INFORMATION PAPER—SUPPLEMENT & DISCUSSION
March-in Rights Request by KEI to NIH and DoD Pertaining to Xtandi®

APPENDIX A
NIH Response And Copies of Letter Submitted by Congressional Members

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

To be e-mailed to: andrew.goldman@keionline.org

June 20, 2016

Andrew S. Goldman
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009

Dear Dr. Goldman:

Thank you for your January 14 letter and your follow-up correspondence to the Department of Health and Human Services, the Department of Defense, and me requesting that each or both federal agencies (1) exercise its march-in authorities found at 35 U.S.C. § 203, or (2) exercise the federal government's non-exclusive royalty-free government use license for Xtandi® (enzalutamide). Based on the information provided in your letter and follow-up correspondence, and information that is publically available, we decline to initiate a march-in investigation or utilize the government's license in the patents.

More specifically, a federal agency that funded an invention has the right, consistent with 35 U.S.C. § 203(a)(1), to grant a license to a third party if "action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time effective steps to achieve practical application of the subject invention in such field of use." Practical application as defined at 35 U.S.C. § 201 is "...to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms."

As set forth in NIH's prior march-in determinations (1997 Cell Pro; 2004 and 2013 Norvir®; 2004 Xalatan®, see www.ott.nih.gov/policies-reports), practical application is evidenced by the "manufacture, practice, and operation" of the invention and the invention's "availability to and use by the public..." Xtandi® is broadly available as a prescription drug. Your letter states that sales of enzalutamide increased 77% from Fiscal Year 2013 to Fiscal Year 2014 and are projected to increase 51% from Fiscal Year 2014 to Fiscal Year 2015 (from your letter, pages 9-10); however, it provides no information and no information was identified from public sources to suggest that enzalutamide is currently or will be in short supply.

In view of the above information presented in your letter and your follow-up correspondence and public information identified by the NIH, we decline to proceed with the government's march-in authorities at this time or utilize the government's license to the patents. Enclosed for your information is the June 7 Department of Health and Human Services response to Representative Doggett on holding a public hearing.

Sincerely yours,

Francis S. Collins, M.D., Ph.D.
Director

Enclosure

cc: The Honorable Ashton Carter
Secretary of Defense

The Honorable Secretary Burwell
Secretary of Health and Human Services

Union for Affordable Cancer
Treatment (UACT)

THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

JUN 07 2016

The Honorable Lloyd Doggett
U.S. House of Representatives
Washington, D.C. 20515

Dear Representative Doggett:

Thank you for your letter of March 28 expressing your and your colleagues' ongoing concerns about the price of Xtandi® (enzalutamide). I can assure you that Dr. Collins and I share your concerns about the rising costs of drugs and the impact these costs have on Americans' access to life-saving treatments.

In your letter, you encourage the National Institutes of Health (NIH) to hold a public hearing on the use of the Bayh-Dole Act march-in authority for the patented inventions funded by the NIH and U.S. Army that cover Xtandi® (enzalutamide). The NIH considers the application of the statutory criteria for march-in very carefully, according to the process outlined in the statute and implementing regulations at 37 CFR 401.6. At this time, NIH believes this process allows the agency to collect sufficient information to consider the petition without a public hearing.

Over the past decade, the NIH has evaluated three prior march-in requests. The NIH's determinations in these cases, which are publicly available at www.ott.nih.gov/policies-reports, demonstrate how the agency evaluates the evidence regarding the statutory conditions that would justify the exercise of its march-in authority.

The Department of Health and Human Services' goal is to foster a health care system that leads in innovation, delivers affordable, high-quality medicines, and results in healthier people. Thank you for your concern and ongoing leadership as we work on our broader efforts to ensure patients have timely access to innovative, quality, and affordable medications.

If you have additional questions or concerns, please contact Jim Esquea, Assistant Secretary for Legislation at (202) 690-7627. I have sent this response to the co-signers of your letter.

Sincerely,

Sylvia M. Burwell

Congress of the United States
Washington, DC 20515

March 28, 2016

The Honorable Sylvia Mathews Burwell
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Francis Collins, M.D., Ph.D.
Director
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Secretary Burwell and Director Collins:

When Americans pay for research that results in a safe and effective drug, an unreasonably high cost should not limit their access to it. New treatments are meaningless if patients cannot afford them. Therefore, we welcome the recent commitment from Health and Human Services Secretary Sylvia Burwell that the National Institutes of Health (NIH) was "prepared to use its [march-in] authority if presented with a case where the statutory criteria are met . . . ."[1] We strongly encourage the NIH to use its authority to hold a public hearing on the request put forth by certain public interest groups to help establish whether or not these criteria are met in the case of Xtandi (enzalutamide).

The 1980 Bayh-Dole Act gives federal agencies, including the NIH, the authority to license a patent when "action is necessary to alleviate health or safety needs which are not reasonably satisfied"[2] or if the invention is not "available to the public on reasonable terms."[3] Price can be a clear barrier to access for consumers, and despite this law being in place for over 35 years, the NIH has never used this broad and powerful authority to protect consumers from excessive prescription drug prices.

NIH was recently petitioned[4] to exercise these march-in rights on Xtandi, a prostate cancer drug developed at the University of California, Los Angeles UCLA through taxpayer supported research grants from the U.S. Army and NIH grants.[5] The petition states that a Japanese licensee,

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[1] March 2, 2016 letter attached, p. 2
[2] 35 U.S.C. § 203(a)(2)
[3] 35 U.S.C. § 201(f)
[4] Letter from Knowledge Ecology International and the Union for Affordable Cancer Treatment to Secretary Sylvia Mathews Burwell, Department of Health and Human Services, Director Francis Collins, National Institutes of Health, and Secretary Ashton Carter, Department of Defense, regarding Xtandi march-in request (Jan. 14, 2016) (online at http://keionline.org/node/2412)
[5] ClinicalTrials.gov Identifiers NCT00510718 and NCT01091103

Astellas, is charging Americans $129,000 for this drug, which sells in Japan and Sweden for $39,000, and in Canada for $30,000. We do not think that charging U.S. residents more than anyone else in the world meets the obligation to make the invention available to U.S. residents on reasonable terms.

An open and transparent public hearing on Xtandi by the NIH[6] would help to provide insight into NIH's decision-making process on this case. In addition, we think that a public hearing is important to allow the public to engage in a dialogue with the Department of Health and Human Services and NIH in order to better understand its position on the use of march-in to address excessive prices. The NIH granted a hearing in 2004 to probe similar issues in a march-in request pertaining to the prices of Norvir (ritonavir), an antiretroviral marketed by Abbott Laboratories. As a result of the march-in request, the company lowered the price of ritonavir for public payors, including AIDS Drug Assistance Programs (ADAPs) and Medicaid, and expanded its patient assistance programs.[7]

The NIH has a powerful tool to hold drug companies accountable for barriers to access to drugs developed through support of U.S. taxpayers, including price. We look forward to your prompt reply and continuing to work with you to ensure all patients have timely access to innovative, quality, affordable medications.

Sincerely,

LLOYD DOGGETT
United States Representative

BERNARD SANDERS
United States Senator

PETER WELCH
United States Representative

AL FRANKEN
United States Senator

ELIJAH E. CUMMINGS
United States Representative

PATRICK LEAHY
United States Senator

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[6] 37 U.S.C. § 401.6(e)

[7] *Abbott Announces Several Initiatives to Further Enhance Patient Access, Address Community Concerns Regarding Re-Pricing of HIV Drug, Norvir (Ritonavir)* (Feb. 2, 2004), (online at http://www.evaluategroup.com/Universal/View.aspx?type=Story&id=48708)

JAN SCHAKOWSKY
United States Representative

SHELDON WHITEHOUSE
United States Senator

ROSA DeLAURO
United States Representative

ELIZABETH WARREN
United States Senator

MARK POCAN
United States Representative

AMY KLOBUCHAR
United States Senator

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APPENDIX B
Key Points Regarding The Bayh-Dole Act

The Bayh-Dole Act[1] (Act) provides the statutory basis for federal technology transfer activities, including the patenting and licensing of inventions made under federal funding agreements by recipients of those funds. The Bayh-Dole Act was enacted into law on December 12, 1980 and established a uniform patent policy towards universities and non-profits, which were given the right to retain title to inventions made as a result of Federal funding. Industry, especially the small business community, applauded an ownership policy that was applied uniformly on a government-wide basis. Also, the Act encouraged universities to collaborate with industry to promote the utilization of inventions; it favored licensing to small businesses; and, to the extent possible, manufacturing in the United States. The Government, in return, permitted universities to file, at their own expense, patent applications on any inventions they elected to own, with the Government retaining a royalty-free, non-exclusive license to practice the invention world-wide, for government purposes. The Government also retained rights to enforce diligent commercial development of inventions.

The right of the recipient to take title is conditioned upon fulfilling its obligations under the Act. Normally, if the recipient takes title to the invention the government retains a royalty-free, nonexclusive license to the invention for government purposes. The government may make or use the invention that was made under the federal funding agreement. In addition, the government may have the invention made or used for it by other parties as long as these actions are for the government's benefit. The government, however, may not grant licenses for commercial exploitation of the invention—unless it exercises its march-in rights or otherwise has an ownership interest.

If the recipient of the federal funding agreement elects to take title, the recipient must file patent applications, seek commercialization opportunities and report back to the funding agency on its efforts to obtain utilization of the invention. If the recipient of the federal funding declines to take title or fails to report the making of the invention within the time limits provided, the Government may take title to the invention. The recipient may request, however, that the Government permit the recipient's employee-inventor to retain rights to the invention.[2]

The Recipient must report the making of and disclose the invention to the Government within a reasonable time after the Recipient's inventor discloses the conception or making of the

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[1] The Bayh-Dole Act, Pub.L. No. 96-517, 94 Stat. 3019 and codified at 35 USC §§200-212.
[2] 35 US.C. § 202(d).

invention to Recipient's representative responsible for the administration of patent matters. 35 U.S.C. §202(c)(1). The Bayh-Dole Act does not define "reasonable time" but corresponding Federal Acquisition Regulation provisions require reporting of the invention to the Government within 2 months after the inventor reports it to his or her employer.[3]

The Recipient must, in writing, either elect to take title or decline to take title within 2 years after reporting the making of the invention to the Government. 35 U.S.C. §202(c)(2). Depending on the terms of the federal funding agreement, federal agencies may recommend or may require the use of certain forms to report and document the election or non-election of title to the invention. Department of Defense (DoD) agencies normally request the use of the DD Form 882, Report of Invention, although any document will do as long as the required information is present.

If the Recipient elects to take title to the invention, the Recipient must file a patent application within 1 year after election or prior to the occurrence of a statutory bar. 35 U.S.C. §202(c)(3). The patent application should include a statement that the Government has an interest in the invention. 35 U.S.C. §202(c)(6). For example, "The U.S. Government has a paid-up license in this invention and the right in limited circumstances to require the patent owner to license others on reasonable terms as provided for by the terms of [federal funding agreement number] awarded by [name of federal agency].

If the Recipient elects to take title to the invention, the federal agency retains a royalty-free, nonexclusive license to the invention by operation of law. 35 U.S.C. §202(c)(4). However, federal agencies generally require the Recipient to execute a document confirming this license to the Government and may recommend or require use of a particular form. Sample language for the confirmatory instrument follows below. In addition, the confirmatory instrument should identify the title of the invention, patent application serial numbers, patent numbers (if any), filing date and inventors. The confirmatory instrument should be signed by the appropriate representative of the Recipient.

Some Government agencies require that the reporting of inventions be made through "Interagency Edison." Interagency Edison is a web-based system that provides federal funding Recipients and participating federal agencies with the technology to electronically manage extramural invention reporting in compliance with the Bayh-Dole Act. Interagency Edison has been designed by the National Institute of Health's Office of Policy for Extramural Research Administration (OPERA) to streamline the invention reporting process to federal agencies that belong to Edison.[4] Interagency Edison can also be used to generate an invention disclosure and the confirmatory instrument (license to the government) required by the federal funding agreement.

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[3] See Federal Acquisition Regulation Part 27.3.
[4] See the website: www.iedison.gov.

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APPENDIX C
Information on Petitions to and Determinations by NIH Regarding Exercise March-in Rights.
Determination In The Case of Petition of CellPro, Inc., August 1, 1997
NIH Public Meeting on Norvir/Ritonavir March-in Request Mary 25, 2004
In the Case of Norvir Manufactured by Abbott Laboratories, Inc.
In the Case of Xalatan Manufactured by Pfizer, Inc., September 17, 2004
Determination In The Case of Fabrazyme Manufactured by Genzyme Corporation, December 1, 2010
Letter to Dr. C. Allen Black Re 2010 Request to HHS to Exercise its Bayh-Dole March-In Authority on U.S. Patent No. 5,356,804, February 13, 2013
Determination In the Case of Norvir Manufactured by AbbVie, November 1, 2013

There have been several petitions directed to the NIH requesting that DHHS exercise its march-in authority, including a previous request by KEI, the Requestor in this action. NIH has declined to exercise march-in rights and has denied all requests it has received. These petitions related to FDA approved pharmaceuticals that were funded, at least in part, by NIH, and all were commercially available. Below are short summaries of three petition arguments and outcomes followed by the NIH determinations for each march-in request made to NIH.

The petitions most closely related to the instant Request are those regarding Norvir, a treatment for HIV/AIDS, and Xalatan, a treatment for glaucoma. The Xalatan case is especially relevant because the petition raised the issue of disparate price between the U.S. and foreign countries

CellPro. On March 3, 1997, CellPro, Inc. filed a petition with the Secretary of Health and Human Services requesting that the government exercise its march-in rights and require the patent owner, Johns Hopkins University (JHU) and Baxter Healthcare Corporation (licensee) to license patented stem cell technology to CellPro or, alternatively, for the government to grant the license itself. JHU had licensed the invention to Becton Dickinson, which sublicensed to Baxter Healthcare.

CellPro alleged that exercise of march-in rights was necessary to alleviate health or safety needs as it had been enjoined from selling its own FDA-approved stem cell invention and the JHU-Baxter device was not yet approved by the FDA and on the market. The injunction imposed against CellPro was a result of a patent infringement suit in which the court found that CellPro

infringed two of the four JHU patents in question.[1] The inventions claimed in the JHU patents arose from research conducted with NIH funding.

The Director of NIH determined that the exercise of march-in procedures was not warranted and issued a decision denying CellPro's petition.[2] The main issues before the NIH were (1) whether JHU and its licensee, Baxter, were taking effective steps, within a reasonable period of time, to achieve practical application of the inventions; and (2) whether there existed a health or safety need which was not reasonably satisfied by JHU and Baxter. With regard to the first issue, NIH concluded that JHU and Baxter were taking appropriate steps to achieve practical application of the invention as the invention had been steadily moving forward in laboratory and clinical trials and Baxter was pursuing an active application for FDA approval.

Regarding the second issue, NIH stated that it had no information to document that either party's invention was better than standard techniques and would not substitute its judgment for that of clinicians and patients. NIH concluded that CellPro's invention did fulfill a heath need and was the only such invention currently for sale and available. But NIH also determined that JHU and Baxter had addressed this issue by agreeing to refrain from enforcing some of their rights against CellPro—allowing the continuing sale of CellPro's technology until Baxter received FDA approval. In addition, Baxter agreed to ensure that patient access to the technology through clinical trials would continue to the fullest extent possible.

CellPro and Baxter had engaged in unsuccessful license negotiations. This was a consideration in NIH's determination that it was inappropriate to intercede in the matter, especially for the purpose of ensuring CellPro's commercial future and assisting it to obtain more favorable commercial terms than it otherwise could obtain from the court or Baxter. NIH realized such intercession in the marketplace could bring about long-term and potentially adverse effects on the innovation, economic and social policies of federally funded research programs.

Norvir. On July 2, 2004, NIH rendered another march-in rights decision regarding the drug, Norvir, an HIV/AIDS drug owned and manufactured by Abbott Laboratories. Norvir was developed partially with NIH funding. Members of Congress and the public "petitioned" NIH by letter and through public meetings to exercise march-in rights by arguing that Norvir's expensive price meant that practical application was not being achieved. Under 35 U.S.C. § 201(f), "practical application" means that the invention is being utilized and that its benefits are available to the public on reasonable terms. NIH concluded that manufacture and utilization of the drug for more than eight years met the practical application requirement. The Petitioner

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[1] U.S. Patent Nos. 4,714,680 (issued Dec. 22, 1987), entitled "Human Stem Cells" and 4,965,204 (issued Oct. 23, 1990), entitled "Human Stem Cells And Monoclonal Antibodies."

[2] National Institutes of Health, Office of The Director, Determination In the Case of Petition of CellPro, Inc. at http://www.nih.gov/news/pr/aug97/nihb-01.htm.
http://www.ott.nih.gov/sites/default/files/documents/policy/cellpro-marchin.pdf

did not present any evidence that health or safety needs were not being met. Again, NIH declined to exercise march-in rights in consideration of long-term effects on the market, stating that the "extraordinary remedy of march-in is not an appropriate means of controlling prices."[3]

Xalatan. The last case, involving Pfizer's glaucoma drug Xalatan, was similar to the Norvir case in that it concerned pricing and involved the same basic arguments for march-in. Xalatan was invented at Columbia University and exclusively licensed to Pfizer. It was FDA approved and available in the United States, Canada and Europe but the price of the drug was higher in the United States than in either Canada or Europe. NIH concluded that the invention had achieved practical application by manufacture, was widely prescribed as both a first and second-line treatment. All health and safety needs had been satisfied by Pfizer. NIH determined on September 17, 2004 that it would not exercise march-in rights and that pricing was an issue for Congress to address if it chose to, especially considering the global implications of disparate prices in foreign countries.[4]

[3] National Institutes of Health, Office of The Director, Determination In the Case of Petition of Norvir at http://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir2013.pdf and Position Paper, http://www.ott.nih.gov/sites/default/files/documents/policy/March-In-Norvir.pdf

[4] National Institutes of Health, Office of The Director, Determination In the Case of Petition of Xalatan at http://www.ott.nih.gov/policy/March-In-xalatan.pdf. Position paper can be found at http://www.ott.nih.gov/sites/default/files/documents/policy/March-in-xalatan.pdf

NATIONAL INSTITUTES OF HEALTH
OFFICE OF THE DIRECTOR

DETERMINATION
In the Case of
PETITION OF CELLPRO, INC.

The National Institutes of Health (NIH) has determined that the initiation of march-in procedures, as requested under the petition outlined below, is not warranted at this time. NIH retains jurisdiction over the instant proceedings until such time as a comparable alternative product becomes available for sale in the United States.

The CellPro Petition

On March 3, 1997, CellPro, Incorporated (CellPro) filed a petition with the Secretary of Health and Human Services (Secretary) requesting that the Government exercise march-in rights under the Bayh Dole Act (Act), 35 U.S.C. §§ 202-212, in connection with certain patents owned by The Johns Hopkins University (Hopkins) and licensed first to Becton-Dickinson and then to Baxter Healthcare Corporation (Baxter).[1] As discussed in greater detail below, the march-in provision of the Act authorizes the Government, in certain circumstances, to require the contractor (or grantee) or its exclusive licensee to license a Federally-funded invention to a responsible applicant on reasonable terms, or to grant such a license itself. CellPro asserts that such action is necessary to alleviate health or safety needs that have arisen because the United States District Court for the District of Delaware (Court) has found the stem cell separation device developed by CellPro, the Ceprate SC, to infringe two of the patents in question and has enjoined its sale.[2] Alternatively, CellPro asserts that march-in is warranted because Hopkins and Baxter have failed to take reasonable steps to commercialize the technology. At the present time, CellPro is the only company that has an FDA-approved device commercially available.

The Department of Commerce regulations implementing the Act are set forth at 37 CFR § 401.6. According to § 401.6(b):

[w]henever an agency receives information that it believes might warrant the exercise of march-in rights, before initiating any march-in proceedings, it shall notify the contractor in writing of the information and request informal written or oral comments from the contractor, as well as information relevant to the matter.

The regulations provide that "the agency shall, within 60 days after it receives the comment, either initiate the procedures below or notify the contractor, in writing, that it will not pursue march-in rights on the basis of the available information." Id. Pursuant to § 401.6, the NIH, which has the delegated authority to make the march-in determination in this case, notified Hopkins of the petition and requested

comment. Hopkins made its initial response on May 7, but in the interim, CellPro had made an additional submission to which Hopkins sought to respond. In sum, CellPro made supplemental filings on April 24, May 8, May 28 and July 2. After its initial response on May 7, Hopkins made supplemental filings on May 19, June 2 and July 2. Because the parties continued to make submissions and insist on the right to comment on the submissions of the other party, the NIH informed the parties that the 60 days set forth in the regulations for a determination by the agency would be calculated from June 2nd, but agreed to review and consider any submissions made by the parties through July 2.[3]

The administrative record in this matter consists of the submissions of the parties, letters from universities, corporations, members of Congress, and other members of the public on this issue, as well as other pertinent materials obtained by the NIH.

Statutory Background and Criteria

The stated policy and objective of the Bayh-Dole Act is:

to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.

Act at § 200. Toward this goal, the Act addresses not only rules governing the licensing of Government-owned inventions, but also addresses Federal contractors'[4] rights to elect title to inventions made with Federal funding. In giving Federal contractors the right to elect title to inventions, Congress altered the preexisting scheme under which the funding agency generally owned patentable inventions made with Federal support unless the contractor obtained a waiver. Congress believed that this change would promote the utilization and commercialization of inventions and would harmonize Federal patent policies. See Senate Rep. No. 96-480 at p.3.

In giving contractors the right to elect title to inventions made with Federal funding, the Act also includes various safeguards on the public investment in the research. For example, the Federal agency retains 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. See 35 U.S.C. § 202(c)(4). In addition, the Act includes march-in rights, which provide a Federal agency with the authority in certain, very limited circumstances, to make sure that a federally funded invention is available to the public. Section 203(1) states:

With respect to any subject invention in which a small business firm or nonprofit organization has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such--

a. action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;
b. action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;
c. action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
d. action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204.[5]

Jurisdiction

In its submissions, Hopkins suggested that NIH did not have jurisdiction in this matter. CellPro disagreed. It is our conclusion that NIH has jurisdiction to determine whether to exercise march-in with respect to the patents in question. The patents which were found by the Court to be valid and infringed are U.S. Patent Nos. 4,714,680 ('680 patent) and 4,965,204 ('204 patent). Documentation submitted by Hopkins clearly establishes that the inventions claimed in these patents were funded by the NIH. For instance, with regard to the '680 patent, Hopkins submitted to the NIH a letter dated October 4, 1984, notifying the NIH that Hopkins had elected title to the invention. In addition, Hopkins provided annual utilization reports filed during the 1980's and early 1990's, and a license from Hopkins to the U.S. Government, which expressly acknowledges that "the invention was made in the course of research supported by the DHHS."[6] Since the inventions were funded by the NIH, as acknowledged by Hopkins well before the patent dispute with CellPro arose, there is a clear presumption of jurisdiction by

the NIH, and Hopkins has not submitted sufficient evidence to rebut that presumption.

Decision

The NIH has evaluated the administrative record with regard to two prongs of the statutory criteria, 35 U.S.C. § 203(1)(a) and (b). The NIH has examined whether, (1) Baxter has failed to take, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject inventions; and, (2) there exists a health or safety need which is not reasonably satisfied by Hopkins or Baxter.[7] Based on these criteria and the available information, march-in is not warranted at this time.

Practical Application of the Subject Inventions

Practical application is defined under 37 C.F.R. § 404.3(d) as "to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms." The administrative record demonstrates that Hopkins and Baxter have clearly met this standard.

This technology was originally developed in the laboratory of Dr. Curt Civin at Hopkins and first published in 1984. Hopkins filed for patent protection and was awarded four patents, the first of which issued in 1987. The technology was first exclusively licensed to Becton-Dickinson & Co. (BD). BD began marketing the first anti-CD34 antibody in 1985 and has sold anti-CD34 antibodies worldwide ever since. Since BD was only interested in the diagnostic applications, the company exclusively sublicensed therapeutic rights to Baxter. Baxter began development of a therapeutic system and sublicensed rights to Applied Immune Sciences (now part of RPR Gencell) and Systemix (now part of Novartis). Baxter also held licensing discussions with CellPro, but no license agreement was signed.

By late 1991, Baxter had developed a prototype stem cell selection device. In 1992, Dr. Civin began clinical trials with the device, and Baxter started its own clinical trials in 1993. In January 1995, Baxter's Isolex 300 System received regulatory approval in Europe (CE Mark of Conformity for Medical Devices). In the United States, Baxter's systems have been installed in numerous transplant centers over the past three years; the Baxter device has been used in clinical trials to process peripheral blood and bone marrow for hematopoietic reconstitution in patients. On February 24, 1997, Baxter filed for Pre-market Approval (PMA) of its Isolex 300SA System.[8] In addition to effectively licensing and developing the technology, Hopkins, BD and Baxter have aggressively defended the patents in court. In 1994, the three parties joined in a suit against CellPro for infringement of the Civin patents.

Accordingly, NIH concludes that Hopkins and Baxter have taken effective steps to achieve practical application, as demonstrated by Hopkins' licensing, Baxter's manufacture, practice, and operation of the Isolex 300, and the device's availability to and use by the public to the extent permitted at this time under applicable law (i.e., foreign sales as well as widespread clinical research use in the U.S.). With regard to FDA approval and commercial sale of the Baxter Isolex 300 in the United States, the administrative record indicates that Baxter is vigorously pursuing an active application. Based on these facts, we conclude that Hopkins and Baxter have met the statutory and regulatory standard for practical application.

