

**Annotations to Model CT CRADAs
Phase I-II and Phase III-IV
June 2007 Version
(and Word "Compare and Merge Instructions")**

These annotations apply equally to Phase I-II and Phase III-IV CRADAs except as described below in Article 6.

Cover sheet:

Negotiator must ensure that the front page is completed including indicating which phase Clinical Trial is involved.

Article 1:

Familiarity with the FTTA is very helpful. Little case law exists, but reading the statute is useful.

Article 2. Definitions:

REVIEW CHANGES TO DEFINITIONS CAREFULLY. THERE IS A HIGH POSSIBILITY THAT THEY MAY BE SIGNIFICANT CHANGES.

Check to be sure any change in a definition makes sense throughout the document.

Background Invention:

The goal is to have the Test Article be a background invention. VA has no interest in having the Test Article become a CRADA Subject Invention. See also Article 5.1.

CRADA Data:

The two preceding provisions (definitions of "Confidential Information" and "CRADA Data") are among the more important provisions with regard to protection of veterans' rights under HIPAA and the Privacy Act. They are negotiable in the sense that the language may be changed, but the same protections would have to remain present. It is important to ensure that the Collaborator's use of data is limited to what is allowed in the HIPAA authorization and the informed consent, and to limit Collaborator ownership of CRADA Data to the case report forms (see also Article 7.1 and 7.2). Be cautious where Collaborator takes an imprecise approach to the definition of "data"; e.g., "data is know-how and the like." What exactly is "know-how" and what exactly is "and the like?"

CRADA Subject Invention:

This is a definition taken from the FTTA statute – “made’ when used with any invention means the conception or first actual reduction to practice of such invention” 15 U.S.C. § 3703(10). We are not happy with it, but because it is a statutory definition, we can’t redefine the term. What we’ve done, under this model, however, is to ensure that the Test Article can never become a CRADA Subject Invention. See definition of “background invention” and Article 5.1.

Individually Identifiable Information:

Be cautious with any changes to this definition in light of the Privacy Act and HIPAA. Any Collaborator wishing to partner with VA must understand our statutory duty to protect veterans’ rights to privacy, and the importance VA ascribes to protecting the security of confidential data like this. Be aware that a Collaborator cannot violate the Privacy Act since it is a Government obligation, nor can Collaborator violate HIPAA. This is also the definition that VHA uses, trains to, and is familiar with.

Protocol:

Make sure the informed consent and HIPAA Authorization provide for release of Individually Identifiable Information or Private Health Information to the NPC for purposes of subject payments and clinical service charges.

Test Article:

See definition of Background Invention and Article 5.1.

Article 3.2. Use and Disposition of Collaborator Materials:

REVIEW CHANGES TO THIS PROVISION CAREFULLY. THERE IS A HIGH POSSIBILITY THAT THEY MAY BE SIGNIFICANT CHANGES.

Article 3.4. Human Subjects Protection:

The content of the above clause has been reviewed and approved by AAHRPP. Avoid making changes if at all possible. It would be acceptable for the Collaborator to require a copy of the written communication, or a chance to review a draft, but the IRB will be the final decision maker on the content.

Article 3.7. Monitoring:

Each facility has detailed local procedures on monitor access consistent with VA’s overarching policy. There is no need to include more details in the CRADA. Collaborator should be made aware of local procedures and may be provided with a copy of the facility policy.

Article 3.8. Registration of Protocol:

VA cannot make this mandatory.

Article 4.1. VA and Collaborator Contributions:

Time limit is negotiable.

Article 5. Inventions and Intellectual Property:

Time limits in this Article are negotiable, but must be consistent.

Article 5.1. Background Inventions:

See also definition of Background Invention. Together, these two provisions ensure Collaborator's Test Article does not become a CRADA Subject Invention and should provide comfort to the Collaborator. Collaborator can be made aware that VA is among a small cadre of government agencies that have taken specific actions in the agreement to protect the Collaborator's invention.

