

## Intellectual Property Issues in a Clinical Trial: A Corporate Perspective<sup>\*,1</sup>

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This paper addresses intellectual property concerns of a corporation when conducting clinical trials of its product with National Institutes of Health's Division of AIDS (DAIDS).

Both industry and Government share the goal of bringing effective AIDS therapies and vaccines to market. Today, a corporation's decision-making is affected by its social conscience, its legal responsibilities to its shareholders under applicable law, and its desire to achieve goals ahead of the competition. All of this must be accomplished without compromising proprietary rights.

A challenge that needs to be met in order to reach the goal of obtaining an effective AIDS therapy is to create a successful collaboration between the public and private sectors. The AIDS Clinical Trial Group (ACTG) was formed with this intention, and it is clear from the large number of protocols in various stages that the corporate sector is impressed with the expertise provided by DAIDS and its network of grantee hospitals and institutions. However, as we gain experience, it becomes evident that there are a number of concerns that need to be addressed to ensure that industry retains control of its proprietary rights. A crucial concern for industrial partners is the adequate protection of their proprietary rights prior to licensure by the FDA.

Typically, in connection with a non-Government clinical study, such concerns regarding proprietary rights are dealt with directly through contracts with a given institution or hospital. However, drug development in the field of AIDS and anti-cancer therapies does not correspond with typical drug development efforts. Because of the devastating effects of AIDS and cancer on the health and welfare of our society, society has demanded, in an unprecedented fashion, that the biomedical research community's efforts to combat these diseases be subjected to both public scrutiny and the direct involvement of the concerned community. We are all accountable.

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<sup>1</sup> This paper was prepared as background for a presentation by Raymond S. Fersko, a member of the Bar of the State of New York, to the Division of AIDS on June 10, 1992. The paper was prepared by Mr. Fersko and M. Jean Connolly, also a member of the Bar of the State of New York. The views expressed here are solely those of Mr. Fersko and Ms. Connolly.

## PRESENT STRUCTURE OF THE ACTG AND HOW INVENTIONS ARE TREATED

The ACTG has standing agreements with its grantee hospitals and institutions to conduct clinical protocols. Those agreements are not renegotiated with every new protocol undertaken or even to meet the specific concerns of a given industrial partner. These standing agreements between the Government and the clinical sites are governed by the Bayh-Dole Act.<sup>2</sup>

Bayh-Dole is applicable to all Federal agencies, and it specifically provides that small business firms and nonprofit organizations can elect to retain title to *any* inventions made pursuant to a funding agreement with a Federal agency.<sup>3</sup> A "funding agreement" is any contract, grant or cooperative agreement between the Federal agency and a contractor for the performance of *experimental, developmental or research work*, funded in whole or in part by the Federal Government.<sup>4</sup>

### LEGISLATIVE HISTORY OF BAYH-DOLE ACT<sup>5</sup>

The Bayh-Dole Act, enacted in 1980, heralded in an enormous change in the Government's prior policy concerning government-funded research and development. Prior to World War II, the Government had a small role in funding research. During the war, and primarily for defense purposes, the Government increased its commitment to R&D. This commitment continued to grow in the decades that followed.

While the stated purpose of Government research efforts was not to develop patentable inventions, inventions were certainly a valuable by-product. Those inventions were made with Government money and remained the property of the U.S. Government. Then, during the 1970s, due in part to Congress' concern about the ability of U.S. industry to maintain its position in the world economy, the validity of this policy was debated.<sup>6</sup> In 1980, the enactment of Bayh-Dole marked a complete reversal of the Government's position on ownership of inventions derived from Federally assisted research. Instead of presuming Government ownership, Bayh-Dole stated that small businesses and nonprofit organizations had a right to elect to retain title to any subject inventions, pursuant to certain terms and conditions.<sup>6a</sup>

On the other hand, opponents of Bayh-Dole felt that whatever the Government acquires through the use of citizens' tax money should be owned by the Government and that assigning automatic patent rights to companies and organizations for inventions developed with Government money was a "giveaway."<sup>7</sup> In a similar fashion, companies entering into a Clinical Trials Agreement (CTA) with ACTG may echo the opponents of Bayh-Dole. Companies do not want the ACTG to "give away" or "take away" any of their proprietary rights; in this case, the rights being given away

<sup>2</sup> Bayh-Dole Act, 35 U.S.C. §§200-211 (1984 & Supp. 1992).

<sup>3</sup> 35 U.S.C. §202 (1984 & Supp. 1992).

<sup>4</sup> 35 U.S.C. §201 (1984).

