

Recommendations Regarding the April 1 OGC Advisory Determinations on CRADAs and Clinical Research Agreements

The VA affiliated nonprofit research and education corporations (NPCs) support a wide range of research programs, all of which are subject to VA review and approval to ensure that they are relevant to veterans. Many of these studies involve new pharmaceutical treatments for conditions prevalent among veterans. Participation in these studies saves VA the cost of standard drugs and affords veterans with additional care and monitoring, again at no cost to VA. Most importantly veterans gain access to cutting edge treatments, some of which are the only treatment available for devastating conditions.

This document offers constructive suggestions for ensuring that the NPCs continue to play an important role in VA research and improvements in veterans care, and that they are not unduly compromised by the determinations of the April 1 OGC advisory on CRADAs and corporations.

Executive Summary

1. Background information about the NPCs – Page 1

Pursuant to 38 USC 7361-7368, eighty-eight VA medical centers have established affiliated nonprofit research and education corporations (NPCs) to serve as “flexible funding mechanisms for the conduct of approved research and education . . .” As reported in June 2004, prior year NPC expenditures of \$179 million supported a wide range of research and educational programs and services.

2. Summary of the findings and implications of the April 1 OGC advisory – Page 2

OGC recently concluded that the clinical research agreements used by NPCs improperly bind VA despite containing language recommended by VA attorneys for more than a decade. To ensure that NPCs’ practices do not conflict with their recent determinations and Cooperative Technology Administration Agreements (CTAAs), OGC has also determined that Cooperative Research and Development Agreements (CRADAs) should be the vehicle for managing intellectual property that may result from industry sponsored research.

3. Rationale for VA Support of the NPCs – Page 3

It is to VA’s advantage to ensure that NPCs are fully able to realize their statutory purpose and their potential as flexible funding mechanisms because 1) the NPCs only support VA-approved research; that is, research conducted to ensure that veterans receive the best possible care now and in the future; 2) the NPCs are VA’s congressionally authorized means to administer non-VA federal and private sector funds in support of VA research and education; and 3) NPC management of sponsored awards affords VA substantial advantages over other administrative entities.

4. Issues for consideration by VHA and OGC – Page 4

CRADAs present an opportunity for addressing what has become in recent years the most contentious issue in clinical research agreements -- intellectual property and licensing. However, in transitioning to this model it is extremely important that all relevant documents fully support the standing of NPCs as active participants in the programs they administer for purposes of 1) their ability to be grantee institutions for NIH awards; 2) preserving their state tax exemptions; and 3) maintaining their congressionally mandated IRS tax-exempt status.

NAVREF encourages VA to reconsider previous analyses that categorically deny NPCs the opportunity to participate in CRADAs as “collaborating parties” and further suggests that the CRADA authority and the NPCs’ relationship with VA do not preclude allowing NPCs to be signatories even if their role would be somewhat atypical in comparison to that of most CRADA funding partners.

5. CRADA Considerations and Recommendations – Page 8

A new paradigm is needed for intellectual property management as well as new means to establish relationships with sponsors. Toward that end, NAVREF offers the following recommendations:

- Each NPC-administered research study should be governed by a clinical research agreement that references a CRADA designed to address solely the intellectual property issues. NAVREF recommends use of a “universal CRADA” and “single collaborator” CRADAs.
- Statements should be incorporated in CRAs to ensure that the CRA is not perceived as binding on the VA. An accompanying VA statement should be used to provide VA assurances as needed.
- VA should develop and disseminate clear policy on VA’s preferred outcome on IP ownership and management appropriate to the type of study proposed. This encompasses a broad spectrum including Phase I-IV, other sponsor-initiated, investigator initiated, VA initiated, etc., studies.
- VA should staff the Technology Transfer Program appropriately in order to ensure expeditious review and approval of CRADAs.
- As quickly as possible, VA should delegate to Regional Counsel Offices approvals of routine CRADAs in accordance with VA guidelines.
- VA and NAVREF should collaborate on training for VA attorneys and NPC personnel in general CRADA principles as well as policies and procedures specific to VA.
- VA should involve NPC representatives and OGC Corporations Panel attorneys in ongoing policy deliberations. VA should also meet with pharmaceutical company personnel and with staff of the Henry M. Jackson Foundation to learn from their extensive experience with intellectual property management, CRADAs and clinical research agreements.

