October 27, 2005

Instructions for Requesting Permission to Conduct International Research as required by VHA Directive 2005-050 "Requirements for Conducting VA-Approved International Research Involving Human Subjects, Human Biological Specimens, or Human Data"

Permission to conduct international research involving human subjects or human biological specimens must be obtained prior to initiating the research as required by VHA Directive 2005-050 "Requirements for Conducting VA-Approved International Research Involving Human Subjects, Human Biological Specimens, or Human Data." The directive defines international research as: 1) any VA-approved human subjects research conducted at international sites (not within the United States, its territories, or Commonwealths) or 2) VA-approved research using either human biological specimens or human data originating from an international site(s). Multi-site trials where a VA facility is only one of the participating sites, is not covered under this definition. However, it would be covered under this definition if:

(1) VA is the sponsor,

(2) VA functions as the coordinating center,

(3) VA subcontracts to a foreign site, or

(4) The principal investigator for the total project is a VA investigator.

The request for permission to conduct international research must include a memorandum from the facility Director indicating his/her approval for conducting the study. *Note: If the research proposal is to be submitted for funding through ORD the memorandum may be submitted with other "just-in-time" documentation.*

For Cooperative Studies Program (CSP) research. For CSP multi-site projects involving international research as defined in Directive 2005-050, review of all required information and approvals will occur during the CSP review process. If the CSP project is approved, the Director, Clinical Science Research &Development (CSR&D) will request the required permission from the CRADO or designee. *Note: For CSP studies the memorandum from the facility director of the performance sites does NOT have to be submitted.*

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For research submitted for VA Merit Review funding. All of the required information specified below under "Required Information" must be included in the proposal submission unless indicated otherwise. Note: If the proposal being submitted is a renewal of a current project and you have submitted information on the project to the Office of Research Oversight (ORO) within the last 6 months, please submit the final communication form ORO with your proposal.

Research projects NOT being submitted for VA Merit Review funding. For those research projects that will not be submitted for ORD funding, four (4) copies of the request for permission and all required information must be sent through the ACOS/R&D to:

Chief Research and Development Officer (12)
Department of Veterans Affairs
810 Vermont Ave., NW
Washington, DC 20420

For additional information or questions concerning Clinical Science R&D or Biomedical Laboratory R&D proposals, please contact Dr. Terri Gleason at (202) 254-0498 (Theresa.gleason@va.gov). For all other proposals, please contact Dr. Brenda Cuccherini at (202) 254-0277 (Brenda.cuccherini@va.gov).

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Required Information for International Research Involving Living Human Subjects

Please note: If the research is being submitted to any of our merit review programs for funding the following items may be submitted during the just-in-time process: 6, 11, 12, and 13. If the proposal is being submitted for funding through CSP, contact Grant Huang, Ph.D. at (202) 254-0252, regarding when items 6, 11, 12, and 13 should be submitted.

1. A copy of the proposal that includes the following:

A. Rationale for conducting the research at an international site(s), including why it cannot be conducted at a VA facility or within the United States. If the research involves a partnership between the VA and an international site, the rationale for this partnership and its benefits to the VA and the U.S. veteran population must be discussed.

B. Required information on Human Studies. The following information must be submitted:

(1) Risk to Subjects

Human Subjects Involvement and Characteristics. Describe the proposed involvement of human subjects in the Research Design and Methods section. For purposes of this Directive including U.S. and international sites. Describe the characteristics of the subject population, including their anticipated number, age range, and health status. Identify the criteria for inclusion or exclusion of any subpopulation. Explain the rationale for the involvement of special classes of subjects, such as pregnant women, institutionalized individuals, or others who may be considered vulnerable populations.

Sources of Materials if Other than the Research Subject Used in the Protocol. Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data, including information on research material that is obtained about deceased individuals or that is de-identified. Indicate whether the material or data will be obtained specifically for research purposes, or whether use will be made of existing specimens, records, or data. If the materials are obtained for research purposes, explain how they will be collected, which ethics review body(ies) reviewed the collection and use of the materials, and by what standards. If the material will be or has been collected for non-research purposes, describe the circumstance or reason for the collection.

Potential Risks. Describe the potential risks to subjects (physical, psychological, social, legal, or other) and assess their likelihood and seriousness to the subjects. Differentiate therapeutic risk from research risk as follows:

Therapeutic risk is the risk or potential risks associated with an intervention that is required for medical care, but occurs as part of the research. An example is an endoscopy that was required for medical follow-up of a specific illness.

Research risk is associated with an intervention that is done only for research purposes regardless if it is an experimental intervention or a commonly used intervention, for example, an extra endoscopy. Where appropriate, describe alternative treatments and procedures, including the risks and benefits of the alternative treatments and procedures to participants in the proposed research.

(2) Adequacy of Protection from Risks

Recruitment and Informed Consent. Describe plans for the recruitment of subjects and the process for obtaining informed consent. Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent.

Protection Against Risk. Describe the planned procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness. Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. For interventional studies, describe the plan for subject data and safety monitoring.

(3) Potential Benefit of the Proposed Research to the Subject and Others. Discuss the potential benefits of the research to the subjects and others, including why the risks are reasonable in relation to the anticipated benefits.

(4) Importance of the Knowledge to Be Gained**.** Discuss the importance of the knowledge to be gained as a result of the proposed research, including why the risks to subjects are reasonable in relation to the importance of the knowledge that reasonably may be expected to result.