Health or Safety Needs

The question of whether the CellPro Ceprate SC fulfills health or safety needs not reasonably satisfied by the Baxter Isolex 300 has been the central inquiry and priority of the NIH in evaluating CellPro's petition for march-in. In this regard, we note the considerable debate among scientists and clinicians as to whether immunoselection of stem cells with selection devices prior to transplantation provides a clinically significant benefit to patients over standard hematopoietic transplantation techniques. The clinical benefit upon which the CellPro Ceprate SC device was approved by FDA consisted of a reduction of infusional toxicity associated with the administration of bone marrow prepared with standard techniques.[9] To date, neither party has presented to the Biological Response Modifiers Advisory Committee any studies documenting that cell separation devices improve stem cell engraftment, disease-free survival, or overall survival.[10] Thus, it is premature for either Baxter or CellPro to claim patient benefits (other than a decrease in infusional toxicities) from stem cell isolation and purification, T-cell, lymphocyte, and tumor cell purging, or other claimed uses.

It is equally premature, and inappropriate, for NIH to substitute its judgment for that of clinicians and patients seeking to avail themselves of an FDA-approved medical device. The FDA has determined that the Ceprate SC is safe and effective for selecting stem cells from autologous bone marrow for hematopoietic reconstitution. Thus, to the extent that the Ceprate SC is the only device that is available for sale in the United States for this purpose, it fulfills a health need for those who wish to use it, until such time as a comparable alternative product becomes available for sale.[11]

As explained more fully below, the administrative record demonstrates that Hopkins and Baxter have taken appropriate steps to reasonably satisfy this need. First, they have refrained from enforcing patent rights to the full extent of the law in order to allow the continuing sale of the Ceprate SC until the Baxter product is approved for sale by the FDA. Second, they have pledged to ensure that the Baxter product is as widely available as possible through clinical trials, and to ensure patient access to the fullest extent possible.

(1) Continuing Sale of CellPro Device

In deference to the health need fulfilled by the CellPro device in the absence of an FDA-approved alternative, Hopkins and Baxter have refrained from enforcing their patent rights to the full extent of the law. Specifically, they modified a proposed order of injunction filed for consideration in the patent litigation in Federal District Court. The Order issued by the Court on July 24, 1997 states, in pertinent part:

CellPro may continue to make, have made, use and sell SC Systems and disposable products (including the 12.8 antibody) for use with SC Systems, within the United States, until such time as an alternative stem cell concentration device, manufactured under a license under the >204 and >680 patents, is approved for therapeutic use in the United States by the United States Food and Drug Administration . . . and for a period of three months thereafter.

Order at p 5. In addition, certain price and volume restrictions contained in the Court's Order specifically do not apply to the provision of products solely for use in clinical trials. Order at pp. 5, 7.

CellPro argues vigorously, however, in documents filed prior to the entry of the Court's Order, that the terms of the proposed order, most specifically the requirement of payments to Baxter for sales of CellPro product, would force CellPro out of business and result in the loss of availability of the CellPro device.

First, we rely on the Court's finding that it is unlikely that the terms of the Order will result in the loss of availability of the CellPro product.[12] This issue was specifically before the Court, supported by an exhaustive factual record resulting from years of litigation. Although NIH is determining whether to open a fact-finding proceeding, as opposed to conducting one, we also found no convincing evidence that CellPro will be unable to supply patients with its product under the terms of the Court Order. The terms of the Order may be unpalatable to CellPro, but CellPro need only operate under those constraints pending a decision on its appeal of the Court's adverse verdict on infringement. The Court specifically found that CellPro "possesses adequate cash reserves to allow it to continue operations during the pendency of its appeal," Memorandum Opinion at p. 24, and determined that it would most likely be in CellPro's interest to continue operations pending the outcome of the appeal. Moreover, the Court has retained jurisdiction and invited the parties to apply to the Court for modification of the terms of the injunction, specifically, the payment of incremental profits to Baxter, if the amount determined by the Court "either provides inadequate relief or works an injustice inconsistent with equitable principles." Id.

Second, the loss of availability of the CellPro product is relevant to the "health need" criteria only during the period prior to FDA approval and availability for sale of a comparable alternative product. In petitioning NIH to open a separate

proceeding on this matter, CellPro argues that its continuing viability and success, even beyond FDA approval of a comparable alternative, should be a matter of concern to the NIH because CellPro has developed and is marketing an important health care product. Invoking our prior caveat as to the investigational nature of these devices, we concur that, as a general matter, NIH supports the development and success of the biotechnology industry. It is indeed very important to the NIH that biotechnology and pharmaceutical companies thrive and compete in order to bring new health care products to the public. Developing and commercializing such products out of federally-funded research is the foundation and essence of the Bayh-Dole Act.

We are wary, however, of forced attempts to influence the marketplace for the benefit of a single company, particularly when such actions may have far-reaching repercussions on many companies' and investors' future willingness to invest in federally funded medical technologies. The patent system, with its resultant predictability for investment and commercial development, is the means chosen by Congress for ensuring the development and dissemination of new and useful technologies. It has proven to be an effective means for the development of health care technologies. In exercising its authorities under the Bayh-Dole Act, NIH is mindful of the broader public health implications of a march-in proceeding, including the potential loss of new health care products yet to be developed from federally funded research.

On balance, we believe it is inappropriate for the NIH to intercede in this matter to ensure CellPro's commercial future. Viability and success in the private sector is appropriately governed by the marketplace, and significantly influenced by management practices and decisions. CellPro had the opportunity to license the invention from Baxter but decided against doing so, and instead risked patent infringement litigation. It would be inappropriate for the NIH, a public health agency, to exercise its authorities under the Bayh-Dole Act to procure for CellPro more favorable commercial terms than it can otherwise obtain from the Court or from the patent owners. CellPro's commercial viability is best left to CellPro's management and the marketplace.

(2) Reasonable Steps to Ensure Widespread Availability of Baxter's Product

Hopkins and Baxter have also pledged to reasonably satisfy any health need created by the loss of the CellPro product in the unlikely event that patient access to this technology is restricted before a comparable alternative product is approved by the FDA and becomes available for sale.

In several of its submissions to NIH, and in a letter from Baxter CEO Vernon Loucks to Secretary Donna Shalala, Baxter committed to ensuring there would be no gap in patient access to stem cell separation technology. Baxter committed to installing its device free of charge at any site from which CellPro might withdraw, and to provide that site with the same level of support on the same terms as

CellPro. Baxter also committed to obtaining all clinical and regulatory approvals necessary to place the Isolex system into operation as soon as possible.

CellPro asserted that Baxter is unable to fulfill this pledge; however, neither party submitted evidence sufficient for a definitive determination, and it would be premature for the NIH to act based on Baxter's failure to accomplish what events have not yet required it to do. In any event, we believe the likelihood of Baxter having to substitute devices in order to ensure patient access is remote, as discussed above. Nevertheless, pending FDA approval and availability for sale of a comparable alternative product, NIH will continue to monitor the situation and will retain jurisdiction to initiate march-in without the filing of a new request, in the event that health needs are not being reasonably satisfied.

Conclusion

The NIH has determined not to initiate proceedings to pursue march-in rights on the basis of the available information. NIH has examined the criteria of 35 U.S.C. § 203(1)(a) and (b) and found that march-in is not warranted under either criteria. Specifically, the NIH has determined that Hopkins and Baxter have taken, or are expected to take within a reasonable time, effective steps to achieve practical application of the applicable patents, as demonstrated by Hopkins' licensing activities and Baxter's manufacture, practice, and operation of the Isolex 300, as well as the pending applications for FDA approval. NIH also finds that the available information fails to demonstrate an unmet health need that is not reasonably satisfied by Hopkins and Baxter.

The NIH will continue to monitor issues related to patient access to the CellPro or Baxter devices during the period prior to FDA approval and availability for sale of a comparable alternative device.

/s/

_____

Harold Varmus, M.D.
Director, NIH

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[1] These patents are: U.S. Patent No. 4,965,680; U.S. Patent No. 5,130,144; U.S. Patent No. 5,035,994 and U.S. Patent No. 4,965,204.

[2] The Order for Permanent Injunction and Partial Stay of Injunction (Order), entered July 24, 1997, includes a partial stay allowing CellPro to continue selling its device under certain restrictions. CellPro has indicated that it intends to appeal the Court's ruling.

[3] Hopkins made an additional submission July 29, which was not considered by NIH.

[4] Defined in the Act as "any person, small business firm or nonprofit organization that is a party to a funding agreement," Act at § 201(c). In 1983, President Reagan issued a memorandum instructing all Federal agencies, to the extent not prohibited by law, to grant all recipients the same right to their inventions as the Bayh-Dole Act provided small businesses and nonprofit institutions.

[5] The legislative history to the Act indicates that Congress anticipated that third parties, such as CellPro in this case, would be likely to inform the Government of the possible need for march-in. However, it is clear that march-in remains a purely government authority. Senate Report No. 96-480 states that:

"[m]arch-in" is intended as a remedy to be invoked by the Government and a private cause of action is not created in competitors or other outside parties, although it is expected that in most cases complaints from third-parties will be the basis for the initiation of agency action.

[6] Although these documents relate specifically to the '680 patent, the '204 patent states that it is a divisional application of the application, serial number 670,740 (the '740 application), from which the '680 patent issued. The claims in the '204 patent are, therefore, based on the original disclosure that was contained in the '740 application, as to which Hopkins had elected title. The other two patents also involved in the patent litigation, U.S. Patent Nos. 5,035,994, and 5,130,144, also issued from divisional applications of the '740 application.

[7] The two other prongs are clearly not relevant. Subparagraph (c) narrowly applies to "public use" required by particular laws. CellPro has not claimed any such law to be applicable in the present case, nor does NIH believe any to be applicable. Subparagraph (d) authorizes march-in when an exclusive licensee of a subject invention has failed to agree (or obtain a waiver of such requirement) that any products embodying the invention or produced through the use of the invention will be manufactured substantially in the United States. Baxter has agreed to manufacture substantially in the United States.

[8] CellPro has argued that the NIH should distinguish between the Isolex SA, an earlier, less automated device, and the Isolex 300i, Baxter's current fully-automated device. The current PMA application to FDA relates to the Isolex SA device. As is customary, the FDA recently discussed the Baxter PMA application for the 300SA device with the Biological Response Modifiers Advisory Committee (July 24, 1997). The majority of the committee members (13 out of 16) voted that the SA device yields an enriched cell population that produces successful engraftments. Thus, NIH finds that the Isolex SA and the 300i have comparable functions for the purpose of this determination.

[9] See, Transcript, FDA Biological Response Modifiers Advisory Committee meeting, February 28, 1996; Package Description, Ceprate SC Stem Cell Concentration System (December 6, 1996).

[10] Transcript, FDA Biological Response Modifiers Advisory Committee meeting, February 28, 1996. At that public meeting, Dr. Richard Champlin, MD Anderson Cancer Center, introducing the CellPro device on behalf of CellPro, stated to the Committee, "[a]gain, one has to remember this is not a treatment for cancer. This is a means to enrich stem cells for a variety of purposes. It has again been shown to be reproducible, safe, and effective for that purpose. And this technology is really critical to allow us to develop the field in a number of other very important applications." Transcript at pp. 21-22.

[11] The Baxter Isolex 300 constitutes such a comparable alternative product. Both the Isolex 300 and the Ceprate SC devices are used in clinical research to isolate and purify stem cells from either bone marrow or peripheral blood, in preparation for stem cell transplantation. Both are under investigation for either autologous (patient's own) or allogeneic (donor) transplantations. We find that performance differences alleged by both parties primarily affect convenience of use, and do not alter the public health impact at issue here.

[12] According to the Court in its Memorandum Opinion at p. 23, "[a]fter evaluating the parties' arguments, and their accompanying declarations, the court finds that in the absence of a conclusive statement from CellPro executives that it will discontinue operations, it has failed to establish that a highly speculative risk of shutdown during the pendency of its appeal to the Federal Circuit outweighs the harm suffered by plaintiffs as the result of CellPro's willful infringement." Nonetheless, the Court modified one of the terms of the injunction, as proposed by Hopkins and Baxter, to require CellPro to pay 60 percent of its incremental profit from infringing sales, as opposed to the 100 percent proposed by Hopkins and Baxter.

FOR RELEASE
Friday, August 1, 1997

Anne Thomas
(301) 496-4461

NIH Director Harold Varmus, M.D., today denied the petition of CellPro, Inc. (CellPro) that the NIH initiate "march-in" procedures under the Bayh-Dole Act in order to give CellPro a license to certain patents owned by the Johns Hopkins University and licensed to Baxter Healthcare Corporation (Baxter).

CellPro asserted that march-in was necessary to alleviate health needs that arise because a Federal District Court found the stem cell separation device developed by CellPro to infringe the patents. The Court has issued an order in that case allowing CellPro to keep its product on the market until an alternative is approved by the Food and Drug Administration and made available for sale.

Dr. Varmus concluded that the initiation of march-in procedures is not warranted based on the available information, but that the NIH will continue to monitor the situation until a comparable alternative product becomes available for sale in the United States. Although the petition was originally sent to DHHS Secretary Donna Shalala, the authority for march-in is delegated to the head of the funding agency, in this case, Dr. Varmus at the NIH.

"The patient care implications of this matter were our first priority and concern," said Dr. Varmus. "Our review indicated that patient needs would be met as long as one or the other cell separation device is available to people in treatment or clinical research programs. Since both devices are currently available under the terms of the Court Order, I do not believe march-in proceedings are warranted." Dr. Varmus added, "The NIH will continue to follow the situation to ensure that patient access to this technology is not compromised."

The NIH recognizes that its decision today will not resolve the legal dispute between CellPro and Baxter, which has been the subject of complex patent litigation. It is the position of the NIH that these companies have full power and authority to resolve this dispute on their own. The NIH has encouraged and will continue to encourage them to negotiate a resolution.

For more information, please read the accompanying backgrounder at (http://www.nih.gov/news/pr/aug97/niha-01.htm). The full text of the determination is available via the Internet at (http://www.nih.gov/news/pr/aug97/nihb-01.htm) or through the NIH Office of Communications at (301) 496-8740.

MEDIA BACKGROUND

CellPro, Inc. Petition to Invoke "March-In" Rights

August 1997

On March 3, 1997, legal representatives of CellPro, Inc. (CellPro) asked the U.S. Secretary of Health and Human Services to invoke Federal "march-in" rights under the Bayh-Dole Act of 1980 with regard to certain inventions made by Johns Hopkins University (JHU) and licensed to Baxter Health Care Corporation (Baxter). The inventions relate to stem cell technology. CellPro submitted its petition after a finding of willful infringement by the U.S. District Court for the District of Delaware.

NIH has prepared the following background information to assist the media in reporting on this matter.

1. What are the Government's "march-in" rights under Bayh-Dole?

The Bayh-Dole Act of 1980 was a patent reform effort designed to harmonize Federal patent policy and to promote the effective commercialization of government-funded research. By strengthening confidence in patent rights and providing a uniform national policy, the Act encourages universities, small businesses and private industry to invest the resources necessary to develop and commercialize inventions supported by public dollars.

Many health care products and services are brought to the market as a result of the patent and exclusive license authorities in the Bayh-Dole Act, which protect private sector investment in costly clinical development and FDA approval processes.

Under the Act, recipients of Federal funding have responsibility for the patenting and licensing new discoveries arising out of publicly funded research. However, the Act reserves certain rights for the funding agency, including "march-in." March-in allows a funding agency to require the grantee, contractor, or its licensee to grant a license on reasonable terms to a responsible applicant. The statute and its implementing regulations provide that an agency may exercise march-in if the agency finds that:

- action is necessary because the grantee or its licensee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the invention;
- action is necessary to alleviate health or safety needs which are not reasonably satisfied by the grantee or its licensee;

- action is necessary to meet requirements for public use as specified by Federal regulations and such requirements are not reasonably satisfied by the grantee or its licensee; or
- action is necessary because the licensee has failed to obtain certain waivers required by the law.

CellPro's petition was assessed under the first two criteria.

2. How did the Director of NIH make this decision? What does the decision mean?

Dr. Harold Varmus, Director of the NIH, has the delegated authority to make a march-in determination as the invention at issue was made with NIH funding. NIH evaluated whether march-in proceedings were warranted based on the statutory criteria. NIH considered the submissions of CellPro and JHU, letters from Members of Congress and the public, and other pertinent material. The Director determined that a march-in proceeding was not warranted. Neither JHU, the grantee, or Baxter, the licensee, will be required to grant a license for the disputed stem cell technology to CellPro.

3. Did the Secretary, HHS or the Director, NIH receive any public comments about the march-in petition and the technologies involved? Are the submissions of the parties available to the public?

Both the Secretary and the Director received numerous letters in support of and in opposition to the march-in petition. Comments were received from Congressional representatives, universities, patient advocacy groups, and interested members of the public. All pertinent communications to the Department were taken into account.

The materials, including the submissions of the parties, will be available for public inspection in the Freedom of Information Reading Room on the NIH campus. For more information, please call the Reading Room at (301) 496-8740 between the hours of 8:30 a.m. and 5:00 p.m. EST.

4. Is there a health threat to patients?

Both the CellPro Ceprate SC and the Baxter Isolex 300, the stem cell technologies in dispute, are currently available to patients either as licensed products or under clinical research protocols. The injunction recently issued by the federal court does not change this. Baxter has committed to ensuring that there will be no gap in patient access to stem cell technology as a result of the injunction. Should CellPro choose to withdraw its Ceprate device from any clinical sites, Baxter has committed to installing their Isolex device in its place. We intend to hold Baxter to these pledges and expect that JHU and Baxter, together, will ensure that there is no threat to patients.

NIH will continue to monitor patient access to the CellPro and Baxter devices during the period prior to approval of a comparable alternative device.

5. The FDA Biological Modifiers Advisory Committee recently met to discuss Baxter's premarketing approval application for the Isolex 300. What is the result of that meeting?

At its July 24 meeting, the Biological Modifiers Advisory Committee (BMAC) discussed Baxter's premarketing approval (PMA) application for the use of the Isolex 300 in concentrating certain stem celcl from peripheral blood to restore the bone marrow in autologous transplants. A majority of the BMAC members found that the data presented adequately illustrated that the device yields a purified cell population, allowing effective transplantation and engraftment. The FDA will take the comments of the BMAC under advisement when making its determination on Baxter's PMA.

NIH will follow FDA activities as part of its effort to monitor patient access to the CellPro and Baxter devices.

NIH Public Meeting on Norvir/Ritonavir March-in Request
May 25, 2004

Agenda

Introductory Remarks by Dr. Mark Rohrbaugh

Written Comments Received:

- Senator Birch Bayh
- Robert Huff, Editor, GMHC Treatment Issues
- Norman J. Latker, former Patent Counsel, HEW
- John Erickson, President & CSO, Sequoia Pharmaceuticals
- Dan Ravicher, Executive Director, Public Patent Foundation
- C. Peter Magrath et al., National Association of State Universities and Land Grant Colleges, Association of American Universities, and American Council on Education
- Carl E. Gulbrandsen, Managing Director, Wisconsin Alumni Research Foundation
- Katharina Phillips, Council on Governmental Relations
- Patricia Harsche Weeks, Immediate Past President, Association of University Technology Managers
- Joseph P. Allen, President, National Technology Transfer Center
- Heather L. Mason, Vice President, Pharmaceutical Specialty Operations, Abbott Labs
- Benjamin Young, OHHP, Organization of Healthcare Providers
- Lynda Dee, Co-Chair, AIDS Treatment Activists Coalition, Drug Development Committee
- Julie Britton Haden, West Virginia Coalition for People with HIV/AIDS
- Rhonda Connard and Amanda Lowther, Co-Coordinators, Covenant House AIDS Program
- Michael Weinstein, President, AIDS Healthcare Foundation
- Stephan E. Lawton, Vice President & General Counsel, BIO
- David D. Ho, Director & CEO, The Aaron Diamond AIDS Research Center
- David Gollaher, President & CEO, California Health Care Institute
- David Miller, President, iBio™
- David Halperin, Attorney Counselor
- James Love, President, Essential Inventions, Inc.
- Jerome Reichman, Bunyan S. Womble Professor of Law, Duke University School of Law

PUBLIC MEETING

National Institutes of Health - Building 50
May 25, 2004

9:00	**INTRODUCTION**
9:05	The Honorable Birch Bayh
9:20	Ted Poehler, Ph.D., Vice Provost for Research, Johns Hopkins University, American Association of Universities
9:35	Daniel Ravicher, Executive Director, Public Patent Foundation
9:50	John Erickson, President & Chief Scientific Officer, Sequoia Pharmaceuticals
10:05	Robert Huff, Editor, *Treatment Issues*, Gay Men's Health Crisis, NYC
10:20	**BREAK**
10:30	Norman J. Latker, former Patent Counsel, Department of Health, Education and Welfare
10:45	James Love, President, Essential Inventions, Inc.
11:00	Andrew Neighbour, Board Member and Chair, Intellectual Property Committee, Council on Governmental Relations
11:15	Jerome Reichman, Bunyan S. Womble Professor of Law, Duke University School of Law
11:30	Benjamin Young, M.D., Ph.D., Organization of Healthcare Providers
11:45	Jeff Leiden, M.D., Ph.D., President and Chief Operating Officer, Pharmaceutical Products Group and Chief Scientific Officer, Abbott Laboratories
12:00	**ADJOURN**

INTRODUCTORY REMARKS

Welcome . . .

My name is Dr. Mark Rohrbaugh and I am the Director of the Office of Technology Transfer at the NIH.

Seated next to me is my Deputy Director, Dr. Bonny Harbinger.

Doris Campos-Infantino, the Deputy Ombudsperson for the National Institutes of Health, will be serving as the moderator for this public meeting.

This public meeting is being held pursuant to requests from various constituencies that the Government exercise its march-in rights under the Bayh Dole Act in connection with patents owned by Abbott Laboratories. The constituencies expressed concern over the price of ritonavir (sold under the tradename Norvir), which is covered by these patents and marketed by Abbott for the treatment of patients with HIV/AIDS.

The purpose of this public meeting is to give us an opportunity to listen to comments from representatives of constituencies and to hear various points of view. These comments and viewpoints then will be considered by the NIH in making the decision of whether we have received information that might warrant the exercise of march-in rights. The NIH will make that initial determination and, if necessary, will initiate any formal march-in proceeding as required under the regulations. We will make every effort to come to a decision as quickly as possible.

I will now turn this meeting over to Ms Campos-Infantino.

STATEMENT OF SENATOR BIRCH BAYH TO THE NATIONAL INSTITUTES OF HEALTH

MAY 25, 2004

I appreciate NIH's invitation to comment on the intent of Congress when it enacted the Bayh-Dole law. I am accompanied by Joe Allen, currently President of the National Technology Transfer Center, and formerly my primary staff member who worked on this legislation. The focus of my comments will be the contention that Bayh-Dole gives NIH the ability to control the price of a product developed under the law by exercising the march-in rights provided in Section 203 of its provisions.

Before proceeding, I should emphasize that I am not being compensated to appear here today. Also, I should note that I am not familiar with the specifics of the drug which is the basis of the petition before NIH, so I will not comment on the merits of this particular case. However, I do know the intent of this legislation which I was privileged to sponsor with my friend, Senator Bob Dole.

As NIH proceeds with this examination of the petition, it should prove informative to the responsible officials here at NIH and the petitioners as well, to be reminded of the history behind the introduction and passage of Bayh-Dole. Particular attention should be given to the economic environment which existed prior to the introduction of Bayh-Dole.

By the late 70s, America had lost its technological advantage:

- We had lost our number one competitive position in steel and auto production. In a number of industries we weren't even No. 2.
- The number of patents issued each year had declined steadily since 1971.
- Investment in research and development over the previous 10 years was static.
- American productivity was growing at a much slower rate than that of our free world competitors.
- Small businesses, which had compiled a very impressive record in technological innovation, were receiving a smaller percentage of Federal research and development money.
- The number of patentable inventions made under federally supported research had been in a steady decline.

What had happened to American innovation, which had sparked generation after generation of international economic success?

Our investigation at the Patent and Trademark Office disclosed that the U.S. government owned 28,000 patents, only 4 percent of which had been developed as a product for use by the consumer.

Close examination disclosed that most patents procured as a result of government research grants, particularly those developed in university laboratories, resulted from basic research. The ideas patented were in the embryonic stages of development. Often millions of dollars were required to produce the sophisticated products necessary for marketability. Since the government refused to permit ownership of the patents, private industry and business refused to invest the resources necessary to bring the products to consumers. As Thomas Edison said: "Invention is 1% inspiration and 99% perspiration." With regard to publicly funded research, government typically funds the inspiration and industry the perspiration.

The well-intentioned voices, such as Senator Russell Long and Admiral Hyman Rickover, opposed Bayh-Dole on the basis "If the taxpayer funds the research, the taxpayer should own the ideas produced." However, the result of this policy was billions of taxpayer dollars spent on thousands of ideas and patents which were collecting dust at the PTO. The taxpayers were getting no benefit whatsoever.

Changes to Bayh-Dole should be made only after giving careful consideration to what has been accomplished by those who have utilized the provisions of the law. The London "Technology Economist Quarterly" called Bayh-Dole "Possibly the most inspired piece of legislation to be enacted in America over the past half century." (I have attached the full text of the article for your information.)

The Economist estimated that Bayh-Dole created 2,000 new companies, 260,000 new jobs, and now contributes $40 billion annually to the U.S. economy. This assessment was made almost six years ago and more progress has been made since then.