6. Other Considerations – Page 12

1. Clear guidance on desired outcomes and appropriate language is needed before NAVREF can be comfortable recommending that NPCs should work with their local VAMCs to negotiate amendments and/or modifications in CTAs to accommodate interim use of CRAs and future use of CRADAs.
2. NAVREF appreciates the commitment of the Office of General Counsel to continue to support the OGC Corporations Panel and encourages OGC to find a way for NPCs to reimburse OGC for VA attorneys’ time spent on NPC issues.
3. If improvements should be made in the NPC statute to clarify the status and authorities of NPCs, as well as to provide VA with the most effective research partners possible, NAVREF welcomes working with OGC toward that end.
4. CRAs and the language used to address issues commonly found in CRAs are similar whether the administrative entity is an NPC or other nonprofit, university or commercial research organization. The April 1 OGC advisory conclusions should be applied consistently to all administrative entities for VA-approved research and not solely to the NPCs.

Recommendations Regarding the April 1 OGC Advisory Determinations on CRADAs and Clinical Research Agreements

Note: This document and all attachments are available electronically at:
http://www.navref.org/library/April_1_Advisory_Recommendations.htm

On April 1, 2005, the VA Office of General Counsel (OGC) issued an advisory (Attachment 1) that has far reaching implications for the mechanisms used to date and in the future to establish research agreements between sponsors and the VA-affiliated nonprofit research and education corporations (NPCs).

The following information is provided. Additional and supporting materials are found in the attachments.

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- Summary of the Findings and Implications of the April 1 OGC Advisory – Page 2
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The National Association of Veterans Research and Education Foundations (NAVREF) looks forward to collaborating expeditiously with VHA and OGC toward establishing and implementing appropriate policy and mechanisms for managing relationships with research sponsors for the benefit of VA and veterans.

Background Information about the NPCs

In 1988 Congress passed legislation that enables VA facilities to establish nonprofit corporations (NPCs) “to provide a flexible funding mechanism for the conduct of approved research and education at the medical center.” Today there are 88 active NPCs. Collectively, prior year NPC expenditures in support of VA research and education were nearly \$179 million according to NPC annual reports submitted to VA in June 2004. Attachment 2 provides details of revenues and expenditures.

NPCs range from those that predominantly administer clinical trials to those that support a full array of research and education awards, including non-VA federal grants from NIH, CDC and DoD. Additionally, many NPCs administer other nonprofit and voluntary health agency awards including those from the American Diabetes Association, the American Heart Association and the Robert Wood Johnson Foundation.

At most VA facilities that conduct research, the NPCs’ support for their affiliated VA medical centers has become an essential component of the VA research infrastructure. These corporations bear much or part of necessary research costs such as IRB activities, compliance officers, investigational pharmacists, research administration staff, IT support, facilities renovation, animal facility staffing and a host of other services that enrich the research environment. Pages 12-14 of Attachment 2 provide specific examples of NPC support.

Typically, NPC support far exceeds its proportionate share of the research enterprise at the facility, and benefits VA more directly than when funds are administrated by other VA affiliated entities. Because VA personnel serve on NPC boards, NPC expenditures can be directed to VA's priority research needs as determined by VA itself. By statute, all NPC expenditures, whether for the direct costs of a research project or for research infrastructure in general, must benefit VA research or education, or support the business operations of the NPC itself.

Additionally, studies supported by NPCs provide veterans with access to cutting edge treatments under carefully controlled circumstances. In some cases, an experimental drug is the only treatment for a veteran's illness and participation in a study offers veterans their only hope.

Since their inception, NPCs have used "clinical research agreements" (CRAs) to establish the terms and conditions of relationships with industry sponsors. Over time, VA attorneys have developed sample clauses containing terms deemed acceptable to VA and many have been made available by postings on the NAVREF web site at (Attachment 3). When negotiating with industry sponsors, NPCs and VA attorneys use these clauses to replace those offered by sponsors which may contain terms that are inconsistent with VA policies or requirements for studies conducted in federal facilities. As recently as June 2004, then Acting Under Secretary for Health Jonathan Perlin, MD, PhD, advised NPCs to use the clauses provided on the NAVREF web site (Attachment 4).