<sup>5</sup> Walterscheid. *The Need for a Uniform Government Policy: The D.O.E. Example*. 3 Harv. J. L. & Tech. 103 (1990). Some of the background information for this section was derived from this article.

<sup>6</sup> H.R. Rep. No. 1307, 96th Cong., 2d Sess., pt. 1, *reprinted in 1980 U.S. Code Cong. & Admin. News* 6460, 6488 (hereinafter referred to as H.R. Rep. No. 1307).

<sup>6a</sup> U.S.C. §202 (1984 & Supp. 1992).

<sup>7</sup> H.R. Rep. No. 1307, 6487.

are not those made with taxpayers' money, but rather are those made with the company's resources.<sup>8</sup>

#### INVENTIONS DERIVED FROM COMPANY'S PRODUCTS—CONFLICT WITH BAYH-DOLE ACT

The specific concern of industry is that Bayh-Dole authorizes the ACTG's grantees to elect to retain title in any inventions made by them, including inventions derived from the company's drug or biologic.<sup>9</sup> The majority of clinical investigators assigned to a given protocol will undertake that protocol as outlined by the ACTG and report the results in accordance with the protocol. It is possible that a clinician may observe a previously unobserved result with the company's product outside of the protocol. For example, during a Phase I trial with asymptomatic individuals, the clinician may note, for example, that the company's AIDS therapy also prevents baldness. If this is a benefit that the manufacturer has not noted, the investigator might claim this discovery of a new use for the company's drug as his *own* invention. Concerns about a clinical investigator discovering a new use for a given compound are more realistic if the characteristics of the given compound are less defined. If the given compound is well defined, it is more likely that the principal investigator will note what the company has noted.

Another, even more inquisitive investigator might consider using the company's product in combination with either a patented or unpatented drug. Perhaps, the clinician might "discover" a new formulation or a new dosage for the drug that is not covered by the company's patent applications. The eager clinician would then disclose his "invention" to the hospital or university with which he is affiliated and that hospital or university would be well within their rights in claiming title to the invention under the Bayh-Dole Act. It is an open question whether any "discovery" by the investigator would ultimately be patentable, but the "discoveries" are clearly based on the company's patentable technology. Here lies the conflict between the company's interest and the law.

While corporations can appreciate that it is not usual for inventions to be made in a clinical setting, it is imperative that there be language in CTAs that address the fair and equitable disposition of proprietary rights, including intellectual property rights.

#### BURROUGHS WELLCOME v. BARR LABORATORIES

Companies are always concerned when transferring proprietary materials to third parties. An example of the issues that might arise when a company "collaborates"

<sup>8</sup> In 1983, President Reagan issued a policy statement that extended the Bayh-Dole Act to *any* organization, not only to small business firms and nonprofit organizations. *Presidential Memorandum to the Heads of Executive Departments and Agencies, Subject: Government Patent Policy, 1983 Pub. Papers 248 (February 18, 1983)*. The Federal Acquisition Regulations, found in 48 C.F.R. Ch. 1, in part contain regulations (part 27) which identify the policies, procedures, and clauses that govern patent rights under Government contracts entered into by any Federal agency. Those regulations parallel the Presidential directives in the Memorandum cited above and the Bayh-Dole Act. In 1986, the Government went further in its efforts to make technology transfer a part of the mission of every Federal laboratory by enacting the Federal Technology Transfer Act (FTTA), 15 U.S.C. §§3701-15 (1984), which permitted Federal agencies to enter into collaborative research and development agreements (CRADAs) with industrial organizations and, thereby, to grant intellectual property rights to those organizations in advance. Those prospective grants included grants of exclusive rights to inventions that were made in whole or in part by employees of "Government-operated Federal laboratories" or "Government-owned contract-operated laboratories."

<sup>9</sup> 35 U.S.C. §202 (1984 & Supp. 1992).

with a third party, particularly, a Government agency, is illustrated by the pending litigation between Burroughs-Wellcome Co. and Barr Laboratories, Inc.<sup>10</sup> This suit was prompted by the NIH's grant of a nonexclusive license to Barr to market AZT and Barr's subsequent submission of an Abbreviated New Drug Application (ANDA) to the FDA.