One is entitled to second guess us and say that we should have allowed the government to have a say in the prices of products arising from federal R&D. However, if changes are believed warranted, we have a process for doing so. That is to amend the law. You simply cannot invent new interpretations a quarter of a century later. This is what is being proposed.

When Congress was debating our approach fear was expressed that some companies might want to license university technologies to suppress them because they could threaten existing products. Largely to address this fear, we included the march-in provisions that are the subject of today's meeting.

The clear intent of these provisions is to insure that every effort is made to bring a product to market. If there is evidence that this is not being done, the funding agency can "march-in" and require that other companies be licensed. If the developer cannot satisfy health and safety requirements of the American taxpayer, agencies may march-in.

It was first brought to my attention that attempts were underway to rewrite history when I saw an article in the **Washington Post** on March 27, 2002, entitled *Paying Twice for the Same Drugs.*. The crux of the article was that:

> Bayh-Dole ... states that practically any new drug invented wholly or in part with federal funds will be made available to the public at a reasonable price. If it is not, then the government can insist that the drug be licensed to more reasonable manufacturers, and if refused, license it to third parties that will make the drug available at a reasonable cost.[1]

This view mistakes how our law works. Bob Dole and I responded in a letter to the editor of the **Washington Post** on April 11, 2002 setting the record straight.[2]

You can imagine my surprise when I see the same arguments were being formally presented in a petition to NIH in an attempt to control drug prices. The quotations in the petition flagrantly misrepresent the legislative history supporting Bayh-Dole. The petition shows complete lack of understanding of how the legislative process works. The current petition says: "The clear language of the Bayh-Dole act requires reasonable pricing of government supported inventions."[3] It later adds: "The legislative history evidences an intent to require that government supported inventions be priced reasonably."[4]

All but one of the citations in the petition used to conclude that march-in rights were intended to control prices actually refer to hearings on bills other than Bayh-Dole. While perhaps interesting, these are not pertinent legislative history. I could find only one citation from the real legislative history. Here is the petition language:

> This consensus was recorded in the Senate's Committee Report on the bill, which explained that march-in rights were intended to insure that no 'windfall profits,' or other "adverse effects result from retention of patent rights by these contractors."[5]

The petition footnote on this section adds "statement of Senator Bayh that the march-in provisions were meant to control the ability of 'the large, wealthy, corporation to take advantage of Government research and thus profit at taxpayers' expense."[6]

Rather than being a statement of fact, my quotation is actually taken from a question I asked the Comptroller General on another topic altogether.

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[1] Peter Arno and Michael Davis, "Paying Twice for the Same Drugs," Washington Post 27 Mar. 2002: A21.

[2] Birch Bayh and Robert Dole, "Our Law Helps Patients Get New Drugs Sooner," Washington Post 11 Apr. 2002: A28.

[3] Petition to use Authority Under Bayh-Dole Act to Promote Access to Ritonavir. Supported by National Institute of Allergy and Infectious Diseases Contract No. AI27220 (Essential Inventions, Inc., 2004) 9.

[4] Ibid., 10

[5] Petition to use Authority Under Bayh-Dole Act to Promote Access to Ritonavir. Supported by National Institute of Allergy and Infectious Diseases Contract No. AI27220 (Washington: Essential Inventions, Inc., 2004) 10.

[6] Ibid.

The petition language taken from the Committee report mixes up references to two different sections of the law so that the original meaning is unrecognizable.

Let's see what happens when the petition quotes are placed in their proper context. I highlighted the following language referred to in the petition as it actually appears in the legislative history.

With regard to the petition's footnote, during his testimony I asked Elmer Staats, then the Comptroller General of the United States, a question regarding concerns expressed about the Bayh-Dole bill. Here it is:

Mr. Bayh: "The other criticism comes from those that feel that this bill is a front to allow ***the large, wealthy corporation to take advantage of Government research dollars and thus to profit at the taxpayers' expense.*** We thought we had drafted this bill in such a way that this was not possible. Would you care to comment on this scenario as a valid criticism?"

Mr. Staats: "Of course, this is the key question. There is no doubt about that. In my opinion, the bill does have adequate safeguards..."

The petition also mixes up Senate Judiciary Committee report language describing two unrelated parts of Bayh-Dole. Here's how the report actually reads with the petition extract highlighted:

> The agencies will have the power to exercise march-in rights to insure that no **adverse effects result from the retention of patent rights by these contractors.**[7]

That was the language on section 203, the march-in rights provision. The report continues:

> The existence of section 204 of the bill, the Government pay back provision, will guarantee that the inventions which are successful in the marketplace reimburse the Federal agencies for the help which led to their discovery. Although there is no evidence of ***"windfallprofits"*** having been made from any inventions that arose from federally-sponsored programs, the existence of the pay back provision reassures the public that their support in developing new products and technologies is taken into consideration when these patentable discoveries are successfully commercialized."[8]

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[7] United States. Congress. Senate. Committee on the Judiciary, University and Small Business Patent Procedures Act: Report of the Committee on the Judiciary. United States Senate, on S.414 (Washington: U.S. Government Printing Office, 1979) 30.

[8] Ibid.

Thus, it is only by inappropriately combining language describing an entirely different section of the law that the words **"windfall profits"** can be made to refer to march-in rights. They clearly do not. Such a representation is highly misleading.

When read in context, the real meaning could not be clearer. Rather than controlling product prices, the language actually provided that the Government should be able to recoup a percentage of its investment when an invention from its extramural funding hits a home run in the market.

In fact, this payback provision of Section 204 was later dropped from the bill altogether because the agencies said that the administrative costs of tracking university royalties would far outweigh any monetary benefits from the one-in-a-million breakthrough invention.

NIH itself has found that price controls are not contemplated by Bayh-Dole. Under pressure in 1989, NIH placed a provision in its intramural collaborations with industry that resulting inventions must demonstrate "a reasonable relationship between the pricing of a licensed product, the public investment in that product, and the health and safety needs of the public."[9]

When industry collaborations began evaporating, and NIH explored the reasons and found:

> Both NIH and its industry counterparts came to the realization that this policy had the effect of posing a barrier to expanded research relationships and, therefore, was contrary to the Bayh-Dole Act.[10]

If NIH found that price controls on its intramural research are "contrary to the Bayh-Dole Act," how can the same provisions be applied to extramural research?

If Congress does decide to amend Bayh-Dole someone must clearly define what is a "reasonable price." Congress must keep in mind that the vast majority of technologies developed under the law are commercialized by small companies that "bet the farm" on one or two patents. Copycat companies are always waiting until an entrepreneur has shown the path ahead. They can always make things cheaper since they have no significant development costs to recover.

What will happen to the start-up companies arising from Bayh-Dole that are driving our economy forward with this sword hanging over their heads? What evidence is there that large drug companies will not simply walk away from collaborations with our public sector? That is what happened to NIH.

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[9] National Institute of Health, NIH Response to the Conference Report Request for a Plan to Ensure Taxpayers' Interests are Protected (Washington: U.S. Government Printing Office, 2001) 9.

[16] Ibid., 8.

NIH wisely realized that the greater good is to allow American taxpayers to have access to important new products and processes, along with the new jobs and taxes they create than to try and regulate prices.

Bob Dole and I made the same choice in 1980. I still believe that we were correct.

I empathize with the countless individuals in the U.S. and around the world who are suffering from AIDS. If it can be shown that the health and safety of our citizens is threatened by practices of a government contractor, then Bayh-Dole permits march-in rights, not to set prices, but to ensure competition and to meet the needs of our citizens. However, such a procedure must be supported by hard evidence that the need exists. Speculative claims and misrepresentation of the legislative history supporting Bayh-Dole will not suffice.

Let me urge the wisdom of approaching such a decision which great caution. The success of Bayh-Dole goes far beyond the efforts of Bob Dole and Birch Bayh. This legislation combined the ingenuity and innovation from our university laboratories with the entrepreneurial skills of America's small businesses. Most importantly, this combination created the incentive necessary for private investment to invest in bringing new ideas to the marketplace. The delicate balance of ingenuity, entrepreneurship, and incentive upon which the success of Bayh-Dole has depended must not be disrupted.

A few of the products which have been produced in the last six years are:

- Taxol, the most important cancer drug in 15 years, according to the National Cancer Institution.
- DNA sequencer, the basis of the entire Human Genome Project.
- StormVision™, which airport traffic and safety managers use to predict the motion of storms.
- Prostate-specific antigen test, now a routine component of cancer screening.
- V-Chip, which allows families to control access to television programming.

It would be the ultimate folly to march in and alleviate the problem addressed by the petition, availability of a drug to treat AIDS today, and in so doing dampen the ingenuity, entrepreneurial skills and incentive necessary to develop a permanent cure for AIDS, or for that matter the cure for other diseases that plague all too many American mothers, fathers, children and seniors today.

As you search for a solution to the problem before us today, be aware of unintended consequences tomorrow. Insuring the health of our citizens requires the wisdom and determination for a long journey. The procedures of Bayh-Dole have saved countless lives and pain and suffering. It provides an incentive for further progress in the future.

Thank you

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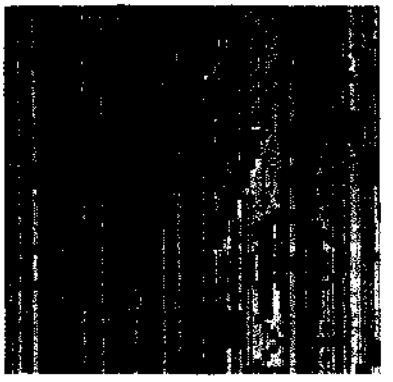
Innovation's golden goose



Contents

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The reforms that unleashed American innovation in the 1980s, and were emulated widely around the world, are under attack at home

REMEMBER the technological malaise that befell America in the late 1970s? Japan was busy snuffing out Pittsburgh's steel mills, driving Detroit off the road, and beginning its assault on Silicon Valley. Only a decade later, things were very different. Japanese industry was in retreat. An exhausted Soviet empire threw in the towel. Europe sat up and started investing heavily in America. Why the sudden reversal of fortunes? Across America, there had been a flowering of innovation unlike anything seen before.

Possibly the most inspired piece of legislation to be enacted in America over the past half-century was the Bayh-Dole act of 1980. Together with amendments in 1984 and augmentation in 1986, this unlocked all the inventions and discoveries that had been made in laboratories throughout the United States with the help of taxpayers' money. More than anything, this single policy measure helped to reverse America's precipitous slide into industrial irrelevance.

Before Bayh-Dole, the fruits of research supported by government agencies had belonged strictly to the federal government. Nobody could exploit such research without tedious negotiations with the federal agency concerned. Worse, companies found it nigh impossible to acquire exclusive rights to a government-owned patent. And without that, few firms were willing to invest millions more of their own money to turn a raw research idea into a marketable product.

The result was that inventions and discoveries made in American universities, teaching hospitals, national laboratories and non-profit institutions sat in warehouses gathering dust. Of the 28,000 patents that the American government owned in 1980, fewer than 5% had been licensed to industry. Although taxpayers were footing the bill for 60% of all academic research, they were getting hardly anything in return.

The Bayh-Dole act did two big things at a stroke. It transferred ownership of an invention or discovery from the government agency that had helped to pay for it to the academic institution that had carried out the actual research. And it ensured that the researchers involved got a piece of the action.

Overnight, universities across America became hotbeds of innovation, as entrepreneurial professors took their inventions (and graduate students) off campus to set up companies of their own. Since 1980, American universities have witnessed a tenfold increase in the patents they generate, spun off more than 2.200 firms to exploit research done in their labs, created 260,000 jobs in the process, and now contribute $40 billion annually to the American economy. Having seen the results, America's trading partners have been quick to follow suit. Odd, then, that the Bayh-Dole act should now be under such attack in America.

No free lunch

There has always been a fringe that felt it was immoral for the government to privatise the crown jewels of academic research. Why, they ask, should taxpayers be charged for goods based on inventions they have already paid for?

That is easily answered. Invention, as TQ has stressed before, is in many ways the easy bit. A dollar's worth of academic invention or discovery requires upwards of $10,000 of private capital to bring to market. Far from getting a free lunch, companies that license ideas from universities wind up paying over 99% of the innovation's final cost.

Then there is the American Bar Association, which has lobbied hard to get the government's "march-in" rights repealed. The government has kept (though rarely used) the right to withdraw a licence if a company fails to commercialise an invention within a reasonable period. This was to prevent companies from licensing academic know-how merely to block rival firms from doing so. The lawyers argue that the government could use its walk-in rights to bully pharmaceutical firms into lowering the price of certain drugs.

Whatever the merits of their case, suffice it to say that the sole purpose of the Bayh-Dole legislation was to provide incentives for academic researchers to exploit their ideas. The culture of competitiveness created in the process explains why America is, once again, pre-eminent in technology. A goose that lays such golden eggs needs nurturing, protecting and even cloning, not plucking for the pot. Readers who agree or disagree can share their own views at www.economist.com/forums/tq. •

Public Meeting at the National Institutes of Health (NIH)

May 25, 2004

The Public Health Impact of Abbott Laboratories' Unreasonable Terms for Norvir

Robert Huff
Editor, GMHC Treatment Issues
Gay Men's Health Crisis
New York

Good Morning.

My name is Bob Huff. I am the editor of GMHC Treatment Issues, a monthly newsletter about HIV treatment research published by Gay Men's Health Crisis in New York, the world's first and largest AIDS service organization.

We've seen a revolution in AIDS treatments over the past ten years, but the therapies we have are not perfect. I'm here today because I am keenly interested to see that the innovation of more effective and less toxic HIV drugs continues.

In the first part of December 2003, the HIV/AIDS treatment community was shocked to hear that Abbott Laboratories was raising the price of its HIV drug, Norvir, five-fold. The price per 100mg pill would increase from $2.14 to $10.71 apiece.

As you've heard, although Norvir was developed and approved by the FDA as an anti-viral drug -- an inhibitor of the HIV protease enzyme -- due to excessive toxicity, it is no longer used as such. Instead it is now used for an off-label indication in much lower doses to take advantage of one of its side effects, namely the inhibition of a metabolic pathway in the liver that effectively improves the concentration of other drugs in the blood. In current clinical practice, most other HIV protease inhibitors are "boosted" by Norvir, which increases their effectiveness. In other words, Norvir enables other drugs to work better.

Here is a before-and-after price chart that shows the six approved HIV drugs that can be boosted by Norvir, and how the price increase has affected their overall cost. Note that the price of Norvir in its approved dosage as an antiviral is far out of proportion to the others. Also note that the price of the drug Kaletra, which is also made by Abbott and contains a small boosting dose of Norvir in each pill, did not change and is now the lowest price boosted protease inhibitor on the market. It is clear that the practical and intended effect of the Norvir price increase was to position Kaletra in advantage to its competitors.

Here is another chart that shows a timeline for the development of some HIV drugs that require Norvir boosting. It includes two protease inhibitors that were approved last year (Reyataz and Lexiva) and several currently in development. It seems clear to me that the Norvir price increase was calculated to come just after these two new drugs received approval. But I'm more concerned about the drugs that are still on the path to approval -- and about potentially useful drugs that may now never enter clinical development -- because they would be at the mercy of Abbott's monopoly on Norvir.

I would like to argue that Abbott's failure to make Norvir available on reasonable terms will adversely affect the development of new drugs that depend on metabolic boosting and will limit the amount of research that will be conducted on existing drugs that require boosting. I believe that the public health is threatened by the restricted availability of Norvir caused by Abbott's unconscionable price increase.

Abbott's abuse of their patent on Norvir will limit patient access to drugs, limit research, limit options for doctors and limit the innovation of new-generation drugs of this type. This is why you are being asked to protect the public against Abbott's unreasonable use of the Norvir patents.

Before a pharmaceutical manufacturer decides to invest hundreds of millions of dollars into bringing a promising compound along the path to FDA approval, the company projects the market for the drug over the entire expected life of the product. While this isn't easy, given the rapid

pace of change in HIV therapy, it is necessary to forecast whether the drug will be competitive and will repay the considerable investment of clinical development. For the makers of Norvir-boosted drugs in the pipeline, Abbott's price increase has thrown these forecasts into chaos.

In seeking to mitigate the impact of the 400% increase in the price of Norvir, Abbott has announced it will make the drug available at the old price for research purposes to companies that are developing a drug that requires Norvir-boosting. However this offer expires once the new Norvir-dependent drug receives FDA approval and goes on the market.

Yet research on these drugs can not and must not end with approval. Post-market research, so-called Phase IV studies, are important to "fill in the blanks" about how a drug behaves in real-world settings and to provide controlled data that helps physicians make the most appropriate use of all the drugs in their armamentarium.

Much of this Phase IV research is mandated by the FDA and some is initiated by the company for marketing purposes. For the recently approved protease inhibitors, the 400% increase in the price of Norvir means that the cost of post-marketing research has now increased dramatically. One pharmaceutical executive estimated that the cost of post-approval research could go up by $20 to $30 million. And this is for drugs that have already been approved, with FDA-mandated post-market research already planned and budgeted.

The impact on drugs still in the pipeline is far more insidious.

A drug company's Phase IV research commitments are decided in negotiations with the FDA. The FDA says it will grant accelerated approval based upon available safety and efficacy data, but only if the company will show a plan for continuing research on the drug after entering the market. These research plans are negotiated based on what the FDA would like to see and what the drug company can afford. The simple fact is that after the 400% rise in the price of Norvir, companies will not be able to afford as much post-market research. And the high price of Norvir will effectively tie the hands of the FDA in what they can ask of companies. This is going to hurt patient care.

There are four Norvir-dependent drugs in the pipeline that this will affect. Abbott's monopoly on Norvir means that there will be less post-marketing research and, consequently, less important real-world medical information produced on how to use these drugs, for example, in women, in people of color, in prisons, in combination with other drugs, in people with hepatitis infections or in people with liver or kidney disease. Much of this research will become too expensive. How much important, useful and desperately needed medical information will never see the light of day because of Abbott's abuse of its patent monopoly on Norvir?

Then there are the government research networks, such as the AIDS Clinical Trials Group (ACTG) at the National Institutes of Health. An investigator might want to use a Norvir-boosted drug in studies of treatment strategies for people with few remaining options, or in women, or in special, under-studied populations. But if they can't afford the Norvir, then they will have to abandon those studies or turn to Kaletra. Even if Abbott would agree to provide Norvir for free ~~(and so far they have refused)~~, these government researchers will have to ask: How useful will the resulting data be down the road if we study drugs that, while promising, will, in practice, be unaffordable and go unused? So, once again, Abbott's Norvir monopoly will hold back research, limit medical knowledge and hurt patient care.

But my main concern is with what Abbott's monopoly on Norvir means for the future. One pharmaceutical executive I spoke to, in evaluating the impact of Abbott's action, posed this as a rhetorical question: "Who would risk developing a Norvir-boosted protease inhibitor after this price increase?" What he meant was that, not only will the high price of Norvir place any new Norvir-dependent drug into an uncompetitive price stratum, but Abbott's unpredictable behavior has made depending on them or their products an unsupportable risk. It's difficult enough to project market conditions for new HIV drugs that don't need Norvir; it's very unlikely that a corporate market analysis will ever again justify investment in drugs of this type. In the words of another pharmaceutical executive, after the

drugs currently in the pipeline empty out, "We've seen the end of the line for boosted protease inhibitors."

And that is a shame, because we desperately need new protease inhibitors to treat drug-resistant HIV. The so-called HIV salvage population is the fastest growing market segment in HIV therapy. Drugs with incremental benefits have continued to trickle onto the market over the past few years, but in practice, this has resulted in many patients simply adding the latest therapy onto a failing regimen, which starts the cycle of resistance all over again. Unless a person switches to multiple drugs that his virus is susceptible to, the development of resistance seems inevitable.

For drugs in the protease inhibitor class -- which are very durable HIV therapies -- Norvir has assumed a crucial, enabling role by assuring that sufficient blood levels of the active antiviral drugs are achieved. Looking ahead, we can foresee the continued need for new protease inhibitors that will have novel resistance profiles, that will have less toxicity, and that are more durable. Some of the drugs in the pipeline have some of these qualities, but none has all of them. Most observers expect the protease inhibitors in the pipeline to continue towards approval because their sponsors have already made substantial financial commitments to their development. But how many important, useful, and desperately needed drugs will now never see the light of day -- because of Abbott's monopoly on Norvir? Abbott's unreasonable terms for Norvir will inhibit innovation, restrict research, limit medical options and hurt people with HIV.

Finally, the pricing issue aside, Abbott has not been a responsible custodian of this drug. Although Norvir's usefulness is as a metabolic booster and not as a protease inhibitor as they had hoped, the company has not made the drug available in dosages that would optimize the use of Norvir for this purpose. With only a 100mg pill of Norvir available, many patients who would only require 50mg or less for boosting are being subjected to unnecessary toxicity. (Kurowski)

Furthermore, Abbott has not sought FDA approval for Norvir as a metabolic boosting agent and continues to represent the drug in medically inaccurate terms, while encouraging continued off-label use.

Also, Abbott has, I have been told by several pharmaceutical executives, been unwilling to offer reasonable terms for licensing Norvir for co-formulation with other companies' drugs, even though a co-formulated pill is widely considered to help simplify drug regimens and improve patient adherence and therapeutic outcomes. The FDA, in a recent guidance document on fixed dose combinations (FDC) said:

"Kaletra (lopinavir/ritonavir), an approved FDC, is an antiretroviral combined with a metabolic booster; a low dose of ritonavir…. Other HIV protease inhibitors are often administered with low doses of ritonavir and may be suitable for co-packaging or co-formulation. *FDA encourages sponsors to develop FDCs for this type of drug combination to help in simplifying regimens.*" (FDA)

Yet Abbott, in order to protect its own, more toxic Kaletra product, continues to resist this.

To sum up, Abbott has behaved unconscionably, and perhaps illegally, in increasing the price of Norvir, and in doing so they have abused the privilege of their patents.

- They have attempted to manipulate the market and restrict patient access to competing drugs that have less toxicity.
- They have increased the financial burden their competitors face in performing important post-market research.
- They have tied the hands of the FDA in how much post-market research can be required of drugs approaching approval.
- They have stifled innovation and have killed the market chances for any new drug candidate that would require Norvir.
- They have not been responsive to the medical need for safer and more rational doses of Norvir.
- They have refused reasonable offers to license Norvir for co-formulation into patient-friendly combinations with other drugs.

With at least ten HIV drugs (and I haven't discussed potential drugs for hepatitis C and other illnesses) dependent on Norvir to achieve optimal efficacy and minimal toxicity, I believe Norvir should be considered a public amenity and be contracted to more responsible custodians.

I'd like to note that I think the case of Norvir is an exceptional one, and that I fully support industry development programs that build on government funded research. It seems clear that the intent of the Bayh-Dole Act was to stimulate innovation, and in this it has been very successful. But it also seems clear that a mechanism was provided to address abuse, and that, in Norvir, we are confronted with that rare case.

Under Abbott's monopoly control of Norvir, drug access (both to Norvir and to dependent drugs), patient care, innovation, research, and medical options are being restricted. The public interest would best be served by making this vital resource more broadly available under much more reasonable terms.

Thank you.