When NPCs are unable to reach agreement on terms consistent with VA policies, they often seek advice as well as review and approval by members of the OGC Corporations Panel which was formed by OGC in 1996 to assist NPCs on legal matters, primarily in negotiating clinical research agreements. The objectives of forming the panel were to ensure 1) compliance with VA policies; 2) consistency in the advice provided; and 3) timely responsiveness so as not to impede the conduct of the research.

Summary of the findings and implications of the April 1 OGC advisory

As summarized by VA Deputy General Counsel Jack Thompson, the OGC email dated April 1, 2005, and entitled "Intellectual Property and Non-Profit Research Corps" concludes:

1. VA has no authority to confer IP rights in advance of disclosure except through CRADAs.
2. VA's nonprofit corporations cannot execute research agreements that legally bind the Department.
3. VA's non-profits cannot execute research agreements that contradict the CTAA's the Department has entered with its affiliates.

Consequently, OGC now takes the position that the clinical research agreements previously advised by VA attorneys for use by NPCs are improper. To ensure that NPCs' practices do not conflict with the above determinations, OGC has decided that Cooperative Research and Development Agreements (CRADAs) should be the vehicle for managing intellectual property resulting from sponsored research awards. OGC also has determined that CRADAs are the only means available to VA to commit ownership and licensing of intellectual property developed by its employees (salaried and WOC), or using VA resources, prior to disclosure. However, in order to make CRADAs feasible, accommodations must be made in the 63 Cooperative Technology Administration Agreements (CTAAs) currently in place with affiliated universities. NAVREF's views on the advisory are summarized in Attachment 5.

In recognition of the far reaching implications of the advisory, the very low level of risk associated with the clinical research agreements (CRAs) used to date, the need to educate both VA and NPC personnel about CRADAs and the uncertain timeline required to modify the CTAAs, OGC has agreed that NPCs will continue to use clinical research agreements, and VA attorneys may assist in their review, during the transition period. Details were provided on April 12 in a memo to OGC attorneys with NPC involvement (Attachment 6).

Rationale for VA Support of the NPCs

It is to VA's advantage to ensure that NPCs are fully able to realize their statutory purpose and their potential as flexible funding mechanisms first and foremost because the NPCs' purpose is to support only VA-approved research; that is research conducted to ensure that veterans receive the best possible care now and in the future. Additionally:

1. By statute, the NPCs are VA's congressionally authorized means to administer non-VA federal and private sector funds in support of VA research and education. This is supported by the March 22, 2004, IG administrative investigation on "Use of Government Funds, Travel, Personnel, Impartiality and Management Issues, Research and Development Office, Veterans Health Administration (Report No. 03-03053-115) Recommendation 1. g) and the July 8, 2004, OGC opinion regarding "Funds Provided by Pharmaceutical Companies to Friends Research Institute for Cooperative Research Studies," under Held, Item 2. Both recommend use of the NPCs to administer extramurally funded research.

Additionally, VA's own Handbook 1200.2 Research Operations mandates:

4. Financial Operations. b. Distribution and Expenditure of Funds. a) Administration of Funds.

NOTE: If approached by a potential donor or grantor interested in supporting VA research, a VA official may not direct the donor to deposit the funds with any entity other than VA or a VA nonprofit corporation.

3. Affiliated schools and universities and nonprofit organizations (other than a VA nonprofit research corporation, discussed above) may administer funds for VA research if authorized by a VA medical center Director. A VA medical center Director may authorize these entities to administer funds for VA research only if administration is a condition of payment of the funds to VA.
2. NPC administration of VA approved research and education affords VA greater awareness, control and oversight of research conducted in its facilities.
3. The NPCs were authorized in part because General Post Funds were found to be an ill-suited mechanism for research administration.
4. Unlike other administrative entities, **all** NPC expenditures ultimately benefit VA. By augmenting hospital and R&D support for VA research, NPCs make VA a more attractive career choice for clinicians interested in pursuing clinical, research and academic careers.

It is a matter of some concern to NAVREF that the NPCs are often placed at a disadvantage to affiliated universities and other potential administrative entities when it comes to research administration. This is in violation of its own policies and is counterintuitive because VA clearly

benefits from NPC administration of both private sector funding and non-VA federal grants. The table provided as Attachment 7 allows one to calculate the approximate cost to VA of non-NPC administration of extramural research support. At a modest indirect cost rate of 15%, this amounts to a loss of as much as \$40 million per year in indirect reimbursement on non-VA federal awards alone. At a 25% rate, this would be as much as \$66 million per year. The typical NPC administrative overhead rate on non-federal awards is 15-25% so the lost benefit to VA on the \$91 million in private sector funding managed by other entities is also substantial.