In May 1991, Burroughs-Wellcome instituted an action against Barr Laboratories seeking a declaration that the Burroughs-Wellcome patents covering AZT were fully enforceable and were being infringed by Barr Laboratories. In its complaint, Burroughs-Wellcome also sought to enjoin Barr from selling any infringing form of AZT.<sup>11</sup>

The NIH granted the license to Barr based on its alleged inventorship interest in the six AZT-related patents which had already been issued to Burroughs-Wellcome.<sup>12</sup> Dr. Samuel Broder and researchers at the National Cancer Institute (NCI) argued that they played a crucial role in determining that AZT is an effective treatment for AIDS.<sup>13</sup> In early 1984, Dr. Broder began to canvas a number of pharmaceutical companies for any anti-retroviral agents that they possessed so that he could screen those agents as a potential AIDS therapy.<sup>14</sup> Dr. Broder and his colleague, Dr. Mitsuya, had developed a method of screening compounds that employed a new human T-cell line designated as ATH-8 to measure for the inhibition of the HTLV-III retrovirus.<sup>15</sup> Drs. Broder and Mitsuya claim to have "discovered" the therapeutic value of AZT by using their screen.<sup>16</sup> They further claim that it was they who discovered the dose at which AZT could be administered to treat AIDS without, in the process, destroying T-cells.<sup>17</sup> According to Barr, Burroughs-Wellcome only knew that AZT had anti-retroviral activity but did not know how to use it in the treatment of AIDS.<sup>18</sup>

In Barr's amended answer to Burroughs-Wellcome's complaint, Barr requested that Burroughs-Wellcome's complaint be dismissed and that the U.S. Government be declared the owner of the six AZT patents pursuant to 35 U.S.C. §§256, 261, and 262.<sup>19</sup> Barr claims specifically that the Burroughs-Wellcome patents are invalid due

<sup>10</sup> *Burroughs-Wellcome Co. v. Barr Laboratories, Inc.*, No. 91-41-Civ-4-H (E.D.N.C., filed May 14, 1991).

<sup>11</sup> Burroughs-Wellcome specifically asserts in its complaint that Barr's submission of an ANDA to the FDA constitutes an act of infringement of the Wellcome patent under 35 U.S.C. §271(e)(2). Compl. ¶14. 35 U.S.C. §271(e)(2) provides, in pertinent part, that it "shall be an act of infringement to submit—(A) an application under §505(j) of the Federal Food, Drug and Cosmetic Act or described in §505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent . . . if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before the expiration of such patent."

<sup>12</sup> According to the NIH, the compound AZT was discovered pursuant to a National Cancer Institute (NCI) grant in the 1960s and is in the public domain.

<sup>13</sup> See, e.g., Compl., Ex. B (Letter dated April 9, 1991 from Thomas C. Pontani, Esq., to General Counsel, Burroughs-Wellcome Co.), pp. 5-6.

<sup>14</sup> *Id.* at 4.

<sup>15</sup> *Id.* at 5.

<sup>16</sup> *Id.* at 4-5.

<sup>17</sup> *Id.* at 5-6.

<sup>18</sup> *Id.* at 4-6.

<sup>19</sup> One of the more interesting issues of fact that arises in this case is whether the essential tests on AZT done by Dr. Broder were begun more than one year before Burroughs-Wellcome made the following statement on July 14, 1986, to the Patent and Trademark Office in response to the first office action in which all claims were rejected as being obvious under 35 U.S.C. §103: "With all due regard to the Examiner's allegations of obviousness, it is quite apparent that the NIH and others skilled in the art have been searching for a drug that will work all apparently with little success to date. It is quite apparent that the art does not teach using AZT as claimed in humans. . . ." Am. Ans. ¶17.

to one or more of the following reasons: derivation,<sup>20</sup> obviousness,<sup>21</sup> and nonjoinder of inventors.<sup>22,23</sup>

As to derivation, Barr claims that in a letter dated February 22, 1985, Broder described his assay to Burroughs-Wellcome and provided Burroughs-Wellcome with his results for AZT.<sup>24</sup> In that February 22, 1985, letter to Dr. Lehrman at Burroughs-Wellcome, Dr. Broder stated, "I believe it looks quite promising."<sup>25</sup> Thus, Broder and Mitsuya communicated their conception of the invention one month before the earliest possible effective filing date that can be accorded to the Burroughs-Wellcome patents.<sup>26</sup> Similarly, on the obviousness argument, Barr alleges that prior to the earliest patent filing date, Burroughs-Wellcome knew that Broder and Mitsuya had found that AZT inhibited HTLV III replication *in vitro* at doses which did not produce a toxic effect in the T-cell population.<sup>27</sup> Further, Barr claims a nonjoinder of inventors in that the essential contributions of Broder and Mitsuya to the inventions claimed in the Burroughs-Wellcome patents warrants that, at the very least, they be named as co-inventors.<sup>28</sup>