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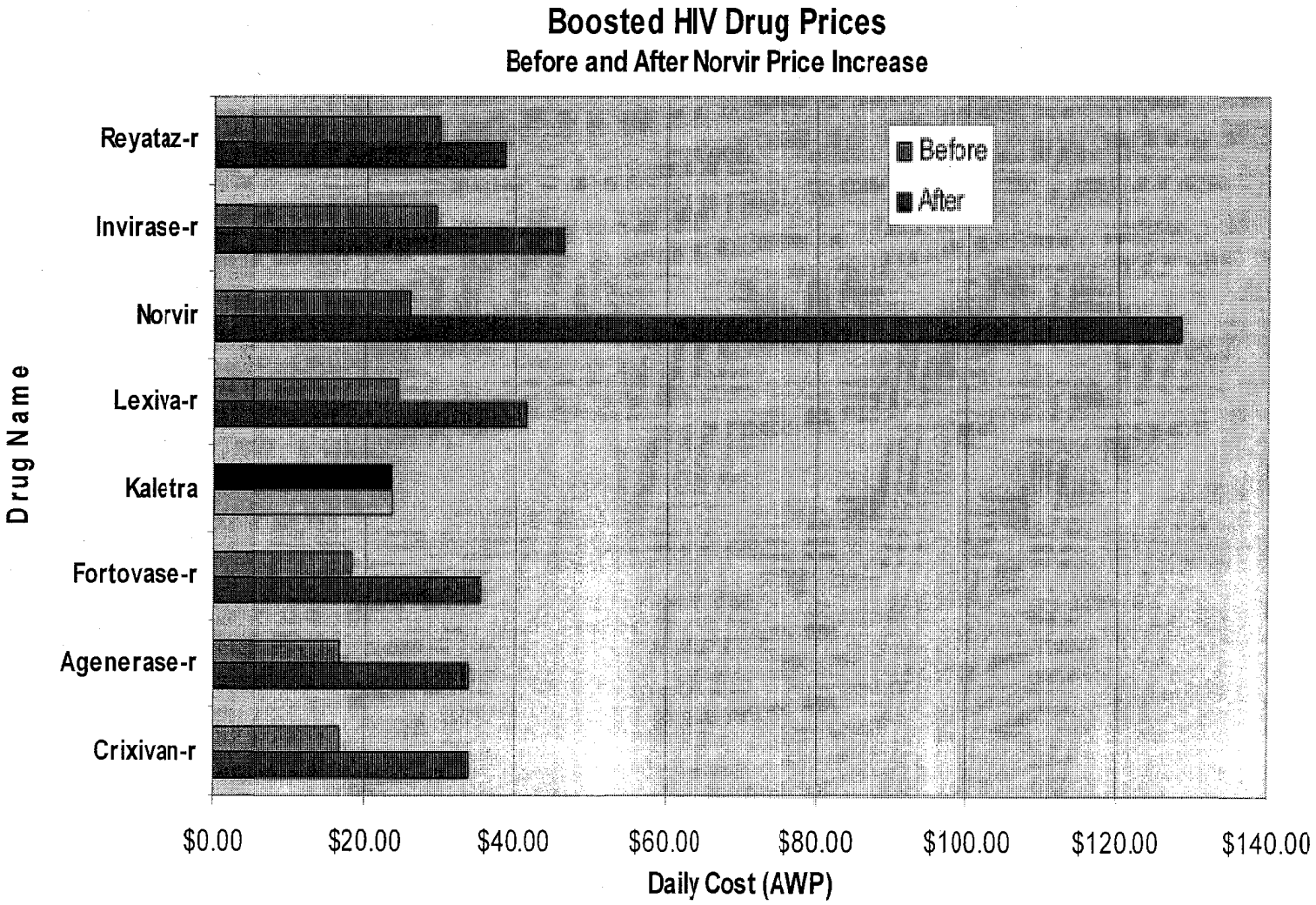
Boosted HIV Drug Prices
Before and After Norvir Price Increase
Reyataz-r
Invirase-r
Norvir
Lexiva-r
Kaletra
Fortovase-r
Agenerase-r
Crixivan-r
Drug Name
Before
After
$0.00
$20.00
$40.00
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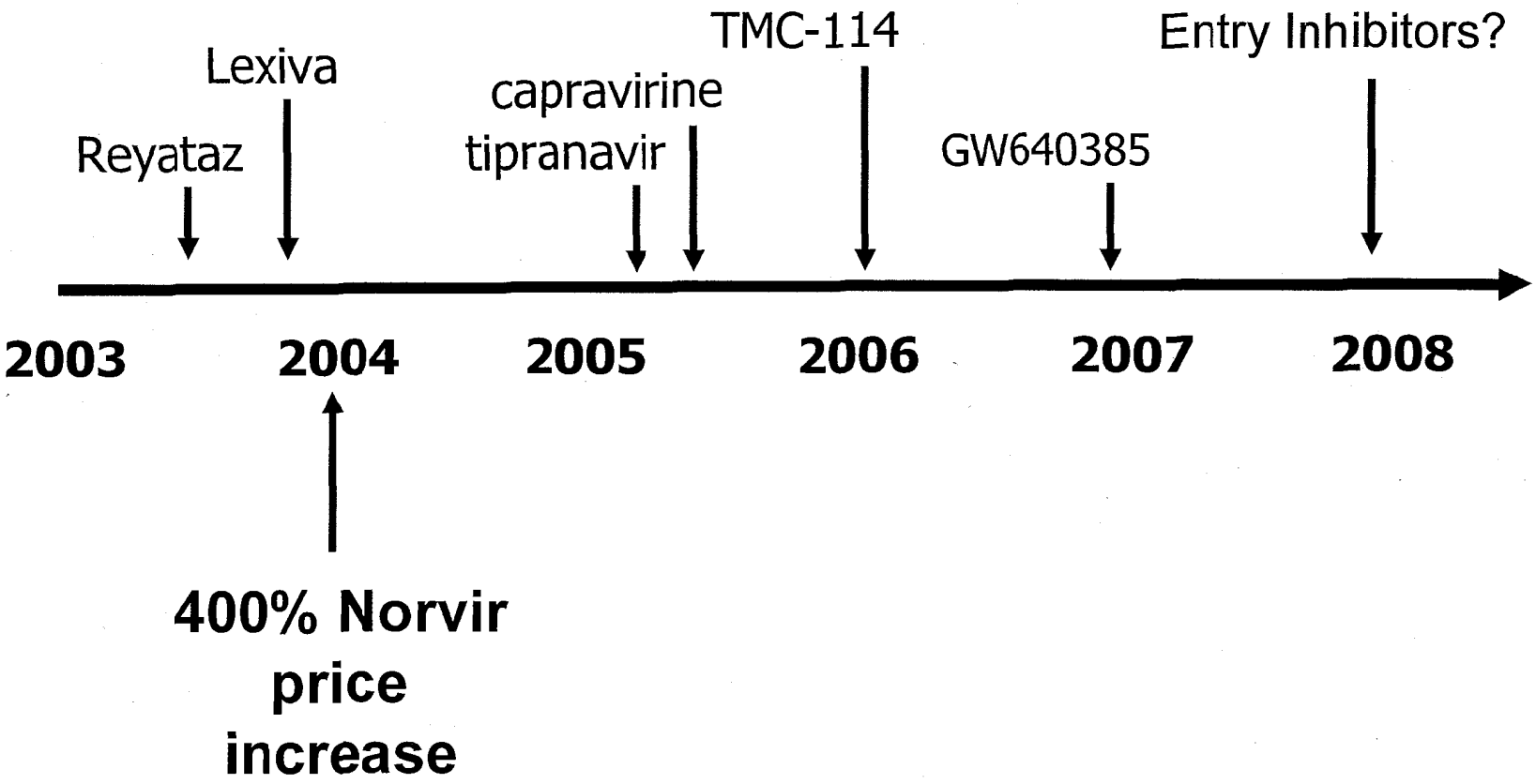
$80.00
$100.00
$120.00
$140.00
Daily Cost (AWP)

HIV Drug Pipeline

Drugs dependent on Norvir boosting



Norman J. Latker

Statement Before NIH On
Essential Inventions Petition Regarding Norvir

May 25, 2004

Hello. I'm Norm Latker, and I'm here to address the petition sponsored by Mr. James Love of Essential Inventions, which asks NIH to end the exclusive title held by Abbott Laboratories for the AIDS drug Norvir.

I thank you for the opportunity to address this issue today.

While I am sympathetic to the efforts of Mr. Love, which I believe are motivated by a desire to enhance the quality of life for the millions of Americans living with AIDS, I must oppose his petition, which, if successful, would undermine the integrity of the Bayh-Dole Act, which I helped to draft back in the 1970s.

Although there was spirited opposition to Bayh-Dole when it was brought before Congress in 1980, a broad political consensus was ultimately built around the notion that market forces would do a far better job of disseminating government-sponsored inventions than bureaucracies ever could.

The Act has been enormously successful. As the Economist Magazine put it recently, it is "the most inspired piece of legislation to be enacted in America over the past half-century."

That may sound like hyperbole, but the impact of the Act has indeed been astounding—and overwhelmingly positive.

It has fostered a potent four-way partnership between researchers, their institutions, government and industry. That partnership has evolved into the most powerful engine of practical innovation in the world, producing innumerable advances that have extended life, improved its quality and reduced suffering for hundreds of millions of people.

Of course, the law isn't perfect. No law is. There have been changes in the three decades since Bayh-Dole's passage—changes that no one could have predicted. But overall it has stood the test of time.

While I feel I can provide some perspective on the Act, there is very little I can say with authority on the underlying issues that have prompted Mr. Love's petition.

Frankly, there are a number of things that I simply do not know.

For example, I don't know how Abbott Laboratories reached its decision to raise the price of Norvir. I don't know whether it was based on legitimate business issues, or as AIDS activists allege, on simple corporate greed.

Nor can I pretend to know what impact the price hike will have on those who need the drug to stay healthy, or on the healthcare finance system. I do not know if some people who need Norvir will now not have access to it. I don't know whether Abbott's promise to provide the drug for free to those who cannot afford it should be taken at face value.

It is worth noting that Senator John McCain has called on the Federal Trade Commission to investigate Abbott Laboratories for possible abuse of its monopoly power with respect to Norvir. Attorneys General in Illinois and New York are also looking into the matter. Again, I do not know precisely what criteria these organs of government might use to determine whether corrective action is warranted.

But I do know this: the Bayh-Dole Act is not an arbiter of healthcare policy or drug pricing, and was never intended to be.

Bayh-Dole defines critically important aspects of intellectual property law, while ensuring that viable government-sponsored research does not go to waste.

It is decidedly ill-suited for any other purpose.

Simply put, the legal philosophy of Bayh-Dole is this: if the government accords broad marketplace prerogatives to the developers of government-funded inventions, such inventions are far more likely to be developed and disseminated to the public.

The law holds that intellectual property rights should be accorded in full to the innovators, rather than to the government agency that financed their research, and that developers should be free to leverage their property rights to their advantage in the market place as intended by the patent system.

There were a few conditions placed on this freedom—conditions which are now the subject of dispute. In layman's terms, the conditions provided that:

a) Reasonable efforts were required to develop the inventions to practical application, and made readily available to society;

b) The inventions should not be used in such a way that might threaten public health;

c) If an invention were subject to a federal order of some kind, the developer must comply with that order; and

d) The marketed invention should be made within the United States.

These conditions were translated into the legal language found in section 203 of the Act—what we now refer to as the "march-in" clauses, because they give the government the power to "march-in" and reassign intellectual property rights. These were conceived as extraordinary measures to be used only when there was overwhelming evidence to show that the public resources invested into an innovation were being wasted or abused.

Obviously, Abbott Laboratories has been enormously successful in bringing the benefits of Norvir to the public at large. The drug may be expensive—perhaps intolerably expensive, given the critical importance it

holds for people with AIDS. But by the criteria established by Bayh-Dole, Abbott has complied with the law.

Mr. Love would of course disagree, both with my interpretation of the march-in clauses and my belief that Abbott has not broken the law.

His petition asserts that Bayh-Dole invests NIH with the authority to determine whether the price of Norvir is too high and, if so, to terminate the exclusivity of Abbott's property rights.

The petition points out that one march-in clause, section 203a, specifies that the invention in question must be made available on "reasonable terms", which the authors interpret to mean "reasonable prices".

None of this is supported by a correct reading of the Act and its legislative history.

In fact, if the drafters of Bayh-Dole had intended such an interpretation, we would have inserted specific criteria into the law to enable NIH—or any government funding agency —to assess what a reasonable price might be. No such criteria are found, because controlling patent rights on the basis of price was antithetical to what the drafters had in mind.

Nor did we envision that the law could authorize government funding agencies to compel private entities to divulge internal accounts or pricing information. If we had foreseen such a process, the Act would have contained enabling language specifically empowering it.

It must be admitted that the law is written in the arcane legalese of the period, and many sections are quite easy to misinterpret unless armed with the correct definitions.

Let me provide some of those definitions now.

The Bayh-Dole Act refers to three key entities involved in the government-sponsored research and subsequent development of an invention.

1) Contractors: These are the organizations that originally used government research funds to make fundamental discoveries

2) Licensees: These are the entities that acquire a license to an invention, develop it and bring it to the marketplace. They pay royalties to the contractor. And bear risk... In the fields of human health and life sciences, these are usually drug companies.

3) Assignees: These are defined by the Act as non-profit patent management organizations, which at the time brokered the license agreements between the contractor and the licensee. Their role has been marginalized in recent years as universities and research institutes have taken on the role themselves.

When reading the march-in clauses, it is important to understand that Section 203a *only* applies to contractors—that is, the original researchers – and assignees.

Section 203a does *not* apply to licensees.

This was not an accidental omission. That licensees are consciously excluded from 203a is obvious, because the next three sections -203b--d explicitly apply to all three entities: contractors, assignees and licensees.

Back in 1980, it was clear that most health inventions could only be practically developed under licenses with the drug industry. Bayh-Dole granted the property rights to the contractor, who would then negotiate a license agreement with the licensee. Of course, drug pricing played *no role* in these negotiations. Pricing a drug which has not yet been tested, approved and marketed is, of course, impossible.

As the phrase "reasonable terms" found in 203a applies to *contractors*, and not to *licensees*, it cannot mean "reasonable prices," because contractors, in the view of the drafters, would not normally be setting prices. Further, they are not required to do so under 202c which sets out all the contractors obligations.

The phrase clearly refers to the terms of the agreement between the contractor and the licensee.

Bayh-Dole wants government-sponsored inventions moved to the marketplace. Towards that end, it obligates the contractor to transfer the invention to the licensee without demanding exorbitant, or unreasonable, *royalties.*

The ultimate price of the drug to be developed had nothing at all to do with section 203a or the contractor's obligations under sec. 202c. Pricing was —and is—left to the discretion of the licensee. It is the licensee, after all, who bears all the risks of developing the innovations—the clinical trials, the FDA approval procedures, the vagaries of the marketplace. They do so because they know that Bayh-Dole guarantees them exclusive rights over the invention.

After explaining all that, I must now point out that Norvir has *never* been licensed, and that Abbott Laboratories is *not* a licensee. It is, in fact, a contractor who obtained title to its invention directly through a contract with NIH.

Again, when the law was written, we thought that in most cases, a contractor would be an academic, research institute or small business that would not have the resources to develop and market the invention on their own. Bayh-Dole therefore emphasizes the licensing process, as is abundantly evident throughout the Act and its implementing regulations.

Abbott Laboratories, as it happens, had no need to license its invention. It had title to the invention and the resources to bring it to the market without any assistance.

This exposes a minor ambiguity in Bayh-Dole. Obviously, "reasonable terms" in this particular case cannot mean "reasonable royalties." But neither can it mean "reasonable pricing", as a requirement under sec.202c.

In other words, we cannot spontaneously reinterpret 203a to mean that when a contractor brings a drug to market itself, it must price the drug

"reasonably". "Reasonable terms" could not mean one thing for a licensee, and another for a contractor, unless the law contained specific language defining these meanings.

The intent of 203a is obvious enough, even if it fails to specifically address the case at hand.

In closing, I'd like to return briefly to the broader issues that have prompted Mr. Love's petition.

It must be plainly understood that medical access problems in the United States stem *not* from the research and development regime, but from the way healthcare entitlements are ascribed and healthcare resources are distributed. Healthcare reform is long overdue. It will be a long, bruising political battle, but the country must, and will, address it.

I confess that I am no fan of price controls, because I believe that they could stifle innovation and drastically reduce the amount of money the drug industry pumps into pharmaceutical research every year. Contrary to what has been published in recent weeks, only a very small portion of the government health research and development funds are channeled directly into drug research and clinical studies. Most is used to sponsor investigations into the life sciences.

It is in fact the private sector that ponies up the resources to develop, test, obtain approval for, and market new drugs. It is an undeniably responsibility of government to create and maintain incentives for these investments, because there is no way the government could manage the job on its own.

In the absence of government price controls, drug companies will seek to maximize their profits by balancing prices with the need for market penetration - and that is exactly what the drafters of Bayh-Dole expected. Pricing freedom is one reason often cited by the pharmaceutical industry for concentrating their research and development activities in the U.S. It is

why the U.S. remains the world leader in medical research, and why so many drugs are made available here first.

That said, the public has an interest in affordable healthcare. I think there are many ways that might be achieved without resorting to outright price controls. State governments, for example, are themselves major purchasers of drugs, and could, through clever use of their market power, help keep prices down.

If a political consensus were to emerge that drug prices need to be controlled by the government, the only legal and appropriate means of instituting such controls would be through a full-fledged legislative process, tested by the courts and administered through empowered organs of government.

Obviously any healthcare reform effort could face resistance from vested interests, and it is tempting for some to look for shortcuts. But twisting intellectual property law into an administrative mechanism to control drug prices would have intolerable consequences for innovation, drug development and healthcare in this country.

It is also legally impossible. A sober reading of the Bayh-Dole Act will leave no doubt that retail drug pricing has nothing to do with the march-in provisions of the Act.

Mr. Love's petition must therefore be denied.

Thank you again for the opportunity to be here today.

ON THE ROLE OF THE US GOVERNMENT IN THE DEVELOPMENT OF NORVIR®

My name is John Erickson. I am the President and Chief Scientific Officer of Sequoia Pharmaceuticals Inc., a small for-profit drug discovery company located in Maryland, focused on the development of new therapeutic approaches to combating drug resistant infections with an emphasis on HIV/AIDS. I am also the Founder of the Institute for Global Therapeutics, a non-profit, 501(c)(3) organization founded by my wife and I to develop safe, effective and affordable new therapeutic approaches to combating drug resistant infections, with an emphasis on HIV/AIDS, for resource-poor settings. I have been involved in HIV/AIDS drug discovery and development for most of my career, first as a researcher and project leader, later as a government laboratory director, and, most recently, as an entrepreneur-scientist, investor and fund-raiser of for-profit and non-profit drug discovery activities. Most of my drug discovery work has focused on the development of new HIV protease inhibitors such as Norvir®.

I was a scientist at Abbott from 1985-1991, during which time I initiated a new research program to discover HIV protease inhibitors. Because we received federal funding for this program, and because this program ultimately led to the development of Norvir, I have been asked to describe the role that US government funding played in the development of Norvir. I am not here to give a learned opinion of the petition, nor on the legal aspects of the petition. I am here out of a sense of civic duty and in the spirit of Abraham Lincoln who said "If you give the people the truth, the [Re]public will be safe". But I cannot help but take the opportunity of this forum to also comment on the larger issue of drug pricing, a powerful market force that has daily and long-term effects on drug discovery activities whether they are in profit or non-profit settings.

Now for some historical facts.

In 1988, Abbott received a grant under a federally chartered program known as the National Cooperative Drug Discovery Group for AIDS (which I will refer to as the

NCDDG program or grant). The NCDDG programs for AIDS were administered by the National Institute of Allergy and Infectious Diseases in the Department of Health and Human Services. The purpose of the NCDDG program was to promote synergy among government, industry and academic laboratories to translate basic research findings on HIV into novel antiretroviral therapies. The NCDDG-AIDS program was a response to the national health crisis that HIV/AIDS represented in the 1980's. At that time, and in sharp contrast to today, targeted antiviral research programs were largely non-existent in the pharmaceutical industry. Thus, the NCDDG program also was a tacit recognition by the government that getting the pharmaceutical industry engaged in this effort would be essential for the rapid development of new and effective antiviral drugs.

The award of the NCDDG-AIDS grant gave the HIV project a much-needed funding boost. In my opinion, it catalyzed the development of the antiviral program. I have often been asked "if not for the NCDDG grant, would Norvir exist today?" A fair question, that no one can answer with certainty. What is certainly true is that the federal grant facilitated the research that led directly to the development of Norvir. Let me explain.

As the Principal Investigator, I was responsible for the conduct of research performed under the grant. I used the funding to recruit a team of scientists to develop a new type of antiviral drug that we hoped would inhibit the spread of HIV infection by blocking a viral-encoded enzyme, called HIV protease. This was an entirely new area of research that required a critical mass of scientists from different disciplines. Without the prestige and dollars that came with the NCDDG award, it is unlikely that the HIV protease inhibitor project would have received internal funding at the time. Interest in HIV as a therapeutic area by pharmaceutical companies was the exception rather than the rule in the late 80's. The NCDDG grant gave us an opportunity to take a risk that management was not yet prepared to take on its own. The helping hand of government risk-sharing was accepted again by Abbott a few years later when it was time to take a drug candidate known as A77003 into the costly clinical development phase of research.

A77003, an early precursor of Norvir, was a highly potent inhibitor of HIV, but could not be administered in oral form. Since we had no idea whether a protease inhibitor would be effective in an HIV-infected patient, we thought it made sense to do a proof-of-concept study to test the drug's efficacy using a parenteral route of administration. However, Abbott was not ready to undertake the clinical development of A77003 because it was concerned that an intravenous compound would not generate sufficient revenue to justify the investment. When the government saw the potential benefit of our new medicine, it agreed to fully fund and to conduct the necessary pre-clinical and clinical development phases up to and through Phase II trials. Abbott agreed to manufacture and provide the necessary drug quantities for the studies. And so, in 1991, a drug development collaboration was born between Abbott, the National Cancer Institute and the National Institute for Allergies and Infectious Diseases. A77003 never made it beyond early Phase I studies; but the commitment of the government to assist Abbott in dollars and in-kind in the development of its protease inhibitor program was never in doubt.

In 1991, I was recruited to the NCI to establish a structure-based drug design research program focused on cancer and AIDS. I continued working with some of my former research team members from Abbott to understand the critical features of how symmetry-based inhibitors interacted with the target enzyme; we published several papers together during the period 1991-1994 or so. I also began a study to evaluate the resistance profile of Norvir when, around 1995, our collaboration was terminated by Abbott, due to a growing concern that the government might try to exert price controls on Norvir. The company [Abbott] worried that if the AIDS community came to perceive that the government had played a major role in the development of Norvir, that it might try to pressure the government to influence the price of Norvir downwards. This demonstrates the powerful influence that even the perception of drug price tampering by the government can have on fragile public-private partnerships.

I want to turn now to the subject of how Norvir is actually used in the fight against HIV/AIDS today. Norvir is not a typical HIV drug. In addition to its antiviral activity, Norvir has the unexpected property of inhibiting its own metabolism, which makes it stay

in circulation longer. Since it inhibits the same metabolic enzymes that are responsible for breaking down and eliminating many other drugs, including competitors' protease inhibitors, co-administration of Norvir with these drugs can lead to higher than normal blood levels and prolonged circulation half-lives. This effect is termed "pharmacokinetic boosting". Because of the boosting effect, low dose Norvir is commonly co-prescribed in all antiviral cocktails that contain a protease inhibitor. It is commonly accepted practice to prescribed Norvir as an "off label" booster with all six FDA-approved protease inhibitors. You might think from what I have said that Norvir would be the ideal protease inhibitor to take all by itself, since it effectively boosts itself. However, due to poor tolerability and adverse side effects Norvir is rarely prescribed in antiviral dosages [1200 mg/day]. Instead, it is taken in 50 or 100 mg 'baby' doses along with one of the other protease inhibitors. Abbott has replaced Norvir by a new first-line protease inhibitor, Kaletra**R**, which is actually a co-formulation of low dose Norvir combined with a high dose of lopinavir, a Norvir analogue that has a superior safety profile.

So, it's important to understand that the price increase of Norvir that is at the center of today's hearing does not really affect the price of Kaletra, even though it contains Norvir. What it does affect, though, is the price of every competing protease inhibitor because they must all be taken with Norvir, which is sold separately at a price comparable to that of the active antiviral agent. The net result of the price increase is that Kaletra has gone from being one of the more expensive protease inhibitor options, before the price hike, to the least expensive protease inhibitor after the price hike. It is also one of the most effective protease inhibitors on the market today, and is responsible for helping to turn AIDS from a death sentence to a chronic, treatable disease. There are still many problems to be solved in HIV therapy, including the growing problem of drug resistant HIV infections.

I would like to turn the focus of my remaining remarks on the issue of drug prices.
It is difficult to find the right balance between the interests of a private company, where success is measured primarily by revenues and share value, and the public interests of the nation, where success is measured by our personal health and well-being. This is a public policy discussion that needs to take place on national, state and local levels. My hope is

that this hearing, catalyzed by the consumer advocacy group Essential Inventions, and convened by the DHHS, will become an important component of an ongoing dialogue on how we, as a nation, deal with the health of our own people.

An important viewpoint was expressed at a meeting I attended in Malaysia earlier this year, in which Mary Robinson, former President of Ireland, stated so eloquently the case for health being a basic human right. If we as a society come to embrace the notion of health as a human right, in the same way as we view the education and welfare of our children as a basic right, then, and only then, will we begin to develop the frame of mind needed to justify directing our public funds to support the costly and high-risk, but essential, R&D required to bring new drugs to the marketplace.

To put it in other terms, if the public wants lower drug prices, the public should be willing to front the risk money for drug development. I don't think we Americans believe in free-riding, but we also don't like being taken for a ride by the rest of the industrialized world whose governments provide price protection. As long as drugs and health care services are considered to be commodities, then drug prices, like energy prices, will be driven by market forces, and may run counter to the public good.

In conclusion, I hope that this historic hearing over whether the government should exercise its statutory 'march-in' rights over Norvir will become part of a record of a thoughtful dialogue between the public and private sectors on how best to share the enormous R&D risks involved in bringing important new drugs to the nation, and eventually to the world's public health marketplaces.

PUBLIC PATENT FOUNDATION
Representing the Public's Interests in the Patent System

PUBPAT

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April 29, 2004

Dr. Mark Rohrbaugh
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Blvd., Suite 325
Rockville, MD 20852

Re: Analysis of Patents Relevant to the Ritonavir Petition

Dear Dr. Rohrbaugh:

As Executive Director of the Public Patent Foundation ("PUBPAT"), a not-for-profit legal services organization working to protect the public from the harms caused by wrongly issued patents and unsound patent policy, I write to provide patent related information and analysis pertinent to Essential Inventions' Petition to Promote Access to Ritonavir ("Ritonavir Petition").

By way of introduction, I am a registered patent attorney with extensive experience litigating, licensing, prosecuting, and otherwise counseling clients with respect to patents. Prior to founding PUBPAT, I practiced patent law with Skadden, Arps, Slate, Meagher & Flom, LLP, Brobeck, Phleger & Harrison, LLP, and Patterson, Belknap, Webb & Tyler, LLP, all in New York, and served the Honorable Randall R. Rader, Circuit Judge for the U.S. Court of Appeals for the Federal Circuit in Washington, D.C. A substantial segment of my experience has focused on pharmaceutical patent issues, including the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Act") and the role of the Food and Drug Administration's Approved Drug Products with Therapeutic Equivalence Evaluations publication ("Orange Book"). In addition to litigating several generic pharmaceutical patent infringement cases, otherwise called ANDA cases, I have also comprehensively evaluated the patent portfolios of pharmaceutical companies and issued opinions regarding the scope and validity of specific pharmaceutical patents.