Ironically, at a time when various determinations are having a negative impact on NPC revenues, the secretary of the Department of Veterans Affairs has on numerous occasions informed Congress that VA research depends on funds other than those appropriated to VA and anticipates large increases in such amounts in the coming year. VA's own FY 2006 budget proposal assumes that VA investigators will successfully compete for an additional \$37 million over the previous year's level of funding from other agencies and \$9 million more from private sector sources. VA support for its own research program, which it contends will amount to \$1.65 billion under the FY 2006 budget proposal, would shrink to 48% of the total, with the R&D appropriation representing less than 24%.

However, according to reports submitted in June 2004, NPC private sector revenues actually declined by 15% or \$17.7 million during the previous year. In part -- though we acknowledge not entirely -- due to continuing difficulties negotiating IP clauses under CTAs and within VA policies, a significant further reduction is anticipated in the reports due on June 1, 2005.

Issues for Consideration by VHA and OGC

CRADAs present an opportunity for addressing what has become in recent years the most contentious issue in clinical research agreements; that is, intellectual property ownership and licensing. It is our understanding that in using CRADAs, VA is agreeable to relinquishing to sponsors the first right to option new intellectual property arising from the Phase III and IV clinical studies that comprise the majority of studies administered by NPCs. If our understanding is accurate, this is a step in the right direction and CRADAs are a means to significantly reduce the time and effort required to negotiate agreements with industry sponsors and to foster an environment conducive to veteran participation in worthwhile studies.

However, CRADAs have not been widely used for the types of studies administered most frequently by NPCs so this is an untested area for VA, the NPCs and industry sponsors. Additionally, the prospects for university cooperation in modifying the CTAs to accommodate CRADAs are uncertain. Finally, it is our understanding that the Office of General Counsel proposes that going forward, intellectual property for virtually every sponsored project will be managed under a CRADA with VA and the sponsor as the only signatories.

NAVREF is concerned that a policy that excludes NPCs from participating in CRADAs as "collaborating parties" or from otherwise being recognized as partners in supporting the research may be problematic for the NPCs and their continued ability to support VA research and education. For purposes of 1) their ability to be grantee institutions for NIH awards; 2) preserving their state tax exemptions; and 3) maintaining their IRS tax-exempt status, it is extremely important that all relevant documents fully support the standing of NPCs as active participants in the programs they administer. Briefly:

1. Considerable benefits accrue to VA from recognition by other agencies that the NPCs are appropriate grantee institutions for receipt of federal awards.

Approximately 41 NPCs currently administer federal funds, most notably NIH funds which carry with them indirect cost support which accrues to the benefit of the VA and VA investigators. It is important for NPCs to be fully “engaged” in research – albeit only VA-approved research subject to VA statutes, regulations and policies – in order for them to be suitable grantee institutions. NIH defines a grantee as:

The organization or individual awarded a grant or cooperative agreement by NIH that is responsible and accountable for the use of the funds provided and for the performance of the grant-supported project or activity. The grantee is the entire legal entity even if a particular component is designated in NGA [Notice of Grant Award]. The grantee is legally responsible and accountable to NIH for the performance and financial aspects of the grant-supported project or activity.

The NIH definition of organizations “engaged” in clinical research involving human subjects is provided as Attachment 8.

Any apparent diminishment of NPC responsibilities puts at risk the \$83.2 million in federal funds administered by NPCs last year (Source: NPC annual reports submitted to VA in June 2004). Should NPCs fail to be recognized as grantee institutions as a result of a perception that they play a minimal role in certain types of studies, such funds would be likely to migrate to the affiliated universities with the loss of substantial direct and indirect support and just as importantly, diminished control over activities conducted in VA facilities. Although a number of NPCs are moving toward administration of NIH funds, at this time the bulk of NIH funds administered by NPCs -- \$50-60 million -- are held by two NPCs that have negotiated HHS indirect cost rates in the 50% range. Each of these NPCs generates substantial NIH reimbursement for NPC administrative costs, indirect programmatic costs and research infrastructure support, over and above the awards themselves.

