings).

(3) Institutions whose employees or agents interact with living individuals for research purposes

(e.g., engaging in protocol-dictated communication or interpersonal contact; conducting research interviews; obtaining informed consent). (See Example (B)(3) below for certain informational activities that do not constitute "engagement" in research and do not require an Assurance.)

(4) Institutions whose employees or agents release individually identifiable private information, or permit investigators to obtain individually identifiable private information, without subjects' explicit written permission (e.g., releasing patient names to investigators for solicitation as research subjects; permitting investigators to record private information from medical records in individually identifiable form). (However, see Example (B)(5) regarding release of such information with subjects' prior, written permission, and Example (B)(6) regarding release of such information to State Health Departments.)

(5) Institutions whose employees or agents obtain, receive, or possess private information that is individually identifiable (either directly or indirectly through coding systems) for research purposes (e.g., obtaining private information from medical records in an individually identifiable form). (However, see Examples (B)(7) and B(8) for certain activities involving the release of information and/or specimens to investigators in non-identifiable form.)

(6) Institutions whose employees or agents obtain, receive, or possess private information that is individually identifiable (either directly or indirectly through coding systems) for the purpose of maintaining "statistical centers" for multi-site collaborative research. Where institutional activities involve no interaction or intervention with subjects, and the principal risk associated with institutional activities is limited to the potential harm resulting from breach of confidentiality, the Institutional Review Board (IRB) need not review each collaborative protocol. However, the IRB should determine and document that the statistical center has sufficient mechanisms in place to ensure that (i) the privacy of subjects and the confidentiality of data are adequately maintained, given the sensitivity of the data involved; (ii) each collaborating institution holds an applicable OPRR-approved Assurance; (iii) each protocol is reviewed and approved by the IRB at the collaborating institution prior to the enrollment of subjects; and (iv) informed consent is obtained from each subject in compliance with HHS regulations.

(7) Institutions whose employees or agents maintain "operations centers" or "coordinating centers" for multi-site collaborative research. Where institutional activities involve no interaction or intervention with subjects, the IRB need not review each collaborative protocol. However, the IRB should determine and document that the operations or coordinating center has sufficient mechanisms in place to ensure that (i) management, data analysis, and Data Safety and Monitoring (DSM) systems are adequate, given the nature of the research involved; (ii) sample protocols and informed consent documents are developed and distributed to each collaborating institution; (iii) each collaborating institution holds an applicable OPRR-approved Assurance; (iv) each protocol is reviewed and approved by the IRB at the collaborating institution prior to the enrollment of subjects; (v) any substantive modification by the collaborating institution of sample consent information related to risks or alternative procedures is appropriately justified; and (vi) informed consent is obtained from each subject in compliance with HHS regulations.

(8) Institutions receiving a direct HHS award to conduct human subjects research, even where all activities involving human subjects are carried out by a subcontractor or collaborator (e.g., a small business receives a HHS award to design a medical device at its own facility and contract with a medical clinic to test the device with human subjects; a foundation receives a HHS award on behalf of an affiliated institution that will actually conduct the human subjects research).

(B) Institutions would not be considered "engaged" in human subjects research (and would not need an Assurance) if their involvement is limited to the following:

(1) Institutions whose employees or agents act as consultants on research but at no time obtain, receive, or possess identifiable private information (e.g., a consultant analyzes data that cannot be linked to individual subjects, either directly or indirectly through coding systems, by any member of the research team).

(a) Should a consultant access or utilize individually identifiable private information while visiting the research team's institution, the consultant's activities become subject to the oversight of the research team's Institutional Review Board (IRB). However, the consultant's institution is not considered to be "engaged" in the research and would not need an Assurance.

(b) Should a consultant obtain "coded" data for analysis at the consultant's institution, the consultant's institution is considered "engaged" in human subjects research, and would need an Assurance, unless a written agreement unequivocally prohibits release of identifying codes to the consultant.