Collaborator does not want the Test Article to become a CRADA Subject Invention because that opens the door to the possibility of VA claiming the Test Article as a joint invention. This possibility could occur because the definition of "made" in the FTTA states: "made" when used in conjunction with any invention means the conception or first actual reduction to practice of such invention." Theoretically, since VA employees carry out the research, it is quite probable that the VA employee will first actually reduce to practice the Test Article, especially in an early phase clinical trial. Under the FTTA, this would make the Test Article a CRADA Subject invention "made" by both the Collaborator and the VA employee, giving VA ownership rights. Understandably, having spent a lot of money on the Test Article, Collaborator wants to avoid even the remotest possibility of VA getting ownership rights.

By removing the Test Article from the definition of CRADA Subject Invention and calling it a background invention, the goal is to place ownership of the pre-existing Test Article under patent law. Under patent law, the Test Article is "made" when conceived and first reduced to practice, which includes constructive reduction to practice by filing a patent application. Since the Test Article usually has been patented or the patent application has been filed before the execution of the CRADA, this will prevent the Test Article from coming under the CRADA and the FTTA definition of "made."

Article 5.2. Ownership of CRADA Subject Inventions:

REVIEW CHANGES TO THIS PROVISION CAREFULLY. THERE IS A HIGH POSSIBILITY THAT THEY MAY BE SIGNIFICANT CHANGES.

Article 6. Licensing (Applies to Phase I, II, III and IV CT CRADAs):
REVIEW CHANGES TO THIS ARTICLE CAREFULLY. THERE IS A HIGH POSSIBILITY THAT THEY MAY BE SIGNIFICANT CHANGES.

Time limits in this Article are negotiable, but must be consistent.

Article 6.1. Collaborator’s Nonexclusive License to CRADA Subject Inventions (Phase III and IV):

This article offering Collaborator a nonexclusive, royalty-free, worldwide license applies only to Phase III and IV CT CRADAs.

The upfront, nonexclusive, royalty free license (NERF) is not offered in the Phase I and II CT CRADA. There is a higher likelihood that new intellectual property (IP) could result out of a Phase I or II clinical trial. However, Collaborator still retains the first option to a nonexclusive or exclusive license. In a Phase I or II trial, such a license for the Collaborator would be subject to negotiation of reasonable license fees.

Article 6.1 in a Phase I or II CT CRADA discusses License Options.

Article 6.1. License Options (Phase I and II):

This Article is numbered 6.2 and called Option for Exclusive License in the Phase III and IV CT CRADA.

The option to choose an exclusive license is a statutory requirement of the FTTA – see 15 U.S.C. § 3710a(b)(1).

Article 6.2. Option for Exclusive License (Phase III and IV):

This Article is numbered 6.1 and called License Options in a Phase I and II CT CRADA.

The option to choose an exclusive license is a statutory requirement of the FTTA – see 15 U.S.C. § 3710a(b)(1).

Article 6.2. Government Rights in CRADA Subject Inventions (Phase I and II) and

Article 6.3. Government Rights in CRADA Subject Inventions (Phase III and IV):

This Article 6.2 (6.3 in a Phase III or IV CT CRADA) is a statutory necessity – Collaborator must agree to a “Government Use License” in a CRADA Subject Invention. The only possible exception is for a sole-Collaborator invention in rare

situations, but a sole-Collaborator CRADA Subject Invention is impossible in a Clinical Trial where VA is performing the work. However, a Government Use License is of little commercial value to VA because the Collaborator holds the underlying patents in the Test Article. In order to make use of the Government Use License, VA would first have to purchase a license to use the Test Article from the Collaborator.

