

VAMHCS HUMAN RESEARCH PROTECTION
STANDARD OPERATING PROCEDURE

SOP# HRP 01.15/PM #047

Version	3.0	Origin	Version 2.0
Author	Jessica Mendoza		
Changes	• Triennial review and updates	New Version #	PM #047
Approved	Thomas Hornyak, ACOS/R&D Date		
File Name	\\CRADA(HRP0115-PM047)2016v3.0_022316		

COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA)

OBJECTIVES:

- To establish procedures to be followed by the VA Maryland Health Care System (VAMHCS) and the Baltimore Research and Education Foundation (BREF) when negotiating and executing Cooperative Research and Development Agreements (CRADAs).
- To ensure that the VAMHCS has a written agreement with the sponsor of each research project that delineates the responsibilities and obligations that the VAMHCS will fulfill for the Sponsor and that the Sponsor will fulfill for the VAMHCS.
- To ensure that the VAMHCS and the Sponsor agree to specified actions that protect research participants, including: medical care for research participants with a research-related injury, reporting of findings that could affect the safety of participants or their willingness to continue participation, influence the conduct of the study, or alter the IRB's approval to continue the study, the publication or disclosure of results, and reporting of study results to participants.
- To protect intellectual property rights due to the VA through work done or data obtained through research projects conducted in VA sites or by VA investigators.
- To establish a procedure for disclosure of potential institutional conflict of interest.

POLICY:

The VAMHCS negotiates and executes CRADAs for all sponsored research in which: 1) there is an issue of pre-assignment of intellectual property rights, and 2) the sponsor owns the investigational new drug or device, 3) designs the protocol; **and/or** 4) funds the project.

CRADAs may be required for other reasons at the discretion of the Specialty Team Advising Research (STAR) component of VA Office of General Counsel (STAR).

BACKGROUND AND SCOPE:

The VAMHCS conducts research funded by various sponsors. As of 12/26/2007, the VA requires that a CRADA be used for all sponsored research: 1) that requires pre-assignment of intellectual property rights, and 2) the sponsor owns the investigational new drug or device, 3) designs the protocol; **and/or** 4) funds the project.

The Investigator, the Associate Chief of Staff for Research (ACOS), Administrative Officer for Research (AO), BREF, and STAR, as needed, negotiate with the Sponsor the terms of the CRADA based on the VA approved model available on the TTP **intranet** website at http://vaww.research.va.gov/programs/tech_transfer/model_agreements/default.cfm. After negotiations are complete, the CRADA must be submitted to STAR for legal review and approval

VAMHCS HUMAN RESEARCH PROTECTION
STANDARD OPERATING PROCEDURE

with changes to the model, if any, shown in tracked changes mode.

If STAR determines that terms negotiated in the CRADA differ significantly from those in the model, STAR will recommend CRADA language consistent with Federal law and policies. Insignificant wording changes the sponsor requests for clarity (wordsmithing) or to meet the sponsor's own needs are permissible and STAR will likely not recommend changes to that language.

For purposes of formally tracking CRADAs and creating an educational resource, the VAMHCS / BREF are required to register CRADAs through the TTP Internet website at http://www.research.va.gov/programs/tech_transfer/crada/resources.cfm when they begin negotiations and again after executing a signed CRADA.

If the CRADA involves a foreign corporation or government, the BREF should notify TTP as soon as possible in order for TTP to initiate clearing the CRADA through the U.S. Trade Representative. Send an email to Noahline Stuart (noahline.stuart@va.gov) providing 1) the title of the study; 2) the name of the company; and 3) the country where the company is doing business. A CRADA with a U.S. subsidiary of a foreign company does not need clearance through the U.S. Trade Representative.

DEFINITIONS

Baltimore Research and Education Foundation (BREF) – the VAMHCS-affiliated non-profit research and education corporation (NPC) created and operated under the laws of the State of Maryland. The NPC's role and obligations are set forth in the CRADA pursuant to its statutory authority under 38 U.S.C. §§ 7361-68 and VHA Handbook 1200.17.