The controversy concerning the inventorship of AZT is similar to the conflicts that arise within most pharmaceutical companies; a chemist will claim to be the inventor of a new compound while the pharmacologist who screened the compound will also assert his rights as an inventor. Typically, in such situations, the contribution of the chemist is given greater weight than that of the pharmacologist. Similarly, Burroughs-Wellcome has argued that its scientists made the unique discovery that AZT could be used to treat AIDS and that they deserve the monopoly created by the six patents which were issued in 1988 to cover various formulations of AZT.<sup>28a</sup> Yet, the fact that Mitsuya and Broder subsequently obtained a U.S. patent on their assay<sup>29</sup> suggests that the creation of the assay was truly an inventive act and that the Government may have contributed more than a "routine" screening.

It remains to be seen how this case will ultimately be resolved. Preliminary motions have been made in the case and discovery is now ongoing. The NIH is hopeful that its license to Barr will increase the availability of AZT, promote competition, and lead to a marked decrease in the price of AZT.<sup>30,31</sup>

<sup>20</sup> Derivation means the claimed subject matter was not invented by the persons named as inventors in the Wellcome patents. 35 U.S.C. §102(f).

<sup>21</sup> Obviousness refers to the fact that the claimed subject matter was obvious to Burroughs-Wellcome as of the March 16, 1985, filing date of the "U.K.I" application. 35 U.S.C. §103.

<sup>22</sup> Nonjoinder means the patents are nevertheless invalid because Wellcome failed to name one or more additional persons as inventors and acted with deceptive intent. 35 U.S.C. §116 and 35 U.S.C. §256.

<sup>23</sup> Am. Ans. ¶¶12, 24, 25-27, 28; Compl., Ex. B, pp. 3-4.

<sup>24</sup> Compl., Ex. B, p. 6.

<sup>25</sup> *Id.*

<sup>26</sup> *Id.*

<sup>27</sup> *Id.* at 5-6.

<sup>28</sup> *Id.* at 7.

<sup>28a</sup> Reply Def. Am. Counterclaim., p. 1.

<sup>29</sup> United States Patent, number 4,704,357, issued November 3, 1987.

<sup>30</sup> Press Release, "Statement by Bernadine Healy, M.D." National Institutes of Health, July 17, 1991.

<sup>31</sup> *Vitamin Technologists, Inc., v. Wisconsin Alumni Research Foundation*, 146 F. 2d 941 (9th Cir. 1945), is of interest even if not directly on point. The case deals with the infringement by Vitamin Technologists, Inc. of a patent held by Wisconsin Alumni Research Foundation for a process of producing Vitamin D in organic substances, which, when consumed, would aid in the prevention or amelioration of rickets disease. The infringer, as Barr Laboratories is alleged to be, asserted that the patentee's licensing policy kept the

## SOLUTIONS

We do not have all of the facts relevant to the parties' contentions in the Burroughs-Wellcome case; however, if a company is in fact the rightful inventor of a drug, it should not find itself in circumstances similar to those now being confronted by Burroughs-Wellcome.

At present, most clinical trial protocols are conducted pursuant to a CTA. The ACTG has a model CTA upon which they base their negotiations. DAIDS has also formed a Working Group with the Pharmaceutical Manufacturers Association (PMA) to finalize a revised model CTA. To date, because of the requirements of Bayh-Dole, it seems that DAIDS has been reluctant to address inventions and intellectual property in the CTAs, except to make a general statement of agreeing to be subject to the laws pertaining to intellectual property created in the course of Federally funded research. However, we are informed that DAIDS has contracted to assist companies in obtaining rights to such inventions from its own employees and the employees of its contractors and grantees.

For a company, this language is far from ideal.

How then can the terms of the DAIDS CTA be modified or supplemented to deal with industry's concerns? One way, which does not really solve the problem—but is a start and ought to be agreeable to DAIDS—would be to strengthen this provision by stating that DAIDS will use its "best efforts" to obtain for the company rights to any inventions from its own employees and employees of its contractors or grantees, as the case may be, to any inventions made as a consequence of the clinical trials. An agreement to use "best efforts" is a definite commitment to do what the DAIDS is able to do in this regard, however, a review of DAIDS actions under this commitment, could be a difficult subjective examination.<sup>32</sup>

*(A) Letters of Understanding*

A better solution would be for the company to enter into separate agreements with each of the clinical trial sites which would provide that any intellectual property rights in inventions made pursuant to a given protocol would accrue to the company. DAIDS would not need to be a signatory to such agreements, but the company could seek their assistance in facilitating such arrangements.