2. The NPC authorizing statute requires that NPCs “shall be established in accordance with the nonprofit corporation laws of the state in which the applicable medical center is located and shall, to the extent not inconsistent with any federal law, be subject to the laws of such state.” (38 USC 7365)

NPCs’ status as state chartered organizations exempt from the respective state, county and city taxes depends on their activities and management being consistent with state requirements. Constraints on the NPCs in these regards may jeopardize their ability to function as statutorily mandated state corporations.

Attachment 9 details issues states typically consider when making decisions about state-incorporated organizations. This State of Washington Department of Revenue determination considers such factors as whether:

- the NPC was “providing administrative services to the VAMC;”
- “the real grantee . . . is the VA Hospital as opposed to the [NPC];” and
- the NPC “is acting as an agent on behalf of the VA Hospital.”

In order to reach a determination favorable to the NPCs, a negative response to each of these queries was essential. The administrative judge considered as findings in favor of the NPC the facts that:

- fifty-five NPC employees were involved in the research;
- “grants are paid to the order of the [NPC], not to the VA Hospital;” and
- the “Congressional purpose in creating the [NPC] was to establish an entirely separate, legal entity.”

3. The NPC authorizing statute requires NPCs to be entities “the income of which is exempt from taxation under the Internal Revenue Code of 1986.” [38 USC 7361 (b)] To meet this requirement, NPCs must obtain IRS tax-exempt status, preferably as medical research organizations.

IRS rules state:

To qualify as a medical research organization, the principal function of the organization must be the direct, continuous and active conduct of medical research in conjunction with a hospital that is described in section 501(c)(3), a Federal hospital, or an instrumentality of a governmental unit referred to in section 170(c)(1).” [IRS Form 1023 Application for Tax Exempt Status]

Thus continuing to be directly involved in the conduct of research is important to the NPCs’ tax status.

IRS definitions of medical research organizations are found at 26 C.F.R. §1.170A-9 (c). See Attachment 10.

It is essential that all documents associated with NPC-administered programs support that they are partners in the conduct of research – again, albeit only VA-approved research subject to VA statutes, regulations and policies – seeking new and improved methods of diagnosis and treatment for disease and disability. Anything that appears to minimize the role of the NPCs in the conduct of research may jeopardize their tax-exempt status.

To date, NPCs have qualified as medical research organizations under IRS regulations, as grantee institutions under NIH rules, and have withstood state attempts to tax their revenues in part because NPCs are signatories on clinical research agreements that explicitly describe the work to be performed as research and because NPCs take responsibility for both private and non-VA federal awards by signing appropriate acceptance documentation. Additionally, NPC employees conduct the research and NPCs provide significant support services for investigators such as managing employees, administering benefits, assisting with grant development, procuring equipment and supplies, modifying research laboratories, securing IT services, etc. In some cases, the research is being conducted in space constructed and owned or leased by NPCs.

Relegating the NPCs to serving as pass through entities or only as “banks” for funds pursuant to CRADAs that are first provided to VA – as provided by VA’s CRADA Guidelines, “Procedures for Handling Funds Associated with CRADAs, item b. – may weaken their ability to withstand relentless challenges by the IRS, state tax agencies, universities and federal funding agencies.

One nonprofit granting organization, the American Cancer Society, already refuses to allow NPCs to administer their grants because it perceives a grant to an NPC to be the same as a grant to VA, and it has a policy of not funding federal agencies. However, the ACS will fund the same grant to the same PI through an affiliated university even when 100% of the work is performed in the VA facility. Another NPC had to demonstrate that it was not an agent of the VA in order to qualify for state bond funding. NAVREF encourages VA not to jeopardize the financial and material benefits of NPC administration of grants, as well as the benefits of veterans' participation in studies, by unnecessarily constraining the NPCs' role in research management.

“Collaborating party” issues: NAVREF encourages VA to reconsider previous analyses that categorically deny NPCs the opportunity to participate in CRADAs as “collaborating parties.” The most relevant one is provided in Attachment 11.