Also, statutorily, VA maintains “march-in rights” which are described at 15 U.S.C. §3710a(b)(1)(B) and (C), but these are for use only in extraordinary situations and have never been exercised by the Government in the history of the FTTA. These rights are not mentioned in the Model because the Model is under the statute and these provisions automatically apply. You may, of course, discuss them with the Collaborator, but needn’t necessarily do so. Again, to exercise march-in rights based on a clinical trial using the Collaborator’s Test Article, VA would have to obtain a license from the Collaborator to use the underlying patents.

Article 7. Ownership and Rights of Access to Data and Publication:

Data ownership and access rights are among the most difficult areas in CRADA negotiations. VA must ensure that veterans’ rights under the Privacy Act and HIPAA are fully protected. Language limiting use of CRADA data to what the subject has allowed in the HIPAA Authorization and informed consent is very important. Be wary of attempts to change the definition of what constitutes “data” and who owns what data. Find out why the Collaborator wants such changes. Emphasize that VA gives the Collaborator ownership of the case report forms and full access to data, Individually Identifiable Information, original notes, documents and records produced by VA, subject to the HIPAA Authorization and informed consent.

The facility bears the responsibility to ensure Collaborator is aware of facility policies on data security.

See also: Definitions of Confidential Information and CRADA Data.

The time limits in this Article are negotiable, but keep them consistent.

REVIEW CHANGES TO ARTICLE 7.1 AND 7.2 CAREFULLY. THERE IS A HIGH POSSIBILITY THAT THEY MAY BE SIGNIFICANT CHANGES.

Article 7.2. CRADA Data and CRADA Materials:

To repeat, this provision may not be changed to give ownership of CRADA Data and materials to Collaborator. In Article 7.1, VA essentially retains ownership. You can explain that VA cannot give away ownership of data it creates. It exists in patient records and VA owns those. The Collaborator has full use, though.

Collaborators may be concerned that VA may use the data accumulated for this CRADA for its own research purposes or may give it to a competitor. The data resides in patient records, so yes, it is possible that VA may access the data in the same way it would for any study involving analyzing patient records. However, you can assure the Collaborator that VA will NOT give the data to a competitor or seek to commercialize it in any way. In the first place, it is scattered among patients' records. The only place it exists in a usable form is in the case report forms and the Collaborator owns those. VA retains copies and will treat them as Confidential Information under the CRADA.

Article 7.3. Presentations and Publications:

Do not give up the right to publish. This is important to NPCs' retention of tax-exempt status as medical research organizations. Also, do not agree to let the Collaborator "approve" presentations or manuscripts. The Collaborator may review and comment on them (primarily for the purpose of ensuring protection of proprietary information), but the Collaborator should not be in a position to prevent publication by withholding approval.

Article 7.3.2. Single Site Data:

The time limits in Article 7 are fully negotiable, but keep time limits consistent throughout the document. You may want to consult the PI about publication review periods so as not to unduly delay publication.

Article 8.2. Disclosure of Confidential Information:

VA is not required by statute to disclose information to an oversight committee, but Congress's control over our budget makes cooperation preferred over forcing them to take extra steps to compel our cooperation.

If the Principal Investigator is a DAP, the VA or NPC negotiator of a CRADA must determine if a CTAA exists with the university affiliate, and if so, whether VA is required to disclose information to the university. If disclosure is required, this Article must be tailored to include such disclosure.

Article 8.3. Duration of Confidentiality Obligation:

The section cited in 8.3.1 is in the FOIA statute. See 8.3.2 for protection of Confidential Information from FOIA requests.

This language takes full advantage of the statutory language in 15 U.S.C. § 3710a(c)(7)(A) and (B) regarding protection of Confidential Information. Although all issues haven't been tested in court, we believe it provides the Collaborator with excellent long-term protection from disclosure under FOIA and the courts agree. See, e.g., *DeLorme*, 917 F.Supp. 867 (1996).

Article 10.3. Unilateral Termination:

The sixty-day time limit is negotiable.

Article 11.1. Settlement:

VA may not agree to binding arbitration absent development of a VA policy on its use in consultation with Department of Justice, 5 U.S.C. § 575.