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treatment from reaching the most afflicted class, the poor. The Court ultimately held that the essential claims in the patents were invalid for various reasons and observed that "the public interest is served better by our decision that the patents are invalid." 146 F. 2d 941, 956 (9th Cir. 1945). One of the issues raised in the Burroughs-Wellcome litigation is the appropriateness of the prices charged by Wellcome for an essential AIDS therapy. See Ackiron, *Patents for Critical Pharmaceuticals: The AZT Case*, 17 AM. J. L. & MED. 145 (1991).

<sup>32</sup> One might question whether the Government itself could simply assign the rights that it has pursuant to the Bayh-Dole Act to the company. However, the rights retained by the Government seem to be limited unless an expansive interpretation could become legally binding. Specifically, the Government will have "a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any subject invention throughout the world: *Provided*, That the funding agreement may provide for such additional rights, including the right to assign or have assigned foreign patent rights in the subject invention, as are determined by the agency as necessary for meeting the obligations of the United States under any treaty, international agreement, arrangement of cooperation, memorandum of understanding, or similar arrangement, including military agreement relating to weapons, development and production." 35 U.S.C. §202(c)(4) (Supp. 1992).

By what mechanism would the invention rights "accrue" to the company? Obviously, the company would prefer that the clinical site make an outright grant of title in any inventions to it, but this would be contrary to the policy behind the Bayh-Dole Act which provides for the contractor or grantee to be able to elect to retain title. Perhaps it would be appropriate to institute efforts to amend the Bayh-Dole Act to add an exception so that companies participating in the AIDS Clinical Trials program would have rights to any inventions reduced to practice during the course of the clinical trials with their product.

Arguments could be fashioned for convincing the Congress of the justification. However, the intense pressure to combat AIDS has already caused companies, governmental entities, and grantee institutions to take extraordinary measures in these preliminary stages of research and development. To a certain degree all concerned should press forward with this important work despite the lack of air-tight agreements and protective legislation. However, there are limits that must be observed when there are these enormous resources being committed. Government must be responsive now rather than later if it wants to solidify the strong partnership it is entering into with industry in the development of AIDS therapies and preventions.

Another alternative beneficial to industry would be to have Letters of Understanding providing that the company will have a right of first refusal to a license or an option to a license to practice any invention conceived or reduced to practice in the course of conducting the clinical trial protocol. Such Letters of Understanding would not supercede the terms of the funding arrangements between the NIH and the clinical sites nor conflict with Bayh-Dole, but would protect the interests of the company whose drug or biologic is being tested. If the company prefers to have an option rather than a right of first refusal, it would be advantageous to the company to set forth in its Letter of Understanding the royalty or royalty parameters that it will pay for an invention.

We understand that the NIH has already brokered such a Letter of Understanding with a company and its contract sites. In that instance, the company already had a Collaborative Research and Development Agreement (CRADA) with the NIH and then also entered into a CTA which further referenced the Letter of Understanding.

One of the more noteworthy clinical trials to be sponsored recently by the NIH, namely, the clinical trials for TAXOL, the anti-cancer drug derived from the bark of Pacific yew trees, also involved the use of Letters of Understanding; it further illustrates the flexibility of the NIH in addressing a company/collaborator's concerns.<sup>33</sup> The TAXOL trials were not conducted by DAIDS but by NCI's extramural program; however, the principles at work there are of importance.

In August 1989, NCI was looking for a private sector collaborator with whom it could enter into a CRADA for the development of TAXOL and who was willing to see the product through to licensing by the FDA. NCI had been having difficulty promoting this product because it could not muster an adequate supply of TAXOL for the human trials. NCI began to negotiate with Bristol Myers; however, NCI had no patent rights to offer. The chemist who had discovered TAXOL decades earlier did not patent it and, therefore, it had entered the public domain. What NCI could offer was an exclusive license to its clinical data and the rights to an exclusive market

<sup>33</sup> The Seattle Times, December 16, 1991, at A1; National Institutes of Health/Pharmaceutical Manufacturers Association, Technology Transfer Conference, June 3-4, 1992. Some of background information for this discussion was derived from the article and conference.

for seven years under the Orphan Drug Act. NCI wanted Bristol Myers to sign its standard form of CRADA but Bristol Myers asserted that the form was not appropriate as it contained language concerning patents, royalty payments, and pricing of the final product. Thus, Bristol Myers drafted its own agreement which guaranteed it exclusive use of both past and future clinical data from NCI's extramural investigators.