- In our view, the September 30, 1996, opinion fails to recognize the substantive contributions NPCs make to VA's research enterprise – not just from funds provided pursuant to the study – as well as to individual research programs, just some of which are noted in Attachment 2, pages 12-14.
- 15 USC 3710a(a) provides that a government laboratory may enter into CRADAs “with . . . nonprofit organizations . . .” NPCs are nonprofit organizations.
- Both the CRADA statute and VA's own CRADA guidelines recognize that there may be more than one collaborating party in a CRADA. [5 USC 3710a(b)(1)]
- Section (b)(2) of 15 USC 3710a provides that a laboratory may “accept, retain and use funds, personnel, services and property from a collaborating party.” These are all items NPCs typically provide in support VA-approved research.
- Section 7364(a)(1) of the NPC authorizing statute provides that NPCs may “enter into contracts with, individuals and public and private entities solely to carry out the purposes of this subchapter.” Because CRADAs are contracts entered into for research purposes and the other collaborating parties would be VA (a public entity) and the commercial sponsor (a private entity), there appears to be no statutory impediment to a three-way CRADA.
- Because the medical center director sits on the board of each NPC, the Associate Medical Center Director could be designated to sign on behalf of VA those CRADAs that involve NPCs in order to avoid the appearance of a conflict of interest and to ensure an arms length relationship. We understand that a re-delegation of signing authority for CRADAs has already been proposed for “national CRADAs” and we suggest it could be expanded to reflect a solution for any CRADA involving an NPC.

As a result, it appears that NPCs may qualify as “collaborating parties” and NAVREF suggests that if having NPCs as signatories is otherwise desirable, there may be sufficient flexibility in the CRADA authority for NPCs to be signatories even if their role is somewhat atypical of most CRADA collaborating parties.

However, in spite of all these points in favor of NPCs being signatories, NPCs value the OGC determination that NPCs are not prohibited sources under the federal ethics regulations pertaining to gifts. This allows NPCs to support VA personnel in certain ways without putting them at risk of ethical violations. If being signatories on CRADAs would make the NPCs prohibited sources, that factor should be weighed against the resulting curtailment of certain types of NPC support.

CRADA Considerations and Recommendations

VA's ability to assert ownership of intellectual property developed by its employees and using VA resources is unquestioned. Further, without objection NPCs have complied with having their employees assign to VA any rights they may have as VA without compensation (WOC) appointees. However, in regard to pre-discovery assertions, VA has appeared to date to treat all research the same regardless of the likelihood of new intellectual property resulting from the study. Clearly, going forward a new paradigm is needed as well as new mechanisms. Toward that end, NAVREF offers the following recommendations:

1. **Each research study should be governed by a clinical research agreement that references a CRADA designed to address solely the intellectual property issues.**

NAVREF recommends that VA should develop two types of CRADAs **specifically for Phase III and Phase IV industry-sponsored studies.**

A. The "Universal CRADA."

- A universal CRADA would govern intellectual property resulting only from Phase III and IV studies as defined in the CRADA and would contain terms likely to be readily acceptable to industry sponsors regarding intellectual property ownership, proprietary and confidential information, copyright and trademark issues, and data ownership and publication rights. It is extremely important for such a CRADA to be perceived as fair and reasonable by sponsors. (Please see the matrix provided as Attachment 12 for sample definitions of Phase I-IV studies.)
- VA would be one party to this CRADA and one or more other "collaborating parties" would be any organization that meets the statutory CRADA definition of a collaborating party, **but would not be specifically named in the CRADA itself.** The definition would encompass pharmaceutical companies, medical device manufacturers and nonprofits providing intellectual capital and/or funds in support of the study. **However, the CRADA would not specifically name the collaborating party(ies). Nor would the non-VA collaborating party(ies) actually sign the CRADA.** Rather, by signing a CRA referencing the CRADA, and attaching a copy to the CRA, the non-VA collaborating party(ies) would accept the terms of the CRADA.
- If OGC determines an appropriate "collaborating party" role for NPCs in CRADAs, NPCs could sign such universal CRADAs, but it may not be necessary.
- The CRADA and CRA would specify that funds should be paid directly to the NPC which will be accountable for their administration.
- A CRA for each study, signed by the NPC and the sponsor, would reference the CRADA as the governing document for intellectual property resulting from that study, subject to any post-discovery CTAA considerations.
- The CRA would address other issues commonly detailed in CRAs, such as payments and notices, termination rights, as well as providing the protocol and budget as attachments. Standard terms and/or principles for each issue could be developed and promulgated, perhaps using the clauses on the NAVREF web site as the starting point.

- The CRA could also contain an explicit statement that the CRA is not binding on VA. If needed by the sponsor, a separate letter from VA could provide assurances of VA support and involvement in the study. A sample letter currently used for this purpose is provided as Attachment 13.