Article 12. Indemnification and Liability

VA will not agree to language requiring VA to report a study-subject injury to Collaborator within a specified time period after the injury. This is because VA does not always know when an injury has occurred – sometimes the veteran is seen by a private physician or the injury is not immediately apparent. A reasonable time limit from the date VA receives notification of the injury may be fair.

Article 12.1. Collaborator’s Indemnification and Liability:

REVIEW CHANGES TO THIS PROVISION CAREFULLY. THERE IS A HIGH POSSIBILITY THAT THEY MAY BE SIGNIFICANT CHANGES.

Article 12.2. VA’s Indemnity and Liability:

The fact that FTCA governs VA’s response to liability claims is non-negotiable.

REVIEW CHANGES TO THIS PROVISION CAREFULLY. THERE IS A HIGH POSSIBILITY THAT THEY MAY BE SIGNIFICANT CHANGES.

Article 12.3. Costs of Subject Injury:

Collaborator’s responsibility is to reimburse VA for costs incurred for an injury. Do not accept language that Collaborator will pay the study subject for costs incurred since VA has a statutory duty to care for any veteran eligible for VA care. 38 C.F.R. § 17.85 further establishes that VA will provide - or provide for - care for veterans and non-veterans injured as a result of participating in VA-approved research. The subject is not out-of-pocket for anything because VA would provide or pay for the care.

REVIEW CHANGES TO THIS PROVISION CAREFULLY. THERE IS A HIGH POSSIBILITY THAT THEY MAY BE SIGNIFICANT CHANGES.

The Collaborator is likely to object to the word “solely” everywhere it appears. Try to negotiate to “substantially” instead. It can be removed from (c) without too

much difficulty. We think contributory fault should not completely absolve the Collaborator from responsibility, but if you must relent, you may.

Article 13.1. Governing Law:

An agency of the federal government cannot agree to be bound by state law. This is non-negotiable.

Article 13.10. Export Controls:

The Federal government cannot agree to be bound by state law.

Article 13.14.4. Payments:

Do not forget to put the NPC's Federal ID # in the CRADA. Also, NPC MUST send a completed IRS Form W-9 to Collaborator.

Appendix A:

Note: Based on the terms of the agreement, among the matters that may be covered in Appendix A are:

- the period of performance
- the Protocol or a summary or synopsis of the Protocol
- contributions of the Parties (materials, capital equipment, etc.)
- disposal of remaining Test Article
- transfer or storage of study records after 5 years
- payment terms
- budget
- identification of background inventions
- identification of confidential information (see Definition of Confidential Information and Article 8.1)

In accordance with local preferences, these matters may be broken up into separate documents within Appendix A (A-1, A-2, etc.).

COMPARE AND MERGE INSTRUCTIONS:

- 1. In a folder, “Save” the document with changes (Document A or the proposed CRADA) and the one to which you want to compare it (Document B or the model CRADA) in order to determine the revisions.**
- 2. If a proposed document (Document A, such as a proposed CRADA reflecting the collaborator’s requested revisions) has tracked changes, on the Edit menu, use “Select All” (Ctrl A) to highlight the entire document. Using “Tracked Changes” on the Tools menu, “Accept” all the changes in the document. Use “Save As” to save this document (Document A) with a new name. If you are starting with a clean document, re-name and “Save As” it. Keep this document (with the new name) open on your screen.**
- 3. On the “Tools” menu, select “Compare and Merge Documents.” Your document directory will appear.**
- 4. In your directory, locate the comparison document (Document B). That is, the one to which you want to compare the one that is already open on your screen (such as the current, prevailing model of the CRADA being proposed). Select the comparison document (the original model CRADA) and click “Merge” or “Compare” on the lower right of the directory.**
- 5. MS Word will create a new merged document that tracks all the differences between the two documents. “Save” this new document (Document C) under a new name.**