Even research data obtained from clinical studies do not belong exclusively to the Government.<sup>34</sup> Generally, the terms of awards for grants to the AIDS Clinical Trial Units (ACTUs) state that data produced pursuant to the clinical studies are the property of the clinical sites, subject to the condition that those institutions can only use the data in cooperation with the ACTG. Bristol Myers was concerned about the autonomy of the clinical sites and their ownership rights in the clinical data. Thus, Bristol Myers entered into a separate supplemental agreement or Letter of Understanding with each clinical site to guarantee that human data were properly collected and transmitted to them.

The Government has justified its agreement with Bristol Myers by stating there was a pressing need to get TAXOL to dying patients. A similar argument can certainly be made for AIDS therapies. Thus, there is a precedent for the NIH lending assistance to companies to see that valuable therapies reach the market.

A company should insist upon the negotiation and completion of all Letters of Understanding with the individual clinical sites prior to entering into a CTA with DAIDS. As lawyers, we cannot assure our clients that their rights will be protected without these letters. However, the difficulty with negotiating separate Letters of Understanding with each ACTU is that it could be very time-consuming, particularly for a large scale study. Each institution may have different concerns and internal policies. Further difficulties will arise if, for example, 9 of 10 clinical sites involved agree to a Letter of Understanding and the final site does not. This mechanism puts an onerous burden upon a company that wishes to protect its intellectual property rights and might discourage it from working with the ACTG.

### *(B) Clinical Trial CRADAs*

Another solution for facilitating a collaboration between the ACTG and industry would be by authorizing the use of CRADAs established for the sole purpose of conducting clinical trials.<sup>35</sup> CRADAs which were created pursuant to the Federal Technology Transfer Act of 1986 allow for prospective protection of intellectual property rights.<sup>36</sup> However, the relevant provisions of the Federal Technology Transfer Act pertain only to Federal agencies.<sup>37</sup> Thus, in order to prospectively grant rights in inventions made by an agency's grantees or contractors—in this case, the ACTUs—the Government would have to designate those grantees as part of the NIH and, thereby, a party to the CRADA.

<sup>34</sup> The general rule with respect to technical data is that the Government acquires unlimited rights in noncopyrightable data which are first produced in performance of a Government contract. Federal Acquisition Regulation, 48 C.F.R. §27.404(a). The Government's rights will be of a limited or restricted nature if the data embody a trade secret or are commercial or financial and confidential or privileged and such data were developed at private expense, i.e., not funded entirely by the Government. 48 C.F.R. §27.404(c).

<sup>35</sup> Personal communications with representatives of National Institutes of Allergy and Infectious Diseases.

<sup>36</sup> 15 U.S.C. §§3701-15 (1984 & Supp. 1992).

<sup>37</sup> *Id.* at §3710a(a).

Typically, a clinical trial site is deemed to be independent of the NIH but it might be designated a "component" of the NIH. This has been done, in a different context, with a company that had an ongoing basic research CRADA with the NIH but wished to have its products tested in a clinical trial with the U.S. Army. Thus, the CRADA was amended to set forth that the U.S. Army was a "sister agency" of National Institutes of Allergy and Infectious Diseases. While it may be easier to make such an amendment to include another Federal agency,<sup>38</sup> an analogous type of arrangement might be undertaken to include government grantees and contractors. Perhaps, pressure should be brought to bear on Congress to extend the Federal Technology Transfer Act to include the transfer of rights in inventions made by contractors or grantees of Federal agencies. Otherwise, it would be necessary, in a clinical trial CRADA, to add a proviso that the CRADA would be paramount to funding arrangements between the ACTG and the clinical sites as well as legislation concerning inventions made with Federal assistance.

Grafting CRADA-like provisions covering intellectual property matters into a CTA is still another alternative. If the CTA was so modified, it might have to be approved according to the typical CRADA approval route, meaning that it would have to be reviewed and approved by the Office of the General Counsel at Health and Human Services, the Office of Technology Transfer at NIH, and a CRADA subcommittee. It is by nature a lengthy process. This process should be streamlined for a clinical trial CRADA and thus, may be another way that ACTG could accommodate the concerns of industry.