PUBPAT has undertaken a review of the patents pertaining to Abbott Laboratories' ritonavir drug products. In total, there are 5 patents listed by Abbott in the Orange Book for its approved ritonavir capsule product. Of those 5, the Ritonavir Petition would, if granted, provide access to 4, leaving only one patent, U.S. Patent No. 6,232,333 ("'333 patent"), as a potential barrier to making an effective generic ritonavir capsule product. Table 1 below sets forth the Orange Book patent listing for Abbott's ritonavir capsule product and also indicates which of those patents are subject to the Ritonavir Petition.

Patent No.	Listed for Abbott's Ritonavir Capsule	Subject to the Ritonavir Petition
5,541,206	Yes	Yes
5,635,523	Yes	Yes
5,648,497	Yes	Yes
5,846,987	Yes	Yes
6,232,333	Yes	No

Table 1: Orange Book Listed Patents for Abbott's Ritonavir Capsule

The '333 patent, unlike each of the other 4 patents listed for Abbott's ritonavir capsule, does not claim the active ingredient, ritonavir, itself. Rather, it merely claims a pharmaceutical composition containing ritonavir. Upon initial review, we have serious doubts about the validity of the '333 patent and its applicability to an effective generic ritonavir product. One issue regarding the '333 patent's validity is that its Abstract and Specification purport to teach an invention providing "improved bioavailability." Yet, no such limitation is present in any of the '333 patent's claims. Such a missing limitation means that the scope of the claims is much broader than what the patent otherwise purports to cover. This breadth of the claims increases the likelihood that they are invalid.

Regardless, the existence of the '333 patent in no way detracts from the importance or utility of the Ritonavir Petition. Access to the technology claimed in the 4 other patents that pertain to ritonavir is absolutely necessary to making an effective ritonavir capsule product available to the American public on fair terms. Further, a potential producer of a generic ritonavir product is much more likely to challenge the '333 patent if it stands alone as the sole patent at issue than if the other 4 patents must also be dealt with. This is especially true since the'333 patent has such glaring validity issues and may be much more easily designed around than the other 4 patents since it does not cover the active ingredient ritonavir itself.

In conclusion, there is absolutely no patent related reason to quell support of the Ritonavir Petition. If PUBPAT can be of any further assistance with respect to this matter, please do not hesitate to contact me.

Sincerely,

Dan Ravicher

cc: James Love
Essential Inventions, Inc.

NASULGC National Association of State Universities and Land-Grant Colleges

April 22, 2004

Dr. Mark Rohrbaugh
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, MD 20852

Dear Dr. Rohrbaugh:

On behalf of the National Association of State Universities and Land-Grant Colleges ("NASULGC"), the Association of American Universities (AAU), and the American Council on Education ("ACE"), we are writing to share our views about the two petitions filed with the National Institutes of Health (NIH) to exercise Bayh-Dole march-in rights to require Abbott Laboratories to lower the price of several drugs developed from NIH extramural research.

The petitions are rooted in the proposition that march-in rights can be exercised to maintain the accessibility and affordability of an essential medical invention. Neither the plain meaning nor the public policies that undergird the Bayh-Dole Act permit a march-in based on affordability. March-in is not a surrogate for government price controls on products that result wholly or in part from federal funding. March-in is reserved only for the purpose of prompt commercialization of federally funded inventions and to avoid the possibility of the stifling of new product development.

The subject of delivering affordable health care to the American public is a serious one, worthy of policy debate; it is ongoing in Congress in the context of Medicare reform and drug reimportation. Debate about the quality and accessibility of health care is especially worthwhile when life-saving drugs involving potentially fatal diseases, such as HIV-AIDS, are involved. But, the Bayh-Dole Act is not the proper forum for this debate. The Act does not confer regulatory authority on the NIH to impose price controls either globally or on a case-by-case basis. Nor should the Patent Act, in which the Bayh-Dole Act resides, be used as a compulsory mechanism for reasonable drug pricing.

If the NIH were to interpret its authority so as to exercise march-in rights, we are deeply concerned that the Bayh-Dole Act, one of this country's most successful statutes, could be subjected to a litany of unintended consequences. The ability of universities to make their federally funded technologies available for public benefit would be undermined, and the incentive for the private sector to invest in federally funded discoveries would be removed. In the final analysis, the synergy between federal funding, university research and the private sector for product development could be lost.

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In short, the Bayh-Dole Act has become a driving force for successful research activities from which the U.S. economy and the American public have benefited. Any administrative action taken by the NIH must recognize the success of the Act and its limitations as a price-control mechanism.

Cordially,

C. Peter Magrath
President, NASULGC

Nils Hasselmo
President, AAU

David Ward
President, ACE

CPM/rh

WARF
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April 15, 2004

Dr. Mark Rohrbaugh
Dir. of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Blvd. Suite 325
Rockville, MD 20852

Dear Dr. Rohrbaugh:

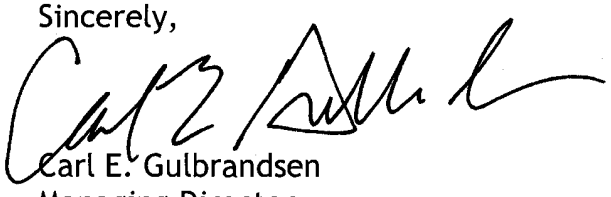
WARF will celebrate its 79th anniversary this year. We were one of the first university affiliated technology offices in the United States. Howard Bremer of WARF was instrumental in the development of the Bayh-Dole Act. Given this history we write to oppose the recent petitions filed by Mr. James Love and Mr. Sean Flynn of Essential Inventions, Inc. requesting the National Institutes of Health invoke the march-in provisions of the Bayh-Dole Act to invalidate exclusive drug patents held by Abbott Laboratories and Pfizer Inc.

The Bayh-Dole Act is a patent law and not a price control law. There is nothing in Bayh-Dole that gives the government authority to march-in to control prices. March-in rights are intended to insure development of important products that improve the human condition and add to the U.S. economy. The Act has achieved tremendous success. When Bayh-Dole was enacted in 1980, less than 30 universities had technology transfer programs. Today, there are over 300 university technology transfer programs that are using local ideas, contacts and initiatives to insure the development and use of federally supported research.

The granting of this petition would be a severe blow for all of the university technology transfer offices. The patent received by universities would be encumbered. The consequence of that would be to make it difficult if not impossible to license technologies to the private sector. The twenty-five years of Bayh-Dole success of partnerships between federal government, university research and private sector development could be lost. How ironic it would be if as countries all over the world are attempting to implement their version of Bayh-Dole, our government would make a decision that could destroy the program that these countries are attempting to implement.

The Bayh-Dole Act is an important catalyst for university private sector collaborators. All sectors of our economy have benefited. Please do NOT take any actions that could put these benefits in jeopardy.

Sincerely,



Carl E. Gulbrandsen
Managing Director

COUNCIL ON GOVERNMENTAL RELATIONS

1200 New York Avenue, N.W., Suite 320, Washington, D.C. 20005
(202) 289-6655/(202) 289-6698 (FAX)

April 5, 2004

Dr. Mark Rohrbaugh
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, Maryland 20852

Dear Dr. Rohrbaugh:

The Council on Governmental Relations (COGR) is an association of 150 of the leading research universities in the United States and several affiliated hospitals and research centers. COGR focuses on understanding federal policies and complying with federal regulations pertaining to sponsored research at universities. Among the most important policies and regulations of interest to our members are those pertaining to the transfer of federally funded research results at universities to the private sector under the Bayh-Dole Act of 1980 (P.L. 96-517; 35 USC 200-212).

The Bayh-Dole Act plays a critical role in enabling university innovations that have been crucial to U.S. economic growth and competitiveness. Bayh-Dole established the major mechanism for successfully transferring federally funded research results from the laboratory to products and services, which benefit all Americans. Bayh-Dole's success is derived from its consistency with America's commitment to free market principles and incentives.

Many studies have demonstrated the phenomenal success of the Bayh-Dole Act. For example, according to an article in the December 12, 2002, *The Economist*, "The Bayh-Dole Act of 1980 is perhaps the most inspired piece of legislation to be enacted in America over the past half-century....this unlocked all the inventions and discoveries that have been made in laboratories throughout the United States with the help of taxpayers' money...."

We understand that NIH has been asked to answer recently submitted petitions for exercise of march-in rights that, according to the authors of the legislation, Senators Birch Bayh and Robert Dole, are based on a fallacious premise. March-in rights accrue to the government only for the purpose of ensuring prompt commercialization of federally funded inventions and to avoid the possibility of companies stifling the development of new products. The legislation does not empower the government in any way to influence or to dictate licensing or commercialization terms for technologies. NIH itself has confirmed this interpretation (NIH Plan to Ensure Taxpayers' Interests are Protected, July 2001).

NIH may feel challenged to review its longstanding interpretation of the conditions under which the government may exercise march-in rights. Given the critical role played by the Bayh-Dole Act in the continuing success of university technology transfer, COGR believes that any proposed change to such a longstanding interpretation should be subjected to close scrutiny. If this were to become necessary, all stakeholders in the continuing success of technology transfer from universities should participate fully in the consideration of the scope of government march-in rights to ensure that the public-private partnership in innovation is maintained.

COGR is concerned that a substantial reinterpretation of the Bayh-Dole's march-in provisions could undermine the ability of universities to make their federally funded technologies available for public use. Any such change in march-in authority or in expanding their exercise by government agencies could result in the loss of the very delicate balance of rights and obligations between the three partners - government, universities and industry - which has been the basis for the success of this legislation. History has proven how important incentives are for encouraging technology transfer from the universities. It would be ironic, indeed, if a change in the current understanding of march-in rights were to impair the dissemination of, and public benefit from, university research results.

For these reasons, COGR urges the NIH to make a strong statement in support of the proper exercise of march-in rights as stated by Senators Bayh and Dole, which was recently reconfirmed in their letter dated April 11, 2002 in the Washington Post. NIH surely is aware of the importance of the Bayh-Dole Act to public-private partnerships in innovation. We see no reason to tamper with this proven platform for promoting government investment in discovery and its application for public use and benefit.

Sincerely,

Katharina Phillips.

Katharina Phillips

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Dr. Mark Rohrbaugh
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, Maryland 20852

Dear Dr. Rohrbaugh:

We are writing on behalf of the Association of University Technology Managers (AUTM®), to comment on the petition to use the authority under the Bayh-Dole act to promote access to: (a) Ritonavir, supported by National Institute of Allergy and Infectious Diseases Contract no. AI27220; and (b) Latanoprost, supported by U.S. Public Health Service Research Grant Numbers EY 00333 and EY 00402 from the National Eye Institute, filed by Essential Inventions, Inc. with Secretary Thompson on January 29, 2004. AUTM® is a nonprofit association with membership of more than 3,200 technology managers and business executives who manage intellectual property at over 300 universities, research institutions, teaching hospitals and a similar number of companies and government organizations.

While the subject of delivering affordable health care is certainly a serious issue for the United States, we believe it must be addressed through other means. There are no expressed authorities in the Act or implementing regulations that would support the petitioner's position for Governmental actions such as those requested. As noted in 35 U.S.C. 200, the general description of the authorities reserved to the government are limited, "...to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against non-use or unreasonable use of the invention..." (underlining added).

The general reservation of rights in the Government is specifically implemented in the march-in provision of 35 U.S.C. §203, which should not be read to be any broader than intended in the general reservation of 35 U.S.C. §200, which would be necessary to grant the requested march-in request. Indeed, such actions as proposed by the petitioner were never contemplated by the Congress and are not reflected in a proper understanding of the legislative history of the law. On the contrary, it is clear that such authorities would actually frustrate the stated policy and objectives of the Act to create incentives for commercial development by assuring, when necessary, an exclusive patent position (see 35 U.S.C. 200).

We believe that an NIH interpretation of the Bayh-Dole Act as advocated by Essential Inventions would disable the Act. The primary basis for the Act lies in the belief of individual action as opposed to government action and the power of the market. Most inventions resulting from government research are conceptual

AUTM

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in nature and require significant investment by the private sector to bring them into practical application. This is particularly true of life science inventions requiring licensure by the Food and Drug Administration. Commercial concerns are unlikely to invest substantial financial resources in the commercial development of any invention, funded in part by the government, knowing that the government could challenge their competitive position after the product was introduced onto the market. As was the experience in the years before the passage of the Bayh-Dole Act, when government policy was to grant only non-exclusive licenses, no drugs for which the government held title were developed and made available to the public.

Currently, exclusive licenses of federally funded inventions are believed to be dependable. This dependability can be maintained only if all those involved in the process retain full confidence that the march-in remedy will be exercised only in those extraordinary circumstances clearly anticipated by the Act. In 1997, Harold Varmus, then Director of the NIH, recognized this potential when he rejected the march-in petition of CellPro after it lost a patent infringement suit brought by Johns-Hopkins University, Becton Dickinson and Baxter. In issuing his determination, he stated:

> *"The patent system, with its resultant predictability for investment and commercial development, is the means chosen by Congress for ensuring the dissemination and development for new and useful technologies. It has proven an effective means for the development of healthcare technologies."*

On May 13, 2003, after a detailed study of technology transfer mechanisms, the President's Council of Advisors on Science and Technology concluded:

> *"Existing technology transfer legislation works and should not be altered."*

Interpreting agency authority to exercise march-in rights as advocated by the petitioner would be a major alteration to the existing technology transfer legislation. Granting a march-in in this instance would, we believe, serve only a narrow interest and be contrary to the broader public interest the Act is intended to serve. While we do not wish to diminish the seriousness of the issue of delivering affordable health care we believe it must be addressed through other means and urge the NIH to reject Essential Inventions's petition.

Sincerely,

Patricia Harsche Weeks

Patricia Harsche Weeks
Immediate Past President
AUTM

Robert C. Byrd
National Technology Transfer Center
at Wheeling Jesuit University

March 31, 2004

Dr. Mark Rohrbaugh
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, MD 20852

Dear Dr. Rohrbaugh:

I recently became aware of a petition addressed to you by Mr. James Love, President of Essential Inventions, Inc. requesting that the National Institutes of Health exercise the march-in rights provision of the Bayh-Dole Act to lower the price of several drugs developed from NIH extramural research.

While the subject of delivering affordable health care is certainly a serious issue, the provisions of the Bayh-Dole Act do not provide for governmental actions such as those requested by Essential Inventions. Indeed, such actions were never contemplated by the Congress and are not reflected in the legislative history of the law.

The interpretation of the intent of Congress in passing this landmark legislation reflected in Mr. Love's petition is, therefore, entirely fanciful.

While serving former Senator Birch Bayh on the Senate Judiciary Committee, I staffed the hearings and wrote the report of the Senate Judiciary Committee on the bill. I also served for many years as the Director of Technology Commercialization at the U.S. Department of Commerce. There I oversaw the implementation of the regulations for Bayh-Dole and chaired the Interagency Committee on Technology Transfer which developed guidelines for utilizing the Federal Technology Transfer Act, under whose authorities NIH develops many of its intramural partnerships with U.S. industry.

Regrettably, Mr. Love and several others making the same case mix up the legislative history of the Bayh-Dole Act with hearings on rival legislation that was not enacted. The **only** legislative history with any bearing on the law are the hearings of the U.S. Senate Judiciary Committee in the 96th Congress on S. 414, the University and Small Business Patent Procedures Act (commonly called Bayh-Dole), the report of the Senate Judiciary Committee on the same, and the Senate debates on S. 414.

Fortunately, we do have an unambiguous opinion from Senators Birch Bayh and Robert Dole themselves on the topic at hand. The *Washington Post* ran an article by Professors Peter Arno and Michael Davis on March 27, 2002, **Paying Twice for the Same Drugs,** making the same arguments as Mr. Love. They wrote:

> *Bayh-Dole is a provision of U.S. patent law that states that practically any new drug invented wholly or in part with federal funds will be made available to the public at a reasonable price. If it is not, then the government can insist that the drug be licensed to more reasonable manufacturers, and, if refused, license it to third parties that will make the drug available at a reasonable cost.*

A joint letter by Senators Bayh and Dole on April 11, 2002, to *The Washington Post* effectively refutes this argument. Here is the complete text of what the authors of the law said was their intent with regard to fair pricing of resulting products:

> *As co-authors of the Bayh-Dole Act of 1980, we must comment on the March 27 op-ed article by Peter Arno and Michael Davis about this law.*
>
> *Government alone has never developed the new advances in medicines and technology that become commercial products. For that, our country relies on the private sector. The purpose of our act was to spur the interaction between public and private research so that patients would receive the benefits of innovative science sooner.*
>
> *For every $1 spent in government research on a project, at least $10 of industry development will be needed to bring a product to market. Moreover, the rare government-funded inventions that become products are typically five to seven years away from being commercial products when private industry gets involved. This is because almost all universities and government labs are conducting early-stage research.*
>
> ***Bayh-Dole did not intend that government set prices on resulting products. The law makes no reference to a reasonable price that should be dictated by the government. This omission was intentional; the primary purpose of the act was to entice the private sector to seek public-private research collaboration rather than focusing on its own proprietary research.***
>
> ***The article also mischaracterized the rights retained by government under Bayh-Dole. The ability of the government to revoke a license granted under the act is not contingent on the pricing of a resulting product or tied to the profitability of a***

company that has commercialized a product that results in part from government-funded research. The law instructs the government to revoke such licenses only when the private industry collaborator has not successfully commercialized the invention as a product. (Emphasis added).

The law we passed is about encouraging a partnership that spurs advances to help Americans. We are proud to say it's working.

Birch Bayh/Bob Dole

In their typically succinct manner, the authors of the law effectively rebut the argument now before you.

The Bayh-Dole Act has become a linchpin of our economy. While not perfect, the U.S. record of commercializing new products and services funded by the Government is the envy of the world. **The Economist Technology Quarterly** said: "Possibly the most inspired piece of legislation to be enacted in America over the past half-century was the Bayh-Dole act of 1980." Any legislative or administrative actions undertaken to alter this Act must be done very carefully.

We have already witnessed well intended Congressional attempts to impose fair pricing clauses on NIH intramural research partnerships. These efforts failed. Technology transfer cannot be a vehicle for trying to control prices. Rather than allowing Government to dictate drug prices, companies simply walked away from partnering with NIH. Wisely recognizing its mistake, Congress rescinded the fair pricing requirement. NIH's subsequent success in building effective partnerships with industry is well documented, and is a great benefit to the public.

President Johnson asked in 1968 how many NIH owned inventions had been commercialized. The answer was none. At that time there were no incentives for industry to undertake the risk and expense inherent in developing such early stage inventions. We should reflect that because of the Bayh-Dole Act, many life saving drugs and therapies are now available for those in need. By altering this delicately balanced law, we may well discover that publicly funded inventions go back to gathering dust on the shelves. Before Bayh-Dole such discoveries were not available at any price.

Sincerely,

Joseph P. Allen
President
National Technology Transfer Center

ABBOTT

Heather L. Mason
Vice President, Pharmaceutical
Specialty Operations

Abbott Laboratories
D-522, AP30
200 Abbott Park Road
Abbott Park, Illinois 60064-6163

Telephone (847) 938-2285
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March 26, 2004

John G. Aubrey, Jr., Ph.D.
Chairman Emeritus
Academy of Medical Art & Sciences
Business Solutions for Medicine
10455 N. Central, Suite 109-131
Dallas, Texas 75231

Dear Dr. Aubrey,

We are responding to your recent correspondence to Miles White on behalf of Business Solutions for Medicine regarding the recent re-pricing of Norvir® (ritonavir). Abbott appreciates your taking the time to contact us and we value your input.

Regrettably, your letter contains considerable misinformation about the re-pricing action and we would like to take the opportunity to provide you with the facts.

Your letter inaccurately states that Norvir's "increase largely gets passed directly to the patient."

In fact, there is little if any, direct impact to the patient. Abbott has taken extraordinary measures to ensure that patients who need Norvir will have access to it. AIDS Drug Assistance Programs (ADAPs) and Medicaid, which provide HIV drugs to uninsured and underinsured patients, are not impacted by the re-pricing.

- Unlike other companies in this area, Abbott has **permanently** frozen Norvir soft gel capsules at its previous price of $1.71 per 100 mg dose for ADAPs, and is the only company to take such a step with one of its drugs. ADAPs provide medication for 20 percent of U.S. AIDS patients.
- Abbott is also the first in the industry to eliminate income requirements for its Patient Assistance Program to ensure that all HIV patients without prescription drug coverage or public assistance can receive Norvir free, regardless of financial status.

208667

- Further, Abbott offers Norvir free to patients who exceed their annual drug coverage maximum, or who are on ADAP waiting lists.

You write that "many times, the patient is responsible for a single co-pay for an HIV drug prescription" and that Norvir's price increase "is potentially serving to empty the wallet of seriously, critically and/or terminally ill HIV/AIDS patients relying upon Norvir as part of their HIV drug cocktail."

Co-payments and premiums for HIV patients with private insurance receiving Norvir remain unchanged, to our knowledge.

- Antiretrovirals comprise 1.5 percent of the nation's private payer pharmacy budget, and at its new price, Norvir accounts for less than .1 percent of this budget.

- Abbott has committed to making a 30-count bottle available to patients as soon as possible, in additional to the 120-count bottle available today. This should address patients with co-insurance who have experienced an increase in their initial out-of-pocket expenses at pharmacies (representing less than 5 percent of privately insured patients). These patients typically have out-of-pocket caps at $1,500 to $2,500, well below the cost of HIV medicines. We are also addressing this issue on a case-by-case basis through our Patient Assistance Program.

It is important to note that Abbott is not aware of *any* patient who has gone without Norvir as a result of the re-pricing. Any patient you are aware of, who does not have access to Norvir should contact Abbott directly at 1-800-222-6885. We will take immediate steps to work toward resolving the situation.

You write that the Norvir re-pricing "raises questions in [your] mind if indeed Abbott has infringed upon regulations set forth in anti-trust legislation." In the same vein, you further note you have "discovered the Attorneys General of New York and Illinois have launched criminal investigations into this pricing practice at Abbott."

In fact, Abbott is in full compliance with both federal and state competition laws. Abbott is cooperating with Attorneys General who have questions about the re-pricing of Norvir.

Keep in mind that at its most commonly used dose (100 mg), Norvir remains most often the lowest-cost component of HIV treatment regimens. Its boosting properties are truly unique as it makes other components of the HIV regimen more effective. Perhaps given your concerns about the cost of therapy, you should also look at these high-cost components of HIV regimens and the respective cost of their daily dose.

Additionally, in order to properly analyze this issue, one would hope that you would look at the full spectrum of HIV drugs and their respective clinical value to patients compared to Norvir, and how their pricing reflects this value. We believe the focus of criticism should properly be on companies who introduce new drugs at premium prices with limited patient benefit. Some of these drugs represent only moderate improvements or reformulations of older medications.

At $8.57 per day, the cost of its most commonly used dose, Norvir has an appropriate clinical value/cost ratio in our opinion. By comparison, other new protease inhibitor drugs, such as Lexiva® (GlaxoSmithKline) and Reyataz® (BMS), both of which Norvir makes more effective – are priced at $19 to $33.50 per dose.

Abbott is proud of its 20-year history of pioneering contributions in HIV therapy. We will continue on this path of excellence as we pursue the next generation of protease inhibitor therapies.

We hope that you will use these facts to help correct any other misinformation.

Sincerely,

Heather L. Mason
Vice President, Pharmaceutical Specialty Operations
Abbott Laboratories

cc: The Honorable Tommy G. Thompson
Secretary, Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

The Honorable Ted Stevens
Chairman, Committee on Appropriations
United States Senate
522 Hart Senate Office Building
Washington, DC 20510

The Honorable C.W. Bill Young
Chairman, Committee on Appropriations
United States House of Representatives
The Capitol, Room H-218
Washington, DC 20515

The Honorable Christopher H. Smith
Chairman, Committee on Veterans' Affairs
United States House of Representatives
335 Cannon House Office Building
Washington, DC 20515

The Honorable William H. Donaldson
Chairman
United States Securities and Exchange Commission
450 Fifth Street, N.W.
Washington, DC 20549

The Honorable Geoffrey S. Connor, Esq.
Secretary of State
State of Texas
P.O. Box 12877
Austin, TX 78701

The Honorable Greg Abbott, Esq.
Attorney General
State of Texas
300 West 15th Street
Austin, TX 78701

The Honorable Eduardo J. Sanchez, M.D., M.P.H.
Commissioner
Texas Department of Health
1100 West 49th Street
Austin, TX 78756

The Honorable Jim Hine
Commissioner
Texas Department of Human Services
701 West 51st Street
Austin, TX 78751

OHHP

Organization of Healthcare Providers

March 10, 2004

The Honorable Tommy Thompson
Secretary, Department of Health and Human Services
200 Independence Ave., S.W.
Washington D.C. 20201

Dr. Mark Rohrbaugh
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Blvd, Suite 325
Rockville, MD 20852

Dear Secretary Thompson and Dr. Rohrbaugh:

The undersigned clinicians write in strong support of the March-In petition filed last month by the nonprofit Essential Inventions, Inc., for an open license for the supply of ritonavir, sold by Abbott Laboratories as Norvir®. An open license would allow full and open competition for the supply of ritonavir, which we believe is a fitting remedy to abusive pricing practices of Abbott Laboratories.

There is widespread dissatisfaction among HIV health care providers nationwide with Abbott Laboratories regarding the decision to increase the price of ritonavir by more than 400%. This increase, if allowed to stand, will have devastating consequences for the future of HIV care in the United States.

Ritonavir is the only effective boosting compound available to increase the effectiveness of existing treatments for HIV/AIDS. Without ritonavir, other compounds are dramatically less effective. Ritonavir is an essential component of almost every protease inhibitor-based antiretroviral treatment for HIV/AIDS.