(2) Institutions whose employees or agents (i) perform commercial services for the investigators (or perform other genuinely non-collaborative services meriting neither professional recognition nor publication privileges), and (ii) adhere to commonly recognized professional standards for maintaining privacy and confidentiality (e.g., an appropriately qualified laboratory performs analyses of blood samples for investigators solely on a commercial basis).

(3) Institutions whose employees or agents (i) inform prospective subjects about the availability of research; (ii) provide prospective subjects with written information about research (which may include a copy of the relevant informed consent document and other IRB-approved materials) but do not obtain subjects' consent or act as authoritative representatives of the investigators; (iii) provide prospective subjects with information about contacting investigators for information or enrollment; or (iv) obtain and appropriately document prospective subjects' permission for investigators to contact them (e.g., a clinician provides patients with literature about a research study, including a copy of the informed consent document, and tells them how to contact the investigator if they want to enroll; a clinician provides investigators with contact information about potential subjects after receiving

explicit permission from each potential subject).

(4) Institutions (e.g., schools, nursing homes, businesses) that permit use of their facilities for intervention or interaction with subjects by research investigators (e.g., a school permits investigators to test students whose parents have provided written permission for their participation; a business permits investigators to solicit research volunteers at the worksite).

(5) Institutions whose employees or agents release identifiable private information to investigators with the prior written permission of the subject (e.g., with written permission of the subject, a clinician releases the subject's medical record to investigators).

(6) Institutions whose employees or agents release identifiable private information or specimens to a State or Local Health Department or its agent for legitimate public health purposes within the recognized authority of that Department. However, utilization of such information or specimens by Department investigators for research purposes would constitute engagement in research, and would require an Assurance from the Department.

(7) Institutions whose employees or agents release information and/or specimens to investigators in non-identifiable (i.e., non-linkable) form, where such information/specimens have been obtained by the institution for purposes other than the investigators' research (e.g., nursing home employees provide investigators with a data set containing medical record information, but the data set contains no direct or indirect identifiers through which the identity of individual subjects could be ascertained, either by the investigators or by nursing home personnel; a hospital pathology department releases excess tissue specimens and relevant medical record information to investigators, but these materials include no direct or indirect identifiers through which the identity of individual subjects could be ascertained, either by investigators or by hospital personnel, including the pathology department; consistent with applicable law or recognized authority, local hospitals or health departments permit State or Local Health Department investigators to access information for research purposes, but the investigators record no direct or indirect identifiers through which the identity of individual subjects could be ascertained, either by the investigators or by local hospital or health department personnel.)

(8) Institutions whose employees or agents receive information or specimens for research from established repositories operating in accordance with (i) an applicable OPRR-approved Assurance; (ii) OPRR guidance (see http://ohrp.osophs.dhhs.gov/humansubjects/guidance/reposit.htm); and (iii) written agreements unequivocally prohibiting of release of identifying information to recipient investigators.

(9) Institutions (or private practitioners) whose clinical staff provide protocol-related care and/or follow-up to subjects enrolled at distant sites by clinical trial investigators in OPRR-recognized Cooperative Protocol Research Programs (CPRPs). In such cases, (i) the CPRP clinical trial investigator (consistent with a registered investigator as defined in Section 14.1

of the NCI Investigator's Handbook) retains responsibility for oversight of protocol related activities; (ii) clinical staff may not accrue subjects or obtain informed consent for research participation; (iii) clinical staff may only provide data to the investigator in accord with the terms of informed consent; and (iv) the informed consent document should state that such data are to be provided by clinical staff as directed by the investigator.

Assurance Coordinators within the Division of Human Subject Protections (DHSP) retain the authority to determine whether institutions are "engaged" in human subjects research consistent with the above guidelines. The DHSP Director and the Assurance Branch Chief should be consulted should Coordinators require assistance in applying these guidelines to specific situations.

J. Thomas Puglisi, Ph.D.

Attachment
cc: Dr. Gary Ellis
Dr. Melody Lin
Ms. Michele Russell-Einhorn

Policy and Assurances | OHRP Home Page

If you have questions about human subject research, click ***ohrp@osophs.dhhs.gov***
If you have questions/suggestions about this web page, click ***Webmaster***

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