### (C) "Exceptional Circumstances" Determination

In light of the difficulties of a company attempting to negotiate separate agreements with all of the clinical trial sites conducting its protocol or of completing a clinical trial CRADA, the ACTG might attempt to invoke the very narrow exception under Bayh-Dole by which Federal rights in inventions can be transferred in advance. This exception is pursuant to an "exceptional circumstances" determination.<sup>39</sup> Section 202(a) of Bayh-Dole states that grantees may elect, within a reasonable time after disclosure, to *retain* title to a subject invention; however, under §202(a)(ii), the Federal funding agreement could provide otherwise

in exceptional circumstances when it is determined by the agency that restriction or elimination of the right to retain title to any subject invention will better promote the policy and objectives of this chapter. . . .

One of the objectives of the chapter is "to ensure that the Government obtains sufficient rights in Federally supported inventions to meet the needs of the Government. . . ."<sup>40</sup>

If a Federal agency did determine that its contractor should not be permitted to retain title to any inventions it develops, the agency would be required to file with the Secretary of Commerce, within 30 days after the award of the funding agreement to that contractor, a copy of the agency's determination, together with an analysis justifying that determination.<sup>41</sup> If the Secretary of Commerce then disapproves of the

<sup>38</sup> The U.S. Army is part of the Department of Defense, which is also a Federal agency.

<sup>39</sup> 35 U.S.C. §202(a) (Supp. 1992).

<sup>40</sup> 35 U.S.C. §200 (1984).

<sup>41</sup> 35 U.S.C. §202(b)(1) (1984 & Supp. 1992).

determination, he will so notify the agency and recommend corrective actions.<sup>42</sup> This 30-day window has probably closed for most clinical trials as the Government's arrangements with ACTUs were probably entered into when the ACTG was formed. However, the ACTG could renegotiate its grantee arrangements with the clinical sites and request that such "exceptional circumstances" determination be made prior to contracting in order to combat the widespread AIDS epidemic, an obvious need of the Government. Such action is not entirely without precedent.

The Department of Energy (DOE) has made such an exceptional circumstances determination in the past.<sup>43</sup> It should be noted that the Department of Energy is distinct from other Federal agencies in that it is bound by a statutory patent scheme that vests all rights to inventions made by DOE collaborators in the Government. However, the DOE can agree to waive its rights to such inventions under a similar exception.<sup>44</sup> In one instance, the DOE formed a consortium between the "Big Three" auto manufacturers to develop a battery for electric cars.<sup>45</sup> Pursuant to an exceptional circumstances determination, the DOE waived its rights in any inventions made during the collaboration and further required its contractors, who were battery manufacturers and not themselves parties to the consortium, to assign title to any inventions that they conceived to the automobile manufacturers as well.<sup>46</sup> Obviously, in this example, the exceptional circumstances determination was probably made prior to the formation of the consortium. This exception seems to have been largely motivated by the fact that the consortium agreed to split the cost of the research and development efforts with the DOE.<sup>47</sup>

#### *(D) A New Patent Policy—Legislative Changes*

As set forth above, the Department of Energy deviates from the Government's uniform patent policy. The basis for the DOE's distinct policy is set forth in the Federal Acquisition Regulation. Those regulations state that each Government funding agreement, one of the purposes of which is the conduct of federally funded experimental, developmental, or research work, must contain a "patent rights clause." Absent special circumstances, the patent right clause must provide that the contractor may, after disclosure to the Government within a specified time, elect to retain title to inventions made in performance of work under the contract.<sup>48</sup> The special circumstances include: (i) when an agency's statutory requirements necessitate a different policy,<sup>49</sup> and (ii) when an agency determines that due to exceptional circumstances, restricting or eliminating the right to retain title in any subject invention will better promote the policy and objectives of the Federal patent law and President Reagan's 1983 Memorandum.<sup>50</sup> In the DOE's case, it determined that the agency's existing statutory requirements necessitated a policy different than that identified in the 1983 Presidential Memorandum.

<sup>42</sup> *Id.*

<sup>43</sup> Personal communication with a representative of the Department of Energy.

<sup>44</sup> 35 U.S.C. §202(a) (Supp. 1992).

<sup>45</sup> Personal communication with a representative of the Department of Energy.

<sup>46</sup> *Id.*

<sup>47</sup> *Id.*

<sup>48</sup> 48 C.F.R. §27.302(b) (1991).

<sup>49</sup> *Id.*

<sup>50</sup> 48 C.F.R. §27.302(b) (1991).

dum and President Reagan's 1987 Executive Order No. 12591<sup>51</sup> and the DOE continues to retain title to inventions made by, among others, large, for-profit grantees.

However, the Federal Acquisition Regulation does provide a basis for other Federal agencies taking exception to the Government's patent policy. The AIDS epidemic ought to be considered such an exceptional circumstance.