Abbott's price increase effectively makes its Kaletra product, which includes ritonavir and was not subject to the price increase, the cheapest boosted protease inhibitor on the market. This will have adverse consequences for the care of patients as doctors and patients will feel pressure to use Kaletra, even when it is not the best treatment for a patient.

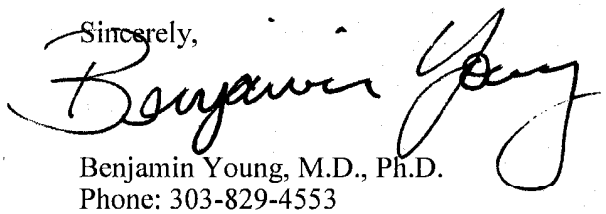
There is no legitimate justification for Abbott's 400% increase in the price of ritonavir, announced just two weeks before Christmas. Abbott is taking advantage of a monopolistic situation, where its product is the only effective protease inhibitor boosting agent.

We are shocked and dismayed that Abbott has raised the price of ritonavir in the U.S., where taxpayer dollars funded its discovery, but not in Europe and other wealthy countries. This fact hardens our opinion that Abbott's price increase lacks any legitimate justification. At least when U.S. taxpayers fund the discovery of a medicine, they should not be subject to

arbitrary and discriminatory prices out of proportion with the prices for the same drug in other comparable markets.

We encourage you to act to remedy this dire situation. Abbott is not making this important government invention available to the public on reasonable terms. Your action is needed to protect the health and safety of people with HIV/AIDS from the effects of Abbott's abusive price increase.

Sincerely,



Benjamin Young, M.D., Ph.D.
Phone: 303-829-4553
E-mail: DenverIDC@aol.com

1. Dorry Norris M.D.
2. Jason Flamm, M.D.
3. Carl Stein, M.D.
4. Joseph Jemsek, M.D.
5. Jennifer Aldrich, M.D.
6. Christopher McMackin, M.D.
7. Richard J Feldman, MD
8. Muhammad R. Sohai, M.D.
9. Robert Killian, M.D./M.P.H.
10. Chad Zawitz, M.D.
11. Kenneth Gould M.D.
12. Ricardo Alvarez, M.D.
13. Barbara Lee Perlmutter, M.D.
14. Wayne Bockmon, M.D.
15. Mario J Fonseca, M.D.
16. Stephen Boswell, M.D.
17. Debrah Archer, F.N.P.
18. William Jay Robbins, M.D.
19. Leslie A. Baken, M.D.
20. Toby Dyner, M.D.
21. Townson Tsai, M.D.
22. Chandra Kantor, A.R.NP.
23. Pablo Tebas, M.D.
24. Charles Steinberg, M.D.
25. Victor Lewis, M.D.
26. James Shearer, PA-C
27. J. Manuel Patino, M.D.
28. Paola Greiger, M,D,
29. Virginia Cafaro, M.D.
30. Martin Kramer, PA-C

AIDS treatment
ATAC
activists coalition

Drug Development Committee

February 26, 2004

Mark L. Rohrbaugh, Ph.D., J.D.
Director, Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard
Suite 325
Rockville, MD 20852

RE: ESSENTIAL INVENTIONS, INC. PETITION TO USE BAYH-DOLE AUTHORITY TO PROMOTE ACCESS TO RITONAVIR, SUPPORTED BY NIAID CONTRACT NIAID CONTRACT NO.: AI27220

Dear Dr. Rohrbaugh:

The AIDS Treatment Activist Coalition (ATAC) is a national coalition of AIDS activists, many living with HIV/AIDS, working together to end the AIDS epidemic. ATAC's Drug Development Committee (DDC) works with government, academia and Industry to provide a community perspective to the development of new HIV drugs and the utilization of HIV therapies. We are writing to support the petition by Essential Inventions, Inc., requesting that you exercise the "march-in" provisions of the Bayh-Dole Act with respect to Norvir, a government funded invention by Abbott Laboratories.

Abbott shocked the AIDS affected community and endangered many lives by increasing the price of Norvir by 400% in December 2003. A full treatment of Norvir will now cost over $46,000, making it by far the most expensive protease inhibitor on the market.

The most common use of Norvir is as a "booster" for other protease inhibitors. For six of the seven non-Abbott protease inhibitors on the market, boosting with Norvir is necessary to achieve maximum medical benefits. Thus, Abbott's price increase has anticompetitively raised the price of its competitors' products.

Abbott did not raise the price of its own Norvir-boosted protease inhibitor, Kaletra. The disparity in the price of Kaletra versus other Norvir boosted protease combinations will negatively impact the health and safety of people with HIV/AIDS in a number of ways. Some insurers may limit people's access to protease inhibitor combinations other than Kaletra and may ban reimbursement for Norvir in its full dose. Many could be left with substandard treatment options, leading to increased risk for illness and even loss of life.

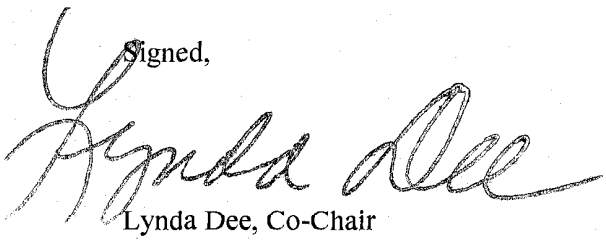
AIDS Drug Assistance Programs, which are already capping enrollment and rationing access to medications because of a lack of needed resources, will see their ranks swell as people are forced out of private sector insurance options and will feel financial strain by commitments to pay private insurance medicine co-payments for many patients. Pharmaceutical assistance programs operated by cities under Title I of the Ryan White Act and non-profit treatment clinics around the country are being saddled with the full price increase to the detriment of their ability to serve their patients.

The price increase will also have a negative impact on the development of new protease inhibitors that require a boosting dose of Norvir. For example, tipranavir, a new protease inhibitor by Boehringer-Ingelheim, needs to be boosted with 400 milligrams of Norvir. At the new Norvir price, the booster component alone for tipranavir will cost over $16,000 a year, destroying the drug's potential to compete with other protease inhibitors for a share of the market for first-line treatments. Therapies that require Norvir boosting may now be abandoned due to the astronomical price of Norvir. This threatens "salvage" patients, the very people who need new anti-HIV drugs the most because they have become resistant or intolerant to all other marketed anti-viral options.

We endorse Essential Inventions' proposed terms for a Bayh-Dole license. First, the license should be open to all qualified applicants so that competitive forces can work to lower prices to consumers to the lowest possible amount, consistent with providing due reward to the patent holder. Second, under the circumstances, we believe that Essential Inventions' proposed royalty term to Abbott of 5% of net generic sales is generous. Third, we endorse the concept of a research and development contribution based on sales of generic Norvir to ensure that use of Bayh-Dole rights does not detract from needed efforts to fund research and development for new HIV/AIDS treatments. We agree with Essential Inventions' petition that there may be multiple ways to structure the fund, and to ensure that the fund is transparent and directed toward research and development of new AIDS drugs.

We urge that you act with great haste to alleviate the negative impacts to health and welfare that people with AIDS are facing because of Abbott's unreasonable and abusive pricing of a government funded invention.

Signed,



Lynda Dee, Co-Chair
AIDS Treatment Activists Coalition
Drug Development Committee
111 N. Charles Street, Suite 500
Baltimore, MD 21201

Gay Men's Health Crisis (GMHC), NYC
Treatment Action Group (TAG), NYC
HealthGap
Center for AIDS, Houston
Test Positive Aware Network, Chicago
The Access Project, NYC
AIDS Treatment Data Network, NYC
The Harm Reduction Coalition, NYC
Being Alive, Long Beach
Program for Wellness Restoration, Houston
AIDS Action Baltimore
Community HIV/AIDS Mobilization Project (CHAMP), NYC
Essential Innovations, Inc.
AIDS Treatment Activists Coalition (ATAC) Save AIDS Drug Assistance Program (ADAP) Committee
Ohio AIDS Coalition

Hyacinth AIDS Coalition, New Brunswick, NJ
Positive for Positives, Cheyenne, Wyoming
Title II Community AIDS National Network (TIICAN)
New Mexico Poz Coalition
Planet Poz, Albuquerque , NM
Wyoming: Positives For Positives
Foundation for Integrative AIDS Research (FIAR), Brooklyn, NY
Being Alive, Los Angeles
Housing Works, Albany Advocacy Center
NYC AIDS Housing Network
Michigan Positive Action Coalition (MI-Poz)
New Mexico AIDS InfoNet
The Peoples Caucus, San Antonio, TX
San Francisco AIDS Foundation
ACT UP/NY
ACT UP East Bay, Oakland, CA
HIV Advocacy Council of Oregon and Southwest Washington
International Foundation for Alternative Research in AIDS (IFARA)
AIDS Action Project Northwest (AAPNW), Portland, OR
Organization of HIV Healthcare Providers
Benjamin Young, M.D., Ph.D., Chair, Denver I.D. Consultants
Edwin, DeJesus, M.D., Vice Chair, Denver I.D. Consultants
Howard A. Grossman, M.D., Secretary, Denver I.D. Consultants
Bill Owen, M.D., Treasurer, Denver I.D. Consultants
Eric Goldman, Esquire

CC: Mark L. Rohrbaugh, Ph.D., J.D.,
Director, Office of Technology Transfer
National Institutes of Health

ATACSignOnMR

WEST VIRGINIA
Coalition FOR People
WITH HIV/AIDS
EST. 1993

The Honorable Tommy Thompson
Secretary
Department Of Health and Human Services
200 Independence Ave, S.W.
Washington, D.C, 20201

Dear Mr. Secretary;

We write to support the request by Essential Inventions, Inc. that you exercise the provisions of the Bayh-Dole Act with respect to Norvir, a government funded invention by Abbott Laboratories.

Abbott shocked the AIDS affected community and endangered many lives by increasing the price of Norvir by 400% in December 2003. A full treatment of Norvir will now cost over $46,000, making it by far the most expensive protease inhibitor on the market.

The most common use of Norvir is a booster for other protease inhibitors. For six of the seven non-Abbott protease inhibitors on the market, boosting with Norvir is necessary to achieve maximum medical benefits. Thus, Abbott's price increase has anticompetitively raised the price of its competitor's products.

Abbott did not raise the price of its own Norvir-boosted protease inhibitor, Kaletra. The disparity in the price of Kaletra versus other Norvir boosted protease combinations will negatively impact the health and safety of people with HIV/AIDS in a number of ways. Some insurers may limit people's access to protease inhibitor combinations other than Kaletra and may ban reimbursement for Norvir in its full dose. Many could be left with substandard treatment options, leading to increased risk for illness and even loss of life.

AIDS Drug Assistance Programs, which are already capping enrollment and rationing access to medication because of a lack of needed resources, will see their ranks swell as people are forced out of private sector insurance options and will feel financial strain by commitments to pay private insurance medicine co-payments for many patients. Pharmaceutical assistance programs operated by cities under Title I of the Ryan White Care Act and non-profit treatment clinics around the country are being saddled with the full price increase to the detriment of their ability to serve their patients.

The price increase will also have a negative impact on the development of new protease inhibitors that require a boosting dose of Norvir. For example, tipranivir, a new protease inhibitor by Boehringer-Ingelheim, needs to be boosted with 400 milligrams of Norvir. At the new Norvir price, the booster component alone for tipranaivr will cost over $16,000 a year, destroying the drug's potential to compete with other protease inhibitors

OUR MISSION

The West Virginia Coalition for People with HIV/AIDS' mission is to assist people of all ages who are infected with and affected by HIV/AIDS to live an independent and integrated life in the community.

600 SHREWSBURY STREET #3 • CHARLESTON, WV 25301
PHONE: 304 344.1479 • FAX: 304.344.1479
jfazzolari@wvcovenanthouse.org

CARITAS HOUSE, INC.
P.O BOX 365
MORGANTOWN, WV 26507
304 598 5121

COMMUNITY NETWORKS
P.O. BOX 5064
MARTINSBURG, WV 25402
304 263 8059

COVENANT HOUSE, INC.
600 SHREWSBURY STREET
CHARLESTON, WV 25301-1211
304 344 0530

206758
(OS incoming)

for a share of the market for first-line treatments. Therapies that require Norvir boosting may now have to be abandoned due to the astronomical price of Norvir. This threatens salvage patients, the very people who need new anti-HIV drugs the most because they have become resistant or intolerant to all other marketed anti-viral options.

We endorse Essential Inventions' proposed terms for a Bayh-Dole license. First, the license should be open to all qualified applicants so that competitive forces can work to lower prices to consumers to the lowest possible amount, consistent with providing due reward to the patent holder. Second, under the circumstances, we believe that Essential Inventions' proposed royalty term to Abbott of 5% of net generic sales is generous. Third, we endorse the concept of a research and development contribution based on sales of generic Norvir to ensure that use of Bayh-Dole rights does not detract from needed efforts to fund research and development for new HIV/AIDS treatments. We agree with Essential Inventions petition that there may be multiple ways to structure the fund, and to ensure that the fund is transparent and directed toward research and development of new AIDS drugs.

We urge that you act with great haste to alleviate the negative impacts to health and welfare that people with AIDS are facing because of Abbot's unreasonable and abusive pricing of a government funded invention.

Sincerely,

Julie Britton Haden

Julie Britton Haden
West Virginia Coalition for People with HIV/AIDS

Covenant House
Working for Justice for All

600 Shrewsbury Street
Charleston, West Virginia 25301-1211
wvcovenanthouse.org

February 2, 2004

The Honorable Tommy Thompson
Secretary
Department Of Health and Human Services
200 Independence Ave, S.W.
Washington, D.C, 20201

Dear Mr. Secretary;

We write to support the request by Essential Inventions, Inc. that you exercise the provisions of the Bayh-Dole Act with respect to Norvir, a government funded invention by Abbott Laboratories.

Abbott shocked the AIDS affected community and endangered many lives by increasing the price of Norvir by 400% in December 2003. A full treatment of Norvir will now cost over $46,000, making it by far the most expensive protease inhibitor on the market.

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AIDS Drug Assistance Programs, which are already capping enrollment and rationing access to medication because of a lack of needed resources, will see their ranks swell as people are forced our of private sector insurance options and will fell financial strain by commitments to pay private insurance medicine co-payments for many patients. Pharmaceutical assistance programs operated by cities under Title I of the Ryan White Care Act and non-profit treatment clinics around the country are being saddled with the full price increase to the detriment of their ability to serve their patients.

The price increase will also have a negative impact on the development of new protease

Emergency Assistance Program
phone (304)344-8433
fax (304)344-9258

Covenant House
phone (304)344-8053
fax (304)344-4331

Residential & Resource Program
phone (304)344-0530
fax (304)344-9259
1-877-470-0752

206759
(OS incoming)

inhibitors that require a boosting dose of Norvir. For example, tipranivir, a new protease inhibitor by Boehringer-Ingelheim, needs to be boosted with 400 milligrams of Norvir. At the new Norvir price, the booster component alone for tipranaivr will cost over $16,000 a year, destroying the drug's potential to compete with other protease inhibitors for a share of the market for first-line treatments. Therapies that require Norvir boosting may now have to be abandoned due to the astronomical price of Norvir. This threatens salvage patients, the very people who need new anti-HIV drugs the most because they have become resistant or intolerant to all other marketed anti-viral options.

We endorse Essential Inventions' proposed terms for a Bayh-Dole license. First, the license should be open to all qualified applicants so that competitive forces can work to lower prices to consumers to the lowest possible amount, consistent with providing due reward to the patent holder. Second, under the circumstances, we believe that Essential Inventions' proposed royalty term to Abbott of 5% of net generic sales is generous. Third, we endorse the concept of a research and development contribution based on sales of generic Norvir to ensure that use of Bayh-Dole rights does not detract from needed efforts to fund research and development for new HIV/AIDS treatments. We agree with Essential Inventions petition that there may be multiple ways to structure the fund, and to ensure that the fund is transparent and directed toward research and development of new AIDS drugs.

We urge that you act with great haste to alleviate the negative impacts to health and welfare that people with AIDS are facing because of Abbot's unreasonable and abusive pricing of a government funded invention.

Sincerely,

Rhonda Connard

Amanda Lowther

Co-Coordinators
Covenant House AIDS Program

Working for
Justice for All

AIDS HEALTHCARE FOUNDATION

Michael Weinstein
President

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Wallace Albertson, Chair
Laurent Frechet, MD, Vice-Chair
Agapito Diaz, Treasurer
Steve Schulte, Secretary
William Arroyo, MD
Mary Ashley
Curley Bonds, MD
Stephen Bowen, MD
Cynthia Davis
Jonathon Kaplan, Esq
Judith Briggs Marsh
Kathy Mendez, Esq
Ron Meyers
Lawrence Peters
Marjorie Richey
Senator Art Torres (Ret.)
Michael Weinstein

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www.aidshealth.org

AHF Healthcare Centers
888.AIDS.CARE

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Chief of Medicine

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El Monte
Hollywood
Los Angeles – Downtown
Los Angeles – West Adams
Los Angeles – Westside
Oakland
Redondo Beach
San Fernando Valley
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Upland
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AHF Prevention & Testing
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Positive Healthcare/California
323.436.5012

Positive Healthcare/Florida
954.522.3132

AHF Research
323.913.1033

Out of the Closet Thrift Stores
323.860.5262

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Tarzana
Venice
Vermont
W. Hollywood
Westside

January 28, 2004

The Honorable Tommy Thompson
Secretary
Department of Health and Human Services
200 Independence Ave., S.W.
Washington D.C. 20201

Re: Release of ritonovir patents under Bayh-Dole due to anticompetitive practices for NIH developed pharmaceutical

Dear Secretary Thompson:

I am writing to express my concern regarding the recent 500% price increase for the AIDS drug Norvir, (ritonavir) a protease inhibitor produced by Abbott Laboratories. As the largest AIDS organization in the United States, caring for over 12,000 patients in California, Florida, and New York, AIDS Healthcare Foundation is writing on behalf and in support of Essential Medicines, Inc., to request that you exercise the US government right (pursuant to the Bayh-Dole Act) to issue licenses to third parties for generic manufacture of ritonovir.

As you know, Norvir is an antiretroviral medication that is used in combination with other medications to suppress the HIV virus. Norvir is rarely used as the sole protease inhibitor in combination antiretroviral therapy because the required dosage, 600 mg, is generally poorly tolerated. However, it is frequently prescribed in smaller doses (100 mg or 200 mg) to boost the effectiveness of other protease inhibitors, including Fortovase (a Roche drug), Crixivan (a Merck drug), Agenerase (a GlaxoSmithKline drug), and Invirase (also a Roche drug, similar to Fortavase). According to the Seattle Times, about 80% of antiretroviral regimens contain Norvir. In addition, Invirase is clinically not recommended to be prescribed *without* a small dose of Norvir, because the Norvir assists with the absorption of Invirase. Ritonovir is an ingredient, along with another protease inhibitor, lopinivar, in Abbott's drug, Kaletra.

With the December price increase, the cost of a typical one day supply (100mg) has grown from $1.17/day to $8.50/ day. This makes a ritonovir-containing regimen much more expensive, *unless* Abbott's Kaletra is used. Abbott has not increased the price of Kaletra. While Abbott has claimed that the price Norvir increase is necessary to fund an upcoming reformulation, it is our contention that the increase is a ploy to force patients off their current regimens and on to Kaletra. This

AIDS HEALTHCARE FOUNDATION

aggressive and anticompetitive move will dramatically increase the price of non-Abbott protease inhibitor regimes that are used with ritonavir as a booster. The price increases for ritonavir and the aggressive pricing for other ARV drugs such as T-20, are placing enormous pressure on third party payers and patients.

Norvir has been available for retail since 1996, making it one of the older available protease inhibitors. Over 20,000 people in the U.S. depend on Norvir, in various combinations recommended by their physicians, for their continued health and well-being. This drastic increase in price is completely unjustified.

Because of Abbott's anticompetitive action and because that substantial NIH funding was used in the development of ritonovir, we urge you to issue a third party patent to Essential Medicines, inc.

Sincerely,

Michael Weinstein
President

BIO
BIOTECHNOLOGY
INDUSTRY
ORGANIZATION

May 24, 2004

Mark Rohrbaugh, Ph.D., J.D.
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, Maryland 20852

Dear Dr. Rohrbaugh:

On behalf of the Biotechnology Industry Organization (BIO), I am writing to express our views regarding two petitions filed by Essential Inventions, Inc., on January 29, 2004 that request that Bayh-Dole march-in authorities authorize third parties to use patents necessary for the manufacture and sale of two drug products, ritonavir and latanoprost. The petitions assert that both products were developed with assistance from NIH funding mechanisms. Both petitions take the position that the prices for the drug products in the U.S. are unreasonable, and that this factor authorizes exercise of march-in authorities. For both legal and policy reasons, BIO strongly disagrees with the petitioners' view that march-in powers should be used to impose price controls.

BIO is a trade association representing more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in the United States. Our members are involved in the research and development of health-care, agricultural, industrial and environmental biotechnology products and as such rely heavily on strong, predictable patent protection around the world. The vast majority of our members have no products on the market: they have patents as their sole assets. Small biotechnology companies use these patent assets to generate the hundreds of millions of dollars necessary to develop and commercialize a biotechnology product. While federal funding of preliminary research is critical to new product discovery, it is private sector funding that enables the development of a biotechnology product. Private sector investors are more likely to invest in product development when they can expect a return on their investment. Thus, any action by the government that undermines the ability of patent holders to exercise their patent rights is of concern to BIO.

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Success of Bayh-Dole

For over two decades, the Bayh-Dole Act has been the cornerstone of sustained progress in the U.S. biotechnology industry, facilitating a remarkably productive partnership between government, academia and industry. As NIH itself has recognized, "[f]ederally funded biomedical research, aided by the economic incentives of Bayh-Dole, has created the scientific capital of knowledge that fuels medical and biotechnology development. American taxpayers, whose lives have been improved and extended, have been the beneficiaries of the remarkable medical advances that have come from this enterprise." [1] According to the Association of American Universities, domestic universities obtained an average of fewer than 250 patents per year prior to Bayh-Dole.[2] Fewer than 5 percent of the 28, 000 patents being held by federal agencies had been licensed compared with 25 percent to 30 percent of the small number of federal patents for which the government had allowed companies to retain title to the invention. By fiscal 2002, survey results showed that two decades of Bayh-Dole had increased the number of university patents issued annually to over 3600 and over 4600 new licenses and options were reported by 219 institutions.[3]

The Bayh-Dole Act has been instrumental in bringing together the public sector and private sector to move innovative federally funded biotechnology from the bench to the bedside. It has done so by encouraging the licensing of federally funded inventions to private enterprise. Since Bayh-Dole's enactment, technology partnerships have led to the founding of more than 1,100 companies based on NIH and university research. More than 370 biotechnology products have been commercialized since the Act's passage. NIH has concluded that "[c]urrent practices in technology transfer have yielded a dramatic return to the taxpayer through the development of products that, without the successful public-private relationship, might not be available."[4] Moreover, Bayh-Dole's technology transfer policies have benefited American universities, which according to one survey received $1.337 billion in gross income from patent licenses in fiscal 2002.[5] This revenue helps to fund new research and training programs at these institutions.[6]

Legal Analysis

The Bayh-Dole Act permits the government to "march-in" and force a patent holder to grant third-party licenses if the patent holder is not taking "effective steps to achieve practical application of the subject invention" or if "action is necessary to alleviate health or safety needs."[7] Neither the plain meaning of the Act, its legislative history nor the

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[1] Department of Health and Human Services, National Institutes of Health, A Plan to Ensure Taxpayers' Interests Are Protected Part F (July 2001), *available at* http://www.nih.gov/news/070101wyden.htm.
[2] Association of American Universitites, *University Technology Transfer of Government-Funded Research Has Wide Public Benefits* (June 2, 1998), at http://www.aau.edu/research/TechTrans6.3.98.html.
[3] Association of University Technology Managers, AUTM Licensing Survey: FY 2002, Survey Summary at 12, available at http://www.autm.net/surveys/02/2002spublic.pdf.
[4] A Plan to Ensure Taxpayers' Interests Are Protected, supra Part F.
[5] AUTM Licensing Survey: FY 2002, Survey Summary, supra at 18.
[6] A Plan to Ensure Taxpayers' Interests Are Protected, supra Part C.2.a.
[7] 35 U.S.C.§ 203(a)(1), (2).

public policies underlying it contemplate use of the march-in authority because of the price of a commercially available product. Yet the march-in petitions suggest that "open licenses" should be granted if prices of commercially available products are higher in the United States than in other countries. Such an interpretation of the Act is without precedent or legal basis.

The report of the Senate Judiciary Committee explained that the Bayh-Dole Act "is designed to promote the utilization and commercialization of inventions made with government support."[8] Accordingly, the Senate bill authorized NIH to take action through the exercise of march-in rights only in the rare case "when the invention is not being used and it appears that there is a public need to use the invention."[9] By contrast, the committee report makes no mention the use of march-in rights as a tool for insuring "reasonable" prices.

The Act's co-authors, former Senators Birch Bayh and Bob Dole, have stated that the law "did not intend that government set prices on the resulting products." Indeed, the Act's authors pointed out that "[t]he law makes no reference to a reasonable price that should be dictated by the government." Furthermore, "[t]his omission was intentional; the primary purpose of the act was to entice the private sector to seek public-private research collaboration rather than focusing on its own proprietary research."[10]

The petitions urge an inappropriate use of march-in powers to impose price controls on products developed with the aid of federal funds. The Bayh-Dole Act's overriding benefit to the public is to make it possible for early-stage research to be leveraged into initial funding for the creation of private companies that will commercialize new products. Simply put, it was never the intention of Congress that the march-in powers of Bayh-Dole Act be used as a method of price setting. To the contrary, Bayh-Dole's march-in authority allows the federal government to compel licensing of a federally funded invention only if the government believes that (1) the patent owner has not commercialized the invention in a reasonable time, (2) a public health need is not being met by the recipient of the federal grant, or (3) a public noncommercial use requires licensing. These measures were included to ensure that the overall goal of the Act--to spur the interaction between public and private research to benefit the public--would be met. Not one word of the march-in provision, or Bayh-Dole's legislative history, suggests that the price charged for a product serves as a basis for exercising march-in rights.