Pros:

- Sponsors would be offered a pre-approved CRADA to expedite initiation of the study.
- An agreement could be negotiated quickly with any sponsor willing to accept the terms provided in the universal CRADA.
- VA would avoid the need to negotiate an individual CRADA with each potential sponsor. Absent such a universal model, it is likely VA would have to negotiate CRADAs with over 100 ever changing sponsors.
- Past experience has shown that pharmaceutical companies change names and ownership frequently. Efforts to negotiate a single, sponsor-specific CRADA, even if only for Phase III and IV studies, could be wasted after a short time and limited use.
- After a few sponsors agree to the universal CRADA, presumably others will, greatly simplifying both CRADA and CRA negotiations.
- Under this proposal, funds would flow directly from sponsors to NPCs, fostering their status as grantee institutions and bolstering their state and federal tax exemptions. Funds would also be available promptly for start up costs, hiring employees, etc.
- By focusing the Universal CRADA only on Phase III and IV studies, it could contain terms suitable for nearly all NPC-administered studies and without the need for VA attorney involvement, greatly reducing the burden on VA attorneys and the TTP for approvals.
- Universities are likely to be amenable to excluding such CRADAs from the CTAAs.

Con:

- Because the concept of sponsors agreeing to a CRADA by reference in a CRA may be unusual, Department of Commerce approval of this approach may be advisable.

B. The “Single Collaborator” CRADA

- Such a CRADA would be offered for Phase III and IV studies when a sponsor declines to accept the terms specified in the Universal CRADA. However, the starting point for negotiations would be the Universal CRADA.
- Such a CRADA would be signed by VA and the collaborating party providing the funds.
- The CRA would reference the CRADA and the CRA terms would be similar to the universal CRADA.

Pro:

- The single collaborator CRADA would offer flexibility to sponsors.

Con:

- Considerable effort would be required to negotiate each CRADA
- VA attorney and TTP involvement would be required.

Providing actual language for the terms of the universal and single collaborator CRADAs is beyond the scope of this document. However, NAVREF would be pleased to participate in their development.

2. **For studies other than industry-sponsored Phase III and IV trials, VA should also develop and disseminate clear policy on VA's preferred outcome on IP ownership and management appropriate to the type of studies** including Phase I and II, investigator initiated, VA initiated, medical device, etc. studies. Such policy should allow negotiators to conduct a cost/benefit analysis in accordance with criteria established with VA, to determine whether VA will assert a pre-discovery ownership right and/or will readily give another interested party – presumably the sponsor – the first right to license new IP and under what terms. The potential royalty gain to VA should be weighed against the cost of losing worthwhile studies. There may be instances when – using a CRADA – in spite of its legal right to ownership, VA should relinquish rights to IP in the interests of participating in worthwhile research programs.

This recommendation for clear policy is based on NAVREF's view that there is no realistic prospect for "one size fits all" CRADA. That is, a single sponsor may simultaneously be involved in different Phase III, investigator-initiated and VA-initiated Cooperative Studies, each of which may require a different approach to IP.

Pros:

- CRADA negotiations and terms would be customized to fit the circumstances of the study.
- NPC personnel and VA attorneys in the field would have the tools necessary to pursue appropriate CRADA terms; that is, terms consistent with pre-established VA policy and criteria.
- The burden on VA attorneys and the TTP would be reduced, reserving their involvement only for studies that don't fit the pre-establish criteria.

Cons:

- Considerable effort would be required to develop clear guidance understandable to NPC personnel and VA attorneys who may not have significant CRADA or scientific experience.
- OGC would have to relinquish some authority to negotiators subject to review and approval of VA attorneys in OGC or Regional Counsel offices.

A matrix such as the one provided as Attachment 12 could be designed to provide guidance to NPCs and VA attorneys as they negotiate CRADA terms. By incorporating appropriate terms in draft CRADAs, final approvals would be greatly expedited.

3. **VA should staff the Technology Transfer Program appropriately in order to expedite CRADA approvals.** Although using universal CRADAs would significantly reduce the number of Phase III and IV CRADAs requiring TTP involvement, it is likely that there will be a significant increase in CRADA requests for other studies. Additionally, during the transition to CRADAs, there are likely to be a number of complex issues in need of resolution. Although VA policies provide that it will respond to CRADAs within 30 days, it typically takes far longer to receive a response.