C. Qualifications of the investigators to conduct this research.

2. For each domestic and international site, any financial arrangements including funding source, any type of payment to subjects, and financial arrangements involving the research site and local investigators at the research site.

3. Discussion of each site in the foreign country(ies) including the foreign investigator(s), the location(s), and a description of the facility(ies) where the research will be conducted.

4. Ethical principles that govern research in each location to ensures the protection of the rights and welfare of human subjects in research.

5. Any research assurances that are in place at the international site(s), including an International (Non-U.S.) Assurance issued by Office of Human Research Protections (OHRP).

6. Copy(ies) of all approvals required by the foreign country(ies) and institution(s). Include information on the IRB or ethics board or other review board that has been established to ensure the ethical conduct of the research and any stipulations of the board(s) that were required to be addressed prior to the initiation of the research in that country. *Note: If the research proposal is to be submitted for funding through ORD, this may be submitted with other "just-in-time" documentation.*

7. Information on how the U.S. VA IRB of record and the foreign IRB decisions will be communicated and reconciled if necessary.

8. Information on VA's liability in relationship to the conduct of the research including a discussion on care for research-related injuries and any compensation available for subjects or others at the site because of research-related injuries.

9. A plan for conducting oversight of the research to ensure ethical conduct, compliance with all applicable regulations, and validity of the data. The plan should include oversight by any foreign country or entity.

10. Frequency and content of monitoring reports, including information on who will review the reports and make any determinations regarding safety of subjects and compliance with applicable regulations.

11. Copy of the U.S. VA IRB minutes that show members in attendance and the action taken on the protocol for the meeting at which the protocol was approved and a copy of the correspondence with the investigator regarding the approval. *Note: If the research proposal is to be submitted for funding through ORD this may be submitted with other "just-in-time" documentation.*

12. Copy of the U.S. VA Research and Development (R&D) Committee minutes that show members in attendance and the action taken on the protocol for the meeting at which the protocol was approved and a copy of the correspondence with the investigator regarding the approval. *Note: If the research proposal is to be submitted for funding through ORD this may be submitted with other "just-in-time" documentation.*

13. Copy of all IRB approved informed consent templates written in English with an indication if it was or will be presented to the subject in a language other then English. *Note: If the research proposal is to be submitted for funding through ORD, this may be submitted with other "just-in-time" documentation.*

14. For any studies that may include children, documentation that a waiver has been granted for their inclusion as required by VHA Handbook 1200.5. *Note: If a waiver has not been requested, the request for waiver may be submitted concurrently with the request for permission to conduct international research.*

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Requirements for International Research that Involves ONLY Human Biological Specimens or Data Derived from Persons

Please note: If the research is being submitted to ORD's merit review program for funding, the following items may be submitted during the just-in-time process: 6 and 7. If the proposal is being submitted for funding through CSP, contact Grant Huang, Ph.D. at (202) 254-0252, regarding when items 6 and 7 should be submitted.

1. A copy of the proposal that includes the rationale for conducting the research at an international site(s) including why the data or samples cannot be collected at a VA facility or within the United States. If the research involves a partnership between the VA and an international site, the rationale for this partnership and its benefits to the VA and the U.S. veteran population must be discussed.

2. For each domestic and international site, any financial arrangements including funding source, any type of payment to subjects, and financial arrangements involving the research site and local investigators at the research site.

3. Discussion of each site in the foreign country (ies) including the foreign investigators and the location(s) of the investigators or research site. If the specimens or data are derived from research projects, give a description of the facility(ies) at which the research was conducted.

4. Ethical principles that govern research in each location in place to ensure the protection of the rights and welfare of human subjects in research.

5. Any research assurances that are in place at the international site(s), including an International (Non-U.S.) Assurance issued by Office for Human Research Protections (OHRP).

6. Copy of the U.S. VA IRB minutes that show members in attendance and the action taken on the protocol for the meeting at which the protocol was approved and a copy of the correspondence with the investigator regarding the approval. *Note: If the research proposal is to be submitted for funding through ORD this may be submitted with other "just-in-time" documentation.*

7. Copy of the U.S. VA Research and Development (R&D) Committee minutes that show members in attendance and the action taken on the protocol for the meeting at which the protocol was approved and a copy of the correspondence with the investigator regarding the approval. *Note: If the research proposal is to be submitted for funding through ORD this may be submitted with other "just-in-time" documentation.*

8. Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data.

a. For the purposes of this Directive, also include information on research material that is obtained about deceased individuals or that is de-identified.

b. Indicate whether the material or data will be obtained specifically for research purposes, or whether use will be made of existing specimens, records, or data.

9. If the materials are obtained for research purposes, explain how they will be or has been collected, which ethics review body(ies) reviewed the collection and use of the materials, and by what standards.

a. Include a copy of the approval by the research ethics committee

b. Include a copy of the consent under which it was collected

10. If the material will be or has been collected for non-research purposes describe the circumstance or reason for the collection. Indicate what applicable ethics review committees have approved the use of the specimens for research purposes?

a. Include a copy of the approval by the research ethics committee

b. Include a copy of the consent in English under which it was collected. If the original consent was not in English, please give information on the language that was used.

11. For any studies that may include children, documentation that a waiver has been granted for their inclusion. Note: If a waiver has not been requested, the request for waiver may be submitted concurrently with the request for permission to conduct international research.