Previous NIH Positions Reject Use of Price Controls

NIH has already concluded that Bayh-Dole does not contemplate the imposition of price controls. In 1995, NIH reversed an attempt to impose a "reasonable pricing" requirement on parties to its Cooperative Research and Development Agreements ("CRADAs").

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[8] S. Rep. No. 96-480, at 3 (1979).
[9] Id. At 18.
[10] Birch Bayh & Bob Dole, Letter to the Editor, Our Law Helps Patients Get New Drugs Sooner, Wash. Post, April 11, 2002 at A28.

Looking back on this experiment, NIH acknowledged that the policy "had the effect of posing a barrier to expanded research and development and, therefore, was contrary to the Bayh-Dole Act."[11] When NIH removed the reasonable price barrier, the number of CRADAs promptly increased.[12]

NIH has likewise previously presented its views on the important policy considerations raised by any grant of march-in rights. In rejecting the march-in petition of CellPro, Inc. in 1997, NIH recognized that the uncertainty created by an exercise of march-in rights could "have far-reaching repercussions on many companies' and investors' future willingness to invest in federally funded medical technologies." Numerous universities and university groups, similarly cognizant of the dangerous uncertainty created by a march-in, opposed the CellPro petition.[13] Many of these groups have already begun voicing their disapproval of the recent march-in petitions, warning that "[t]he ability of universities to make their federally funded technologies available to the public would be undermined, and the incentive for private sector to invest in federally funded discoveries would be removed."[14]

In denying CellPro's petition, NIH was particularly "mindful of the broader public health implications of a march-in proceeding, including the potential loss of new health care products yet to be developed from federally funded research." Its written decision emphasized that "[t]he patent system, with its resultant predictability for investment and commercial development, is the means chosen by Congress for ensuring the development and dissemination of new and useful technologies. It has proven to be an effective means for the development of health care technologies."[15]

In October 2000, Congress instructed NIH to "prepare a plan to ensure that taxpayers' interests are protected" in light of "the mounting concern over the cost to patients of

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[11] A Plan to Ensure Taxpayers' Interests Are Protected, *supra* Part C.6.

[12] *Id.* Part C.6 & App. 4.

[13] See Letter from Gerhard Casper, President, Stanford University, to Harold Varmus, Director, NIH (June 10, 1997); Letter from David J. Ramsay, President, University of Maryland at Baltimore, to Harold Varmus, Director, NIH (July 10, 1997); Letter from Richard K. Koehn, Vice President for Research, The University of Utah, to Donna E. Shalala, Secretary, Department of Health and Human Services (July 11, 1997); Letter from E. Gordon Gee, President, The Ohio State University, to Harold Varmus, Director, NIH (July 21, 1997); Letter from Cornelius J. Pings, President, Association of American Universitites, to Harold Varmus, Director, NIH (May 30, 1997); Letter from Jlordan J. Cohen, President, Association of American Medical Colleges, to Harld Varmus, Director, NIH (May 30, 1997); letter from Milton Goldbert, President, Council on Governmental Relations, to Harold Varmus, Director, NIH (June 26, 1997).

[14] Letter from National Association of State Universities and Land-Grant Colleges, Association of American Universities and American Coucil on Education to Mark Rohrbaugh, Director of the Office of Technology Transfer Center, NIH 2 (April 22, 2004); *see also* Letter from Joseph P. Allen, President , National Technology Transfer Center, *supra*; Letter from Katharina Phillips, President, Council on Governmental Relations, to Mark Rohrbaugh, Director of the Office of Technology Transfer, NIH (April 5, 2004) (stating that any "change in march-in authority or in expanding their exercise by government agencies could result in the loss of the very delicate balance of rights and obligations between the three partners – government, universities and industry - which has been the basis for the success of this legislation").

[15] Determination in the Case of Petition of CellPro, Inc., http://www.nih.gov/news/pr/aug97/nihb-01.htm

therapeutic drugs."[16] NIH's response to this Congressional directive emphasized the incredible success of the system created by the Bayh-Dole Act and concluded that "contravening the provisions of Bayh-Dole may have a deleterious effect on biotechnology development."[17] The same report matter-of-factly observed that "neither NIH nor universities have a role in drug pricing."[18]

Conclusion

In the biotechnology industry, the vast majority of funding necessary to develop new products comes from the private sector. But private sector investors will not invest in the development of research that they do not believe will yield a return on their investment. As such, the exercise of march-in powers to set price controls would defeat the overarching goal of the Act—which is to facilitate commercialization of government funded research.

As the public debate continues on the use of march-in authorities, NIH must be careful not to alter the Bayh-Dole landscape in such a way as to introduce a level of uncertainty that would lead private enterprise to withdraw from the Bayh-Dole equation. Because the Bayh-Dole Act was never intended as a price-control mechanism, any interpretation allowing price-based march in would destroy the essential fabric of the Act.

For the reasons outlined in this letter, BIO urges the NIH to (1) adopt a policy that makes it clear that a company's pricing decision does not serve to trigger march-in authorities under Bayh-Dole; and (2) deny both petitions submitted by Essential Therapeutics.

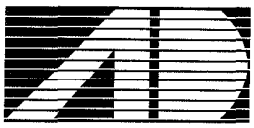
Thank you for the opportunity to provide comments on this important matter. Please call me at (202) 962-9215 or Lila Feisee, BIO's Director for Intellectual Property, at (202) 962-9502 to discuss any questions you may have.

Sincerely,

Stephan E. Lawton
Vice President & General Counsel

SL:fz

[16] A Plan to Ensure Taxpayers' Interests Are Protected, *supra* Part A.
[17] *Id.* Part F.
[18] *Id.* Part D.1.




THE AARON DIAMOND AIDS RESEARCH CENTER

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May 24, 2004

Dr. Elias A. Zerhouni
Director
National Institutes of Health
9000 Rockville Pike
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Dr. Mark Rohrbaugh
Director of the Office of Technology Transfer
Office of Intramural Research
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, MD 20852

Dear Drs. Zerhouni and Rohrbaugh:

I am writing out of concern related to the issues raised in connection with the petition regarding Abbott Laboratories and the exercise of march-in rights under the Bayh Dole Act. As an independent researcher at the Aaron Diamond AIDS Research Center in New York, I began collaborating with Abbott Laboratories in 1991 and was one of the investigators working on the testing of protease inhibitors for safety and efficacy throughout all the phases of clinical development. While I do not wish to express any legal opinion with respect to provisions of Bayh Dole, I do think it important for those faced with rendering a decision on this petition to recall both the circumstances and the climate related to the discovery of protease inhibitors in general, and Norvir in particular.

First, it is valuable to put the development of protease inhibitors in their historical context by recalling the early days of the HIV epidemic. Quite simply, large numbers of people were dying painful deaths at an alarming rate after an AIDS diagnosis. Treatment options were limited to a few medications that simply were not potent enough to make an impact on the mortality rates at the time, and the demand for new treatments was intense. For researchers and for the pharmaceutical industry, the task of finding these new treatments represented an enormous investment and a significant gamble. For example, during my work on Abbott's protease inhibitors, it was determined that one such compound showed promise, but later was found not to work well enough when tested in patients. Another looked more promising, but again when tested in patients; it fell short in its efficacy. While the literature reflected great excitement about the promise of protease inhibitors in 1994 and 1995, in 1993 nothing about their efficacy was certain.

When protease inhibitors were being investigated, there was no way to know if they would work – and even if they did work - we weren't yet sure how they could be used. It involved a great deal of trial and error to reach the point where experimental discoveries such as protease inhibitors actually became useful drugs. In today's environment, it is easy to forget what those days were like. The grim treatment options of the early days contrast with today's array of effective therapies because of the advances made in therapeutics over the last 15 years.

I think it particularly important at this point to draw some emphasis as well to the role that the National Institutes of Health played at the time when it awarded grants to assist in protease inhibitor research efforts. Abbott was a recipient of such a grant. However, when it came to the actual clinical testing of protease inhibitors, the development of Norvir was accomplished through the investment of the company and through the institutional resources of investigators such as myself. The amount of money used in discovery is but a fraction of the sum spent to fully develop a drug for market. The discovery may have been subsidized, but the testing and development were not.

After Abbott tested various molecules, Norvir emerged as its most effective compound. Once Norvir was introduced into infected subjects during clinical trials, we saw a reduction in viral load that was unprecedented and it then seemed logical to combine this with 3TC and AZT. The eventual result is the very different AIDS epidemic that still challenges us today, though in a vastly different way. Mortality dropped significantly. Lives were extended. Quality of life was vastly improved. Eventually, Norvir's role as a boosting agent to other anti-viral therapies became known, extending the benefit of its role beyond what was conceived during its initial use.

The development of Norvir is a prime example of the benefits of a public-private partnership. The investment in discovery on the part of the National Institutes of Health - and Abbott itself - was followed up by the much more significant investment by private industry to test and develop the discovery and bring it to market.

As a witness of this development, I felt compelled to write and share this perspective with you. If you have any follow-up questions, please do not hesitate to contact me.

Sincerely,

David D. Ho

David D. Ho, M.D.

C·H·I
CALIFORNIA HEALTHCARE INSTITUTE
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May 19, 2004

Elias A. Zerhouni, M.D.
Director
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Zerhouni:

On behalf of the California Healthcare Institute (CHI), whose more than 220 members include our state's premier life science companies and academic research institutions, I would like to express concern regarding the recent action to impose the march-in provision of the Bayh-Dole Act (Bayh-Dole) against Abbott Laboratories.

Healthcare access and affordability is a serious national issue, and was the focus of the recently enacted Medicare Prescription Drug and Modernization Act of 2003 (MMA). This landmark legislation will improve prescription drug coverage for our nation's seniors and most needy. Bayh-Dole, however, is not the proper vehicle for addressing concerns about drug access and costs.

Bayh-Dole was intended to stimulate the transfer of medical technology between academic institutions and commercial companies. In passing this law, Congress recognized that federal funding of basic science was, by itself, insufficient to bring new medicines to the bedside. The complex and expensive process of transforming discoveries into products required a legal framework in which the intellectual property derived from federally-funded research could be licensed by a university to a company in exchange for royalties or other appropriate considerations. To ensure that important innovations would not languish, march-in provisions were built into the law to allow government to broaden the scope of patents in order to move inventions into the market place if a commercial company lacked the resources necessary to do so. Neither Bayh-Dole nor its march-in provision pertains to the issue of affordability in the marketplace. Certainly Bayh-Dole was not intended to act as a price control mechanism.

Allowing march-in rights based on price would go against the very aim of Bayh-Dole. Indeed, the product in question, Norvir, is already available on the market and has been used effectively by patients. The government cannot encourage industry to bring products to market by extending patents only to take them away once the product is commercialized. The result would be a return to the status quo prior to enactment of Bayh-Dole when taxpayer dollars were invested in research that had minimal chance of reaching the market. By weakening intellectual property rights, the exercise of march-in rights in this case would have devastating effects on the future of medical innovation in the United States

I strongly urge NIH to consider not only the original intent of the Bayh-Dole march-in provisions but the original aim of the Bayh-Dole Act itself – to stimulate the commercialization of discovery, not stifle it – and reject exercise of march-in rights in this case.

Sincerely,

David Gollaher

David Gollaher, Ph.D.
President & CEO

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David E. Miller
President

May 21, 2004

Elias A. Zerhouni, M.D.
Director
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

Dear Dr. Zerhouni:

The Illinois Biotechnology Industry Organization, better known as iBIO™, represents scores of biotechnology companies in this state that work to develop and bring new life-saving and –enhancing drugs and medical products to market.

I am writing out of concern regarding the recent petitions requesting imposition of the march-in provisions of the Bayh-Dole Act against Abbott Laboratories' license for the invention it has productized as the drug Norvir. Such an action would subvert both the language and underlying legislative intent of Bayh-Dole.

The purpose of the Bayh-Dole Act was to stimulate the transfer of technology between university researchers and private sector firms with the resources to develop these inventions and bring them to market so as to benefit the public. The idea was that licensing of federally- funded inventions would provide an incentive for private industry to develop products through the grant of commercialization rights.

Absent these incentives, Congress reasoned, there was little chance of many such potentially useful inventions ever reaching the market. There exists widespread agreement that the incentives provided by the Act have been hugely successful in making new products, including many new drugs, available to the public.

Congress was concerned that in some instances licensed inventions might languish in the hands of the licensees. It therefore built march-in provisions into the law to allow the government to step in if a private company lacked the resources necessary or otherwise failed to bring a product to market or to address public health needs after obtaining its license. The march-in provisions would, in those limited instances, allow the government to grant additional licenses for the same product.

There is nothing in the Act that provides for substitution of a funding agency's judgment on appropriate pricing of the product or allowance for the agency's imposition of price controls through exercise of march-in rights. The only relevant questions under Bayh-Dole are: Is the firm actively making the invention publicly available, and is it benefiting public health needs?

In my research on this matter I have found no claims by any party that Abbott has failed to take, in the Act's language "within a reasonable time, effective steps to achieve practical application of the subject invention" in its "field of use", or that Norvir has failed to effectively address public health needs. Norvir is widely available and has been used effectively by the target HIV patient population. Norvir has strengthened the ability of other drugs, provided by both Abbott and Abbott's competitors in this highly competitive category, to suppress the effects of HIV infection. In some instances, Abbott has made the drug available to people worldwide at no charge and reduced charge.

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The petitions for imposition of march-in processes were brought by parties complaining about the price of the product, not its market availability or effectiveness in addressing health needs; what they are saying, in effect, is that Bayh-Dole requires licensees to distribute their products so that every person in every circumstance can access them.

Granting the petitions based on this reasoning would effectively re-write the provisions of Bayh-Dole. Doing so would also subvert the Act's legislative intent.

Widely quoted studies from Tufts University and the Boston Consulting Group indicate that pharmaceutical companies require hundreds of millions of dollars and an average of 10 years to bring a new drug to market. (Abbott reports that it spent more than $300 million dollars to develop Norvir.) More recently, the Bain research group has calculated that, taking into account the many failures for each successful drug candidate, the true cost of each successful drug is over one billion dollars.

Imposing ad-hoc pricing judgments as a pretext for invocation of march-in rights, after a licensee has made substantial investments in testing and product development, would obliterate the very incentives Congress sought to create by enacting Bayh-Dole. The result would be a return to the previous status quo, when taxpayer dollars were invested in research that sat on the shelves.

I therefore urge you to reject these petitions and, in so doing, uphold the language of the Act and its underlying intent to spur development of inventions that benefit the public. Please do not hesitate to contact me if you have any questions regarding this matter.

Sincerely,

David Miller
President

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The Bayh-Dole Act and March-In Rights

David Halperin[1]

May 2001

I. Summary

The Bayh-Dole Act, 18 U.S.C. section 200 et seq., enacted in 1980, was aimed at turning federally-funded research and development into useful patented inventions, in order to benefit American research institutions, industries and consumers. From the beginning, a stated objective of the Act was to protect the American public against "unreasonable use" of government-funded inventions. 18 U.S.C. section 200. The march-in rights provision was included as a means to vindicate that interest. It gives the federal agency under whose funding agreement an invention was made the right to grant a license to a responsible new applicant if, among other things, the current manufacturer has failed to make the product "available to the public on reasonable terms," 18 U.S.C. sections 201(f), 203(1)(a), or if "action is necessary to alleviate health or safety needs which are not reasonably satisfied" by the current manufacturer. 18 U.S.C. section 203(1)(b).[2]

The research and development needed to create numerous drugs now on the market was funded primarily by the American people through their tax dollars. The key patents to many of these drugs were filed by universities, and then licensed to private companies. In many cases, these private corporations have provided only a small fraction of the overall R&D investment in the products, but charge high monopoly prices. These prices do not reflect the cost of production of the drugs, which are routinely only a fraction of the sale price. In some cases, generic competitors in other countries sell the drugs at prices less than 5 percent of the U.S. price.

The exact outlay by industry licensees for licensing, research, development, production, and other expenses is typically unknown, because the licensees generally refuse to disclose such data. However, in the course of a governmental review of a product under Bayh-Dole, it should be possible to make the data public, so a complete, rational and fair assessment can be made.

Even without such disclosures, the high prices of many products currently on the market is *prima facie* unwarranted in terms of the purposes of Bayh-Dole and of federal patent law. If these laws are meant to encourage and reward investment and innovation, then the windfall profits obtained by industry licensees turn that purpose on its head:

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[1] Attorney and Counselor, Washington, DC. Special Assistant for National Security Affairs and speechwriter to President Clinton (1998-2000); fellow, Harvard Law School Berkman Center for Internet & Society (1997); solo legal practitioner (1994-97); co-founder, Progressive Networks (now RealNetworks) (1993-94); counsel, Senate Intelligence Committee (1991-93); law clerk, U.S. District Judge Gerhard Gesell (1989-91). Yale Law School JD 1989, Yale College BA 1984. The author prepared this paper at the request of the Consumer Project on Technology, Washington, DC.

[2] Regulations governing the procedures for the exercise of march-in rights are at 37 CFR section 401.6.

Companies which contributed comparatively little to the R&D for particular drugs receive a monopolist's price *as if they undertook all of the R&D themselves*.

The losers under this arrangement are the American people, who have been forced to pay twice for the drugs: first, through taxpayer funding for R&D; and today, through higher Medicare and other government program expenditures, higher insurance premiums, and, higher patient out-of-pocket expenses and other costs associated with the exorbitant prices.

No federal agency has ever asserted its march-in rights with respect to a Bayh-Dole-conferred patent. Indeed, only once has a federal agency ever been petitioned to do so. (See below.) Now the Government should apply a brake to runaway prices for critical medicines created with taxpayer money.

The Secretary of Health and Human Services should take action to help restore appropriate balance to federal policy under Bayh-Dole; to help ensure that overall U.S. policy with respect to research and patents is rational and effective; and to uphold the interests of American taxpayers, insurers, and government.

II. Argument: The Case for Exercising March-in Rights

The 1980 Bayh-Dole Act embodied a new approach to intellectual property rights in the fruits of federally-sponsored research. Under the previous approach, much of this research remained government property or was placed in the public domain. But there was a perception that federal inventions were often underutilized. There was concern that a failure to remedy this problem would weaken the ability of U.S. firms to compete with foreign companies. There also were substantial differences among the procedures and standards used by federal agencies with respect to a funding recipient's right to obtain title to an invention created with federal monies. The process by which a contractor sought to obtain such rights was often burdensome and delayed the transformation of research into useful products.[3]

The new approach posited that encouraging patenting of the results of federal research, and licensing to private firms, would prompt greater use of federally-sponsored inventions, spur U.S. industries, and create American jobs. The Bayh-Dole Act gave incentive to non-profit entities and small businesses to patent the products of government-funded research by authorizing them to retain patent ownership for themselves, to license those patents, and to retain royalties from them.[4] Subsequently, a

[3] See S.Rep. 96-480 at 15-25; Barbara M. McGarey and Annette C. Levey, Patents*, Products, and Public Health: An Analysis of the CellPro March-In Petition*, 14 Berkeley Tech.L.J. 1095, 1097-98 (1999); Peter S. Arno & Michael H. Davis, *Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed upon Patents Derived in Whole or in Part from Federally Funded Research*, 75 Tulane L. Rev. 631, 640, 656 (2000); Mary Eberle, *March-In Rights Under the Bayh-Dole Act: Public Access to Federally Funded Research*, 3 Marq.Intell.Prop.L.Rev. 155 (1999).
[4] Federal regulations implementing the Bayh-Dole Act are at 37 CFR section 401.1 et seq.

1983 Executive Memorandum and 1987 Executive Order extended the benefits of Bayh-Dole to all government contractors, including larger businesses.[5]

The objectives of the Bayh-Dole Act, as set out by Congress are as follows:

> to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.

35 U.S.C. section 200.

The Bayh-Dole Act sought to create a uniform, streamlined process across all federal agencies for patent license transfers. Under the Act, federal contractors generally have the right to elect ownership rights to any invention created with federal funds.

As one scholar has put it, the Bayh-Dole approach is, in fundamental ways, "counterintuitive ... [I]t seems to require the public to pay twice for the same invention -- once through taxes to support the research that yielded the invention, and then again through higher monopoly prices and restricted supply when the invention reaches the market."[6]

To address such concerns, Congress built into the Act a number of obligations aimed at ensuring that the public's investment would be used in the public interest. Under the Act, contractors must disclose each subject invention to the funding agency

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[5] Memorandum to the Heads of Executive Departments and Agencies: Government Patent Policy, Public Papers of the Presidents 248 (Feb. 18, 1983); Executive Order 12591, 52 Fed.Reg. 13414 (1987).

[6] Rebecca S. Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research*, 82 Va.L.Rev. 1663, 1666 (1996). Professor Eisenberg further states:

> Second, by calling for exclusive rights in inventions that have already been made through public funding (and thus, presumably, without the need for a profit incentive), it contravenes the conventional wisdom that patent rights on existing inventions result in a net social loss ex post, a loss that we endure only to preserve ex ante incentives to make future patentable inventions. Third, by promoting the private appropriation of federally-sponsored research discoveries as a matter of routine, it calls into question the public goods rationale for public funding of research. And fourth, by providing incentives to patent and restrict access to discoveries made in institutions that have traditionally been the principal performers of basic research, it threatens to impoverish the public domain of research science that has long been an important resource for researchers in both the public and private sectors.

Id., at 1666-67.

within a reasonable time after discovery. They must elect within two years of disclosure whether or not to retain title. They must agree to file patent applications prior to any statutory bar date. If a contractor fails to meet any of these obligations, it risks forfeiting title to the Government.[7] Moreover, under the Act the Government reserves for itself a nonexclusive, paid-up license to practice or have practiced on its behalf any subject invention, in the United States or in other countries.

In addition, the Bayh-Dole statute includes the march-in provision that is the focus of this paper. Section 203 provides, in relevant part:

> With respect to any subject invention in which a small business firm or nonprofit organization[8] has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such
>
> > (a) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use; [or]

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[7] A recent study by the U.S. General Accounting Office shows that contractors and universities in fact engage in regular violations of Bayh-Dole requirements, particularly widespread failure to report the patents that they obtain through government-funded research. U.S. Gen.Accounting Office, GAO/RCED-99-242, Technology Transfer: Reporting Requirements For Federally-Sponsored Inventions Need Revision 6, 10-12 (1999); see Arno & Davis at 676-679, 686-687.

[8] After the 1983 Executive Memorandum extended Bayh-Dole benefits to all federal contractors, including large corporations, Congress by statute expressly extended the march-in rights provision, along with other aspects of the Bayh-Dole law, to such entities:

> Nothing in this chapter [35 U.S.C. sections 200 et seq.] is intended to limit the authority of agencies to agree to the disposition of rights in inventions made in the performance of work under funding agreements with persons other than nonprofit organizations or small business firms in accordance with the Statement of Government Patent Policy issued on February 18, 1983, agency regulations, or other applicable regulations or to otherwise limit the authority of agencies to allow such persons to retain ownership of inventions except that all funding agreements, including those with other than small business firms and nonprofit organizations, shall include the requirements established in [section] 202(c)(4) and section 203 [the march-in rights provision] of this title. Any disposition of rights in inventions made in accordance with the Statement or implementing regulations, including any disposition occurring before enactment of this section, are hereby authorized.

P.L. 98-620, codified at 35 U.S.C. section 210(c).

> (b) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees ....

The phrase "practical application," used in subsection 203(a), is defined elsewhere in the Act to mean:

> to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms.

18 U.S.C. section 201(f).

The march-in rights provision of the law was contained, essentially verbatim, in the original version of the bill as it was introduced by Senators Bayh and Dole on February 9, 1979.[9] However, the concept of government march-in rights, and the "reasonable terms" standard for exercising them, were much older. In 1963, President Kennedy issued a Presidential Memorandum on patent policy that allowed for exclusive licensing of government patents in some circumstances but required that such licensing be "on reasonable terms."[10] A 1968 government-commissioned report supported the use of march-in rights when a contractor failed to offer the invention "on reasonable terms."[11] President Nixon's Patent Policy Statement of 1971 tied the exercise of march-in rights to whether a licensed invention "is being worked and ... its benefits are reasonably accessible to the public."[12]

Another provision in the original Bayh-Dole bill, section 204, provided for automatic recoupment of part or all the government investment in R&D after the subject invention had earned a particular level of profits.[13] Although at least one of the bill's sponsors, Senator Thurmond, considered this provision "[p]erhaps the most significant feature of the bill,"[14] and it was included in the Senate-passed version of the bill[15], it was eventually dropped.