Cooperative Research and Development Agreements (CRADA) - Established under the Federal Technology Transfer Act of 1986, Public Law (Pub. L.) 99-502, CRADAs were created to serve as a flexible form of agreement between Federal and non-Federal organizations for establishing the terms of collaborative research efforts. CRADAs were specifically designed to respect both government and non-government organizations' rights to intellectual property in order to foster translation of research results into commercial products. CRADAs, which are legally binding on all parties, allow the Department of Veterans Affairs (VA) to establish ownership and licensing rights to inventions in advance. A template is available at the VA Technology Transfer Program intranet site.

Technology Transfer Program (TTP) - The mission of the VA Technology Transfer Program (TTP) is to serve the American public by translating the results of worthy discoveries made by employees of VA into practice. This requires a program that educates inventors concerning their rights and obligations, rigorously evaluates all inventions, obtains patents, and assists in the commercialization of new products. It also requires consistent policies that govern the necessary relationships between investigator (i.e., inventor), academic partners, local VA medical centers, industry, and the Department of Commerce. It requires close collaboration between ORD and the VA Office of General Counsel (OGC).

VAMHCS HUMAN RESEARCH PROTECTION
STANDARD OPERATING PROCEDURE

RESPONSIBILITIES

AO/R&D and/or Executive Director (ED) of BREF

- When notified by an investigator of intentions to participate in a research to be funded by a non-VA sponsor, decides whether CRADA requirements apply;
- Negotiates with Sponsor the terms of the CRADA.

Principal Investigator

- Is responsible for notifying the ACOS, Deputy ACOS, AO/R&D, and/or ED of BREF when s/he has decided to participate in a research study to be funded by a non-VA Sponsor.

Specialty Team Advising Research (STAR) of the VA Office of General Counsel

- May assist in negotiation of CRADA with sponsor.
- Performs legal review and approval with changes to the model (if any) shown in tracked changes mode.

PROCEDURES:

1. At the time that an investigator decides to initiate or participate in research study to be sponsored by a non-VA sponsor, s/he informs the AO/ACOS and/or and the Executive Director of BREF prior to entering into negotiations with the Sponsor.
2. No CRADA involving an investigator who is a dually appointed personnel (DAP) holding both a VAMHCS a University of Maryland position may be entered into unless either 1) the applicable Cooperative Technology Administration Agreement provides that VA will take the lead on patenting, marketing, and licensing any invention made under the CRADA; or 2) VAMHCS and the University agree on a case-by-case basis to VA taking the lead on managing CRADA subject inventions. BREF personnel will confirm any necessary university approvals prior to entering into a CRADA involving a DAP.
3. The investigator completes a Conflict of Interest survey (see #17 below).
4. To initiate development of a CRADA for a project, BREF personnel provide the Sponsor with a copy of the most recent version of the appropriate model CRADA downloaded from the TTP **Intranet** website at http://vaww.research.va.gov/programs/techtransfer/model_agreements/default.cfm. With the involvement of STAR, as needed, they negotiate terms to arrive at a proposed CRADA acceptable to the Sponsor and ready for submission to STAR. Involving STAR in negotiations where the Sponsor's legal counsel is involved is highly recommended. The CRADA template ensures that:
 - 4.1. there is an agreement that the organization will follow the protocol and applicable law;
 - 4.2. there is an agreement on who would provide care and who is responsible to pay for the care;
 - 4.3. there is an agreement that obligates the sponsor to promptly report to the VAMHCS any findings that could:
 - 4.3.1. Affect the safety of participants,
 - 4.3.2. Affect the willingness of participants to continue participation,
 - 4.3.3. Influence the conduct of the study,
 - 4.3.4. Alter the IRB's approval to continue the study.
 - 4.4. there is an agreement that obligates the sponsor to follow the DVA's policies and procedures regarding the publication of findings from sponsored research
 - 4.5. there is an agreement on how results from a research study will be communicated to participants when those results directly affected their safety or medical care.