Pros:

- Prompt review and approval of CRADAs is needed to ensure that VA is not shut out of worthwhile studies simply because non-VA collaborators can negotiate agreements more quickly and are willing to be more flexible on IP issues.

- An adequately staffed TTP will help to restore sponsor confidence in research collaborations with VA.

Con:

- VA will have to invest scarce dollars in hiring additional, qualified technology transfer staff. However, see below for recommendation regarding NPC reimbursement.

4. **As quickly as possible, VA should delegate to Regional Counsel Offices approvals of routine CRADAs in accordance with VA guidelines as suggested in the sample matrix.** OGC review and approval should be reserved only for those CRADAs likely to result in significant royalty revenues and requiring complex terms. However, Regional Counsel staff should be apprised that time is of the essence in executing CRADAs and performing CRA reviews when requested. Timeliness in VA attorney and TTP responsiveness is the primary concern expressed by NAVREF members in regard to the transition to CRADAs.

Pro:

- OGC and TTP involvement in CRADAs and CRAs would be reserved for situations outside the norm.

Con:

- A formal delegation of authority is required and may take some months to accomplish.

5. **VA and NAVREF should collaborate on training for VA attorneys and NPC personnel in general CRADA principles as well as policies specific to VA.** NAVREF has already offered to partner with VA to sponsor such training in the fall of 2005.

Pros:

- By collaborating on a single training session, both VA and NPC personnel would undergo the same training.
- With the involvement of VA personnel in the planning, the content could be customized according to VA policies and requirements.
- The per person cost of the training should be lower than that charged by trainers when conducting sessions offered to the general public.
- NAVREF will undertake administration of the workshop (hotel contract, registration, contracting with the speakers, etc.)

Con:

- VA will have to underwrite the cost of training VA attorneys and other VA personnel.

6. **VA should involve NPC representatives and OGC Corporations Panel members in ongoing policy deliberations and should meet with pharmaceutical company representatives and staff of the Henry M. Jackson Foundation** to learn from their extensive experience with intellectual property management, CRADAs and clinical research agreements. In meetings with NAVREF last year, HJF staff members were extremely generous in sharing their expertise and resources.

Pro:

- VA can benefit from insights from NPC personnel and the HJF's longstanding experience.

Con:

- None

Other Considerations

1. During a NAVREF Annual Conference presentation on April 12, Acting Assistant General Counsel Lorrie Johnson encouraged NPCs to negotiate **amendments and/or modifications in CTAs** to accommodate interim use of CRAs and future use of CRADAs. However, NAVREF is uncomfortable recommending that NPCs do so in the absence of guidance on the optimum outcome and appropriate language. Also, because universities and the Chief Research and Development Officer are the CTA signatories, we are uncertain of NPCs' authority to negotiate revisions or amendments.
2. NAVREF appreciates the commitment of the Office of General Counsel to continue to support the **OGC Corporations Panel**. Our members have expressed an interest in finding a way to reimburse OGC for VA attorneys' time spent on NPC issues. Would use of the Intergovernmental Personnel Act (IPA) authority be a tool that NPCs could use to provide OGC with the resources necessary to increase staffing and reduce the impact of NPC related work on OGC budgets?
3. NAVREF believes that mechanisms for future clinical research agreements and CRADAs recommended above are consistent with the NPC authorizing statute and other statutory requirements. However, should OGC feel that **improvements could be made in the NPC authorizing statute** to clarify the status and authorities of NPCs, NAVREF would welcome working with OGC toward that end.
4. CRAs and the language used to address issues commonly found in CRAs, are similar whether the **administrative entity** is an NPC or other nonprofit, a university or even a commercial research organization. Unless VA applies the April 1 conclusions to agreements used by all administrative entities for VA-approved research, the NPCs will be at a distinct disadvantage. VA should carefully weigh whether selectively applying these determinations is in VA's best interests.

Conclusion

NAVREF appreciates the opportunity to raise the above points with VHA policymakers and OGC, and to make recommendations. We hope the background information provided above and the issues discussed will assist in the prevention of unintended consequences that could be detrimental to VA research as new policies and methodologies are developed. NAVREF, its board and its members welcome involvement in deliberations on these matters as VA considers new policy and mechanisms for interactions with research sponsors. If you have questions or need additional information, please contact NAVREF Executive Director Barbara West.