The legislative history of the Bayh-Dole Act and similar bills introduced in the same period shows that the march-in rights provision was repeatedly cited by bill

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[9] S.414, 96th Cong., 1st Sess.
[10] Subcommitee on Domestic and International Scientific Planning and Analysis of the House Committee on Science and Technology, 94th Cong., Background Materials on Government Patent Policies: The Ownership Of Inventions Resulting From Federally Funded Research and Development (Committee Print 1976) at 6.
[11] Id., at 196.
[12] Id., at 10, 14-16.
[13] Id.
[14] The University And Small Business Patent Procedures Act, Hearings Before the Senate Committee on Judiciary, 96th Cong., 1st Sess., 1979, at 34 (statement of Sen. Thurmond).
[15] See S.Rep. 96-480, at 34.

advocates as a meaningful and appropriate guarantee that the public interest would be protected.[16]

For example, there is this testimony from Dr. Betsy Ancker-Johnson, vice president of General Motors and former Assistant Secretary of Commerce:

> DR. ANCKER-JOHNSON. Mr. Chairman ... you have written into this legislation march-in rights which, should something go wrong, gives the Government an absolute method to correct it. It seems to me that you have made the possibility for abuse virtually nonexistent by including this section in the bill.
>
> Senator BAYH. How do you perceive those march-in rights would accomplish what you suggest?
>
> DR. ANCKER-JOHNSON. Should there be any abuse, Mr. Chairman, whatsoever, these criteria would be applied by the Federal Government and so make it possible for the Government to ... obtain the rights to that patent and distribute them to whoever it deemed best for the exploitation of that technology for the welfare of the people. So you have this excellent guarantee written into the bill, and it seems to me you have fully provided for any remote possibility of abuse.

It is notable that the witness spoke not of patent non-use -- the danger that the government contractor would simply leave the technology on the shelf -- but patent *abuse*.

As Professors Arno and Davis, who exhaustively reviewed the legislative history, conclude, "there was never any doubt" that the "reasonable terms" standard for march-in rights "meant the control of profits, prices and competitive conditions."[17] As they note[18], there are many references in the legislative record to the value of march-in rights for maintaining competitive market conditions. James E. Denny, Assistant General Counsel

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[16] See The University And Small Business Patent Procedures Act, Hearings Before the Senate Committee on Judiciary, 96th Cong., 1st Sess., 1979, at 44 (statement of Elmer B. Staats, Comptroller General of the United States), 70 (statement of Dr. Hector F. DeLuca, chairman, biochemistry department, University of Wisconsin Madison), 187 (statement of Howard Bremer, president, Society of University Patent Administrators); Patent Policy, Hearings Before the Subcommittee on Science, Technology, and Space of the Senate Committee on Commerce, Science and Transportation, 96th Cong., 1st Sess. at 182 (statement of Gerald J. Mossinghoff, Deputy General Counsel, NASA); Patent Policy, Hearings Before the Subcommittee on Science, Technology, and Space of the Senate Committee on Commerce, Science and Transportation, 96th Cong., 1st Sess., at 366 (statement of Dale W. Church, Deputy Under Secretary of Defense for Acquisition Policy); Government Patent Policy, Hearings Before the Subcommittee on Science, Research and Technology of the House Committee on Science and Technology, 96th Cong., 1st Sess., 1979, at 54 (statement of John E. Maurer, director, Patent Department, Monsanto Corp.) ; Government Patent Policy, Hearings Before the Subcommittee on Science, Research and Technology of the House Committee on Science and Technology, 96th Cong., 1st Sess., 1979, at 182 (statement of Dr. Ralph L. Davis, Purdue Research Foundation); 1977 Small Business Hearings at 189-95 (statement of John H. Shenefield, Asst. Attorney General, Antitrust Div., Dept. of Justice).

[17] Arno & Davis, at 662.

[18] Id.

for Patents, U.S. Energy Research and Development Agency, testified that march-in rights were appropriate "where the contractor is misusing the invention to the detriment of competitive market forces."[19] Ky P. Ewing, Assistant Attorney General for the Antitrust Division, testified, "'[M]arch in' provisions should help assure that the availability of exclusive rights ... does not disrupt competition in the marketplace."[20]

Harry F. Manbeck, General Patent Counsel for General Electric Company, emphasized the connection between unwarranted prices and the exercise of march-in rights: "[I]f [a contractor] fails to supply the market adequately at a fair price, then there is reason for requiring it to license both the background patents and the patents stemming from the contract work."[21]

Other testimony expressly linked the invocation of march-in rights to the existence of "windfall profits" on a subject invention. Written responses to the Senate from U.S. Comptroller General Staats reported that the Department of Energy "said that march-in rights to protect the public's interest were developed to take care of and address the patent policy issues of *contractor's windfall profits*, suppression of technology, *and the detrimental effects to competition from granting contractors rights to inventions*."[22] Mr. Manbeck of General Electric testified as to march-in rights, "We think it is part of the answer to the so-called windfall situation."[23]

Questioning Comptroller General Staats, Senator Bayh noted that a criticism of the bill, "comes from those that feel that this bill is a front to allow the large, wealthy, corporation to take advantage of Government research and thus to profit at taxpayers' expense. We thought we had drafted the bill in such a way that this was not possible." Staats replied, "In my opinion, the bill does have adequate safeguards."[24]

Another witness, R. Tenney Johnson, who had served as chief or deputy legal counsel to five cabinet departments or agencies (and subsequently served in the Reagan Administration as general counsel at the Department of Energy), discussed the bill's

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[19] Patent Policy: Hearings on S.1215 Before the Subcommittee on Science, Technology and Space of the Senate Committee on Commerce, Science and Transportation, 96th Cong. 150 (1979).

[20] Patent and Trademark Law Amendments of 1980: Hearings Before a Subcommittee of the House Committee on Government Operations at 102 (1980)

[21] Government Patent Policy: Hearings Before the Subcommittee on Science, Research and Technology of the House Committee on Science and Technology, 96th Cong. at 48 (1979)

[22] The University And Small Business Patent Procedures Act, Hearings Before the Committee on Judiciary, 96th Cong., 1st Sess., 1979, at 56 (responses of Mr. Staat). Mr. Staat's further characterized DOE's view as follows: "The Department believes that march-in rights, although available to the Government for more than 10 years, have not been utilized because such problems are illusionary and not actual. If and when negative effects result from allowing a contractor to retain title to an invention of commercial importance, march-in rights are there to address them. Otherwise, DOE believes they will never be used." Id. We submit that the situation posited by this discussion -- negative effects result from allowing a contractor to retain title to an invention of commercial importance -- has now become reality and compels Government action.

[23] Patent Policy, Hearings Before the Subcommittee on Science, Technology, and Space of the Committee on Commerce, Science and Transportation, 96th Cong., 1st Sess. At 317 (statement of Mr. Manbeck).

[24] The University And Small Business Patent Procedures Act, Hearings Before the Senate Committee on Judiciary, 96th Cong., 1st Sess., 1979, at 44.

provision for the assertion of government rights in connection with need for the Government to take action to protect public health or safety[25]:

> Whenever you discuss patent policy, you very quickly come up with the question of what do you do with a cure for cancer? Are you going to let one company have that? Obviously, a priceless invention. As I say, you are likely not to have a single patent on that, but you need to have some protection against that possibility.
>
> I think that such a possibility might arise in a contract where the work was expressly at the point of discovering whether there was an answer to cancer. The Government might need to acquire title, because that would be an exceptional circumstance.

Admiral Hyman Rickover, the father of the nuclear Navy and an opponent of the Bayh-Dole approach ("These inventions are paid for by the public and therefore should be available for any citizen to use or not as he sees fit"[26]), had a different view. He prophetically argued that the march-in rights provision would not be enforced[27]:

> The Government has had march-in rights since 1963, but to my knowledge has never used them. To be in a position to exercise these rights a Government agency would have to stay involved in the plans and actions of its patent holders and check up on them.
>
> If a Government agency ever decided to exercise its march-in rights and the patent holder contested the action, no doubt the dispute could be litigated for years. For this reason, I believe this safeguard is largely cosmetic. It would result in much additional paperwork but would probably be used no more than in the past.

In fact the legislative history of the Bayh-Dole Act reveals at least one instance where a government agency, the Department of Defense, had exercised march-in rights.[28] But Admiral Rickover's cynicism on this point now appears, unfortunately, well-grounded. The bill's sponsors and supporters were not cynical about the march-in rights provision, and their expectations deserve to be vindicated now.

The record also reveals that the march-in rights provision was retained despite the fact that a number of industry representatives argued aggressively against that provision,

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[25] Patent Policy, Hearings Before the Subcommittee on Science, Technology, and Space of the Committee on Commerce, Science and Transportation, 96th Cong., 1st Sess. At 44 (statement of Mr. Johnson).

[26] The University And Small Business Patent Procedures Act, Hearings Before the Senate Committee on Judiciary, 96th Cong., 1st Sess., 1979, at 157 (statement of Adm. Rickover).

[27] The University And Small Business Patent Procedures Act, Hearings Before the Senate Committee on Judiciary, 96th Cong., 1st Sess., 1979, at 159-60 (statement of Adm. Rickover).

[28] Patent Policy, Hearings Before the Subcommittee on Science, Technology, and Space of the Committee on Commerce, Science and Transportation, 96th Cong., 1st Sess., at 366 (statement of Dale W. Church, Deputy Under Secretary of Defense for Acquisition Policy). ("Only once can I recall there was a case where we exercised march-in rights. It was a case involving two patents held by MIT. There was a complainant who felt as though the patents were not being utilized. As to one of the patents, it was found that MIT was using it and was allowed to retain exclusive title. In the case of the other, we found that MIT was not effectively using it, and they did provide for the complainant to use the patent.")

as well as the provision allowing the government to revoke a contractor's license.[29] The fact that Congress, in the face of industry complaints, nevertheless retained the march-in rights provision demonstrates that these provision were not included casually, that they were not simply boilerplate.

In the course of the hearings on the legislation, the Electronic Industry Association urged Congress to redefine the phrase "practical application" -- a trigger for the exercise of march-in rights -- to reduce the obligations of the contractor and thus the risk that the government would actually assert march-in rights: "The definition of 'practical application' appears too stringent. We would suggest a rewrite to indicate that 'application' means ... 'that the invention is being worked *or* that its benefits are available to the public either on reasonable terms or through reasonable licensing ...."[30] Congress declined to adopt this change, and maintained the standard that a "practical application" is achieved -- and march-in rights conditions are avoided only if the invention is being practiced *and* it is available to the public on reasonable terms. [31]

There is nothing to suggest that Congress kept the provision and yet expected it to lay dormant forever. Indeed, the language of the Senate report suggests an expectation that march-in rights would indeed be asserted from time to time: "'March-in' is intended as a remedy to be invoked by the Government and a private cause of action is not created in competitors or other outside parties, although it is expected that *in most cases complaints from third-parties will be the basis* for the initiation of agency action." S.Rep. No. 96-480, at 34 (1979) (emphasis added).

It also is worth noting that the Bayh-Dole bill, as enacted in 1980, limited benefits to non-profit institutions and small businesses. The bill's sponsors believed that to extend benefits to large corporations would doom the bill, because consumer and antitrust advocates worried that big companies, on balance, did not need the help and in fact could use Bayh-Dole benefits to weaken market competition and hurt the public welfare.[32] The extension of Bayh-Dole to large corporations came not through a carefully-considered legislative process, but through executive action by the Reagan Administration. In 1984, Congress effectively ratified this action by the Administration, but at the same time it expressly provided that, if the Government was going to give Bayh-Dole benefits to large

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[29] See, e.g., Government Patent Policy, Hearings Before the Subcommittee on Science, Research and Technology of the House Committee on Science and Technology, 96th Cong., 1st Sess., 1979, at 169-71 (statement of Patrick Iannotta, president, Ecolotrol, Inc.); Government Patent Policy: Hearings Before the Subcommittee on Domestic and International Scientific Planning and Analysis of the House Committee on Science and Technology, 94th Cong. At 173 (statement of Charles S. Haughey, Patent Counsel, Hughes Aircraft Co.); 1980 Joint Hearing at 523-24 (testimony of Robert B. Benson, Director, Patent Dept., Allis-Chambers Corp.). As James E. Denny, Assistant General Counsel for Patents, U.S. Energy Research and Development Agency, stated, "[I]ndustry does not like either the concept of a revocable license or the 'march-in' rights, and views them with great suspicion." 1976 Hearings at 435.

[30] Patent Policy: Hearings on S.1215 Before the Subcommittee on Science, Technology and Space of the Senate Committee on Commerce, Science and Transportation, 96th Cong. at 221 (1979) (statement of Peter F. McCloskey, President, Electronic Industry Assn.) (emphasis added).

[31] See Arno & Davis, at 666.

[32] See Eisenberg, 82 Va.L.Rev. at 1695-96; Bradley Graham, Patent Bill Seeks Shift To Bolster Innovation, Washington Post, Apr. 8, 1979, at .

businesses, then the Government would retain the rights it had with respect to other Bayh-Dole inventions: (1) a nonexclusive, paid-up license to practice on behalf of the United States the subject invention; and (2) march-in rights.[33] The views expressed in 1980 -- regarding the potential for large corporations to abuse Bayh-Dole rights -- should be taken into account: In the case of large corporations, the Government has a particularly strong obligation to consider whether Bayh-Dole patent monopolies are serving the public interest.

American pharmaceutical companies have profited greatly from the Government benefits provided under Bayh-Dole and the subsequent extension of Bayh-Dole to large corporations. And these benefits to drug companies have come on top of other substantial federal aid through the tax code.[34] A company's own R&D expenditures can be deducted annually from taxable income. Internal Revenue Code section 174. The pharmaceutical industry, in particular, has benefited enormously from specific tax code provisions, including the foreign tax credit, the orphan drug tax credit, the general business tax credit, and a tax code provision that offers substantial benefits for manufacturing products in Puerto Rico. A 1999 analysis concluded that pharmaceutical makers have one of the lowest effective tax rates and one of the highest after-tax profit rates of any industry.[35]

The American public has received little direct financial return on its investment in health care research and development. Indeed, in the years 1985 through 1994, NIH received slightly less than $76 million in royalties, $40 million of which came from a single license for the HIV antibody test kit. From 1993 through 1999, royalties reached a total of nearly $200 million, reaching $45 million in 1999. But that figure still represents less than one percent of NIH's funding for 1999.[36]

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[33] The provision, codified at 35 U.S.C. section 210(c), states:

> Nothing in this chapter is intended to limit the authority of agencies to agree to the disposition of rights in inventions made in the performance of work under funding agreements with persons other than nonprofit organizations or small business firms in accordance with the Statement of Government Patent Policy issued on February 18, 1983, agency regulations, or other applicable regulations or to otherwise limit the authority of agencies to allow such persons to retain ownership of inventions except that all funding agreements, including those with other than small business firms and nonprofit organizations, shall include the requirements established in paragraph 202(c)(4) and section 203 of this title. Any disposition of rights in inventions made in accordance with the Statement or implementing regulations, including any disposition occurring before enactment of this section, are hereby authorized.

[34] See U.S. Office of Tech. Assessment, Pharmaceutical R&D: Costs, Risks and Rewards 183-99 (1983); Arno and Davis, 75 Tulane L.Rev. at 638-39.

[35] Memorandum from Gary Guenther, Analyst in Business Taxation and Finance, to Joint Economic Committee 1-7 (Dec. 13, 1999), cited in Arno and Davis, 75 Tulane L.Rev. at 639.

[36] Arno & Davis at 639-40, citing Nat'l Insts. Of Health, NIH Technology Transfer Activities FY 1993-FY1999, available at http://ott.od.nih.gov/newpages/webstats99.pdf; Nat'l Insts. Of Health, Federal Obligations For Health R&D, By Source or Performer: Fiscal Years 1985-1999, available at http://silk.nih.gov/public/cbz2zoz@www.awards.sourfund.htm.

Of course, the public has also benefited from Bayh-Dole in other ways -- to the extent the law has helped create jobs, spur research, and bring to market useful products.[37] But in at least some cases the price for these benefits has been too high.

Two scholars who recently conducted a careful review of the overall record under the Bayh-Dole regime conclude[38]:

> [P]erhaps more important than the absence of any [direct return on taxpayer investment] is the inevitability of even greater public or consumer expenditures demanded by the monopolies obtained by industry over publicly financed inventions, and the resulting supracompetitive profits and prices. The public has already paid for the costs of research. The government's failure to police these economic abuses is the untold scandal of federally financed inventions and of the failure of the Bayh-Dole Act, which was meant to provide that policing.

In many instances, the taxpayers have not received their due benefits from the Bayh-Dole bargain. That is because industry licensees have ignored their obligations under the statute to sell the fruits of taxpayer research on reasonable terms and consistent with public health and safety needs. As a result, the only way for the taxpayers' interests to be vindicated, the only way to bring publicly-funded medicine to citizens at a fair price, is for the Secretary to take action and exercise march-in rights.

Only once before has the Government received a petition for Bayh-Dole march-in rights: a petition filed with the Secretary of Health and Human Services in 1997 by CellPro, Inc. seeking a license for certain patents for stem cell separation technology created by Johns Hopkins University with support from the National Institutes of Health ("NIH").[39] CellPro was already manufacturing an FDA-approved device based on the

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[37] One recent scholarly account summarizes the following progress in the years since Congress enacted Bayh-Dole: Although the federal government still provides the bulk of funding for university research, industry funding for such research has grown by a factor of five since passage of the Act. Licenses granted by universities have increased by a factor of ten. Royalties paid to universities increased nearly four-fold from 1981 to 1992 and more than doubled between 1991 and 1995. However, as this account notes, it is not clear how much of this expansion is the result of Bayh-Dole and how much expansion would have occurred in any case, because of a general increase in intellectual property patenting and licensing and advances in biotechnology and other fields. Tamsen Valoir, *Government Funded Inventions: The Bayh-Dole Act and the Hopkins v. CellPro March-in Rights Controversy*, 8 Tex.Intell.Prop.L.J. 211, 234-36 (2000). As this account notes, though the Bayh-Dole era has brought substantial increases in patents, licensing and royalties in fields that have benefited from the law, "this growth parallels that seen in other industries that are generally independent of government funding." Id. at 239.

[38] Arno & Davis at 640.

[39] As Barbara McGarey, Deputy Director, Office of Technology Transfer, National Institutes of Health has noted, the legislative history of Bayh-Dole shows that Congress anticipated that the petition of a private party would be the likely trigger for the Government to consider asserting march-in rights. McGarey and Levey, 14 Berkeley Tech.L.J. at 1099, citing S.Rep. No. 96-480, at 34 ("'March-in' is intended as a remedy to be invoked by the Government and a private cause of action is not created in competitors or other outside parties, although it is expected that in most cases complaints from third-parties will be the basis for the initiation of agency action.") McGary and Levey report in their article that, though they are aware of no

technology.[40] Hopkins' licensee, Baxter, had obtained approval to market and was marketing its device in Europe, had filed for U.S. FDA Pre-Market Approval with respect to its device, and its device was in use in clinical trials in the United States. Determination In The Case of Petition of CellPro, Inc., National Institutes of Health, Office of the Director, August 1, 1997, at 5. Dr. Harold Varmus, director of NIH, concluded that the exercise of march-in rights was "not warranted at this time." Id., at 1. But NIH retained jurisdiction over the matter "until such time as a comparable alternative product becomes available for sale in the United States." Id.

The facts and equities in the CellPro case were very different than they are with respect to some drugs today. That case was about alleged failure to exploit a patent, while today there are products that are widely available to the public but not, it appears, on reasonable terms and not in accordance with public health and safety needs. In CellPro, NIH concluded that Baxter had met the requirements of Bayh-Dole, because it was "vigorously pursuing" FDA approval of its product. Id., at 5. Moreover, in separate civil proceedings, a court had held CellPro liable for willfully infringing Hopkins' patents, after negotiations between Baxter and CellPro for a licensing agreement had failed. Id., at 1, 5. Finally, Hopkins and Baxter changed the equities in the CellPro case by agreeing, notwithstanding their victory in the civil patent case, to refrain from enforcing their patent rights in order to allow the continuing sale of the CellPro device until the comparable Baxter product was approved for sale by the FDA. Id., at 6-7. In those circumstances, it would have been difficult for NIH to justify the need for march-in rights.

The Bayh-Dole Act calls for the assertion of federal march-in rights where such action "is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in [the applicable] field of use." In terms of specific request for the exercise of march-in rights, this is the standard to which decision-makers must look.

"Practical application" means "that the invention is being utilized *and* that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms." (emphasis added). 18 U.S.C. section 201(f).

The requirement that a Bayh-Dole contractor make inventions available "on reasonable terms," must be read to include the obligation to sell at a reasonable price. In comparable legal contexts, the phrase "reasonable terms" has been considered to include price. See, e.g., *Byars v. Bluff City News Co*., 609 F.2d 843, 864 n. 58 (5th Cir. 1979) (in applying a reasonable terms requirement in a particular antitrust context, citing "[t]he difficulty of setting reasonable terms, especially price"); *American Liberty Oil Co. v.*

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other formal petitions for march-in rights, "There have been various inquiries to federal agencies from third parties regarding possible march-in, but all have been resolved informally." 14 Berkeley Tech.L.J. at n.79.

[40] See McGarey and Levey, 14 Berkeley Tech.L.J. passim; Mary Eberle, *March-In Rights Under the Bayh-Dole Act: Public Access to Federally Funded Research*, 3 Marq.Intell.Prop.L.Rev. 155 (1999); Tamsen Valoir, *Government Funded Inventions: The Bayh-Dole Act and the Hopkins v. CellPro March-in Rights Controversy*, 8 Tex.Intell.Prop.L.J. 211 (2000).

Federal Power Commission, 301 F.2d 15, 18 (5th Cir. 1962) (holding that, under statute authorizing the FPC to establish reasonable terms and conditions, the "price ... must be reasonable").

A reasonable price for a product is one that covers costs, accounts for risk, and allows a reasonable profit. See, e.g., *Williston Basin Interstate Pipeline Co. v. FERC*, 165 F.3d 54, 57 (D.C.Cir. 1999). In evaluating whether the price of a medicine, one critical to keeping people alive, is reasonable, one should consider also whether the price imposes substantial hardships on patients who need it and the health care system working to support those patients.

In the context of a medical product, risk factors would include: the risk that research and development might not produce a safe and effective product; the risk that the FDA might fail to approve a product for such reason; and the possibility that a competitor might produce a comparable product that is better, cheaper or both.

A reasonable profit would be one that accounted for risk and ensured that the assignee of the patent would indeed have sufficient incentive to make the product. In the Bayh-Dole context, a reasonable profit would be less than a "windfall" profit, a level of profit comparable to that enjoyed by a monopolist who had done all the research and development itself.

Given the strong concern expressed throughout the legislative history of Bayh-Dole that taxpayers' interests be vindicated, when it comes to a critical, life-saving medicine, evaluation of the reasonableness of the price must also take into account the ability of purchasers to afford the good. In the Bayh-Dole context, it is reasonable to assert that a reasonable price for critical good financed by the public is not a price that creates hardship for the overall public or for individual members of the public.

These factors must be assessed on a case-by-case basis.

The government might be reluctant to engage in the practice of scrutinizing the prices of goods offered by government contractors. But such practice is a regular responsibility of government -- agencies as well as courts -- in many spheres. And it is a practice that is manageable in this context. Moreover, as discussed above, it is a practice that is part of the applicable law, under the march-in rights and "reasonable terms" provisions of the Bayh-Dole Act.

Government evaluates and sets prices or rates in a number of contexts. Price-setting is standard procedure for utilities and other regulated industries that are granted monopoly or substantial market power by government. Section 2-305(1) of the Uniform Commercial Code provides that if a contract price is not settled, "the price is a reasonable price at the time for delivery...." The UCC, in force in 49 states, gives courts the authority to determine reasonable prices where the parties have failed to set prices, and courts have regularly done just that. See, e.g., Koch Hydrocarbon Co. v. MDU Res. Group Inc., 988 F.2d 1529, 1534-35 (8th Cir. 1993) (evaluating, pursuant to UCC section

2-305, what constitutes a reasonable price for natural gas); N.Cent. Airlines, Inc. v. Cont'l Oil Co., 574 F.2d 582, 592-93 (D.C.Cir. 1978) (evaluating under UCC section 2-305 what constitutes a reasonable price for aviation fuel). The Patent Act directs courts, upon a finding of infringement, to award at least "a reasonably royalty" to the patent owner.

After public outcry over the pricing of AZT, the first Bush Administration adopted the policy of requiring firms to sign "reasonable pricing" clauses in return for entering into Cooperative Research and Development Agreements (CRADAs) with the federal government, or exclusive licenses to federal government owned research on pharmaceuticals.[41] This policy went further than the Bayh-Dole Act in some respects. First, it created reasonable pricing requirements even in cases where there were no patents to license. Second, the policy introduced a specific obligation to demonstrate that prices were reasonable in light of the government support for the development of the product.[42]

One of the first drugs to be commercialized with this reasonable pricing clause was the cancer drug Taxol, which was subject to a US government CRADA with BMS. The US government did not own patents on Taxol, but gave BMS the exclusive rights to data from US government funded clinical trials, which BMS used to establish safety and efficacy of Taxol with the US FDA. This effectively gave BMS a five year monopoly on Taxol sales in the US. The NIH was criticized by consumer groups for its management of the Taxol reasonable pricing obligation, and specifically for allowing BMS to charge prices that were roughly twenty times the prices the U.S. government had previously paid for generic supplies of Taxol.[43]

In 1995 the NIH decided that it would abandon the reasonable pricing clause, rather than enforce it. There were several efforts in the U.S. Congress to restore the reasonable pricing clause, but those efforts failed.

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[41] An account of the experience and debate over this policy is found in the *Reports of the NIH Panels on Cooperative Research and Development Agreements: Perspectives, Outlook, and Policy Development,* July 21, 1994 and September 8, 1994, National Institutes of Health.

[42] The Public Health Service (PHS) adopted, as Section 16 of Appendix A of the model PHS CRADA Agreement, a statement that "NIH/ADAMHA have a concern that there be a reasonable relationship between the pricing of a licensed product, the public investment in that product, and the health and safety