VAMHCS HUMAN RESEARCH PROTECTION
STANDARD OPERATING PROCEDURE

5. Prior to initiating negotiations, BREF should check the CRADA registry to determine if a similar study has already been negotiated with another VAMC. If the same study is listed on the registry, the BREF should contact the other facility to ensure consistency in the agreements and expedite negotiations.
6. Upon initiating negotiations for CRADAs, BREF should complete the CRADA registry Excel spreadsheet at http://www.research.va.gov/programs/tech_transfer/crada/resources.cfm to the extent possible and send it to TTP (Noahline.stuart@va.gov) via e-mail. The information provided will be integrated into the master Excel registry and posted on the TTP Internet website.
7. Upon completion of negotiations with the Sponsor, BREF forwards an electronic copy of the proposed CRADA showing tracked changes and the Conflict of Interest survey to STAR for review and approval.
8. In addition, BREF forwards to the STAR a draft memo (the "justification memo") from the STAR to the Director of the VAMC or local equivalent that:
 - 8.1. states that there are no changes that are believed to be "significant," that the STAR concurs in the proposed CRADA and recommends that the Director sign it, or
 - 8.2. identifies changes that are believed to be "significant" and contains justification for the approval of the significant changes identified, including an explanation of the factors deemed to be important in the particular case, or
 - 8.3. identifies changes that are believed to be significant and contains a statement that the proposed CRADA represents a best effort, although it contains significant variation for which there is not available justification. See Guidance below.
 - 8.4. STAR then forwards the proposed CRADA found by the STAR not to contain significant changes to the MCD for signature, together with a final of the justification memo, concurring in the CRADA
9. In any case in which the proper documents are provided, the STAR will complete its review in 10 working days or less. Where the documentation requires additional work, or is particularly complicated, the STAR will complete its review and move the CRADA on in no more than 20 working days.
10. After the CRADA is approved, the BREF will prepare a sufficient number of originals (one for each party) for signature. Each original must be signed by:
 - an authorized representative of the Sponsor;
 - an authorized representative of the BREF when applicable;
 - the Principal Investigator; and lastly
 - the Medical Center Director (see 12.1-12.3 below).
 - 12.1 After the CRADA has been signed by the Sponsor, the PI, and the BREF, it is forwarded to STAR.
 - 12.2 The STAR returns the signed CRADA with a cover letter stating that the CRADA is ready for MCD signature.
 - 12.3 The CRADA and cover letter are routed through the Chief of Staff office to the MCD for signature and return to the BREF.
11. The BREF will distribute the executed CRADA and copies thereof as follows:
 - Copies to Director TTP, ACOS and STAR
 - One original to each signatory of the CRADA.
12. As soon as CRADAs are executed, BREF must add the remaining information to the Excel spreadsheet and re-send it to TTP. If negotiations terminate without an executed CRADA, the BREF should notify the TTP office and it will be noted on the CRADA Registry.
13. The total amount of CRADA funds (broken down per CRADA) received by the VAMHCS/BREF during the previous twelve months from October 1 through the following September 30 shall be reported to TTP every October.
14. Conflict of Interest:
 - 14.1 The Conflict of Interest (COI) survey is available at the TTP website:
http://www.research.va.gov/programs/tech_transfer/model_agreements/conflict.doc.
 - 14.2 VA requirements regarding employee conduct standards in general and the avoidance

VAMHCS HUMAN RESEARCH PROTECTION
STANDARD OPERATING PROCEDURE

of conflict of interest in particular are contained in 5 C.F.R. §735. Conflict of Interest laws are criminal statutes and are found in title 18 of the United States Code. In order to comply with these statutes and regulations and the Federal Technology Transfer Act, any potential conflict identified in the conflict of interest survey or arising during the negotiation and conduct of a CRADA or in the commercialization of inventions resulting from a CRADA should be immediately discussed with STAR.

14.3 A copy of the COI survey must be provided to STAR with the CRADA submission. The original must be maintained in the CRADA file at the VAMHCS.

REFERENCE:

VHA Directive 2007-044

Use of a Cooperative Research and Development Agreement
(CRADA) (December 26, 2007)