### *(E) March-In Rights*

Another alternative by which the ACTG could protect a company's intellectual property rights would be for the NIH to invoke its march-in rights to alleviate AIDS.

The Bayh-Dole Act gives the Federal agency under whose funding agreement an invention has been made the right to require the contractor to grant a license to a responsible applicant(s) if the Federal agency determines that such action is necessary to "alleviate health or safety needs which are not reasonably satisfied by the contractor. . . ."<sup>52</sup>

Thus, the industrial partner, in its CTA with DAIDS, could negotiate specifically that the Government, when requested, will invoke march-in rights if an invention made during the performance of the company's protocol is necessary for the company to promote its AIDS therapy and/or if the grantee institution has made it financially or otherwise unfeasible for the company to develop its product. However, it must be pointed out that the Government has never invoked its march-in rights.

## OTHER CONCERNS—CONFIDENTIALITY AND PUBLICATIONS

Two other concerns relating to the proprietary rights of a company in its product that need to be addressed in negotiations with the ACTG are confidentiality and publication rights. The ultimate end-point of an ACTG protocol is a publication. Companies are justifiably concerned that detailed information on its product and the product's formulation should not be disseminated to the public. The FDA is prevented by law from disclosing Investigational New Drug Application(s) (INDs).<sup>53</sup> However, the ACTG is not similarly bound and there is a possibility that protocols could be obtained pursuant to a Freedom of Information Act request. The CTA should be strengthened to state that confidential information provided by the company should not be released to the public.

As for publication of data, it is necessary that publications be carefully monitored to protect the company's potential patent rights. The ACTG has a Publications Policy, but it does not provide for protection of intellectual property rights. Safeguards should be addressed and all concerned with the clinical trial should be required to comply with such an amended Publications Policy.

<sup>51</sup> Presidential Memorandum to the Heads of Executive Departments and Agencies, Subject: Government Patent Policy, 1983 PUB. PAPERS 248 (Feb. 18, 1983); Exec. Order No. 12,591, 3 C.F.R. 220 (1987), *reprinted in* 15 U.S.C.A. §3710 (Supp. 1992). President Reagan's Executive Order No. 12591 states that each agency shall promote the commercialization of the patentable results of Federally funded research by granting to all contractors, regardless of size, the title to patents made in whole or in part with Federal funds in exchange for royalty-free use by or on behalf of the Government.

<sup>52</sup> 35 U.S.C. §203 (1984 & Supp. 1992).

<sup>53</sup> 21 C.F.R. §312.130 (1991).

Similarly, insofar as assessments of the impact of other studies is considered by statisticians of Statistical and Data Analysis Center, this may compromise the confidentiality concerns of a company. Adequate safeguards addressing these concerns should be put in place.

TABLE 1

## Intellectual Property Issues in a Clinical Trial—A Corporate Perspective

- 
- (1) Government should prosecute patent applications diligently
  - (2) Industry must engage in fair and commercially reasonable pricing
  - (3) Product liability protection for AIDS vaccines and therapeutics
- 

TABLE 2

## Legal Framework

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- (1) Bayh-Dole Act—1980
  - (2) 1983 Executive Order
  - (3) Federal Acquisition Regulation (1983)
  - (4) Federal Technology Transfer Act (1986)
- 

TABLE 3

## Concerns of Industry

- 
- (1) Under Bayh-Dole, grantee organization elects to retain title in inventions which could include inventions derived from company's drug or biologic
  - (2) Burroughs-Wellcome situation
  - (3) Adequate protection for patent rights, confidential information and data (confidential information provided by company should not be released to the public and publication of data should be carefully monitored so as to protect company's potential patent rights.)
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TABLE 4

## Solutions or How ACTG Should Address Intellectual Property Issues Directly

- 
- (1) Agree in CTA to assist company in obtaining rights to inventions of employees of DAIDS and/or its grantees
  - (2) Best efforts to obtain rights should be employed by DAIDS
  - (3) Letters of Understanding directly with clinical trial sites
    - (3a) Legislative change to Bayh-Dole to ensure company receives rights for inventions reduced to practice with company's product
    - (3b) Right of first refusal to license or option to license
  - (4) Clinical site agreement—ensuring data properly collected and transmitted, e.g., TAXOL clinical trial
  - (5) Clinical trial CRADA
  - (6) "Exceptional circumstances" under 35 U.S.C. §202(a)(2) of Bayh-Dole
  - (7) Federal acquisition regulation is precedent for finding of *special circumstances* to justify development of special patent policy because of AIDS
  - (8) March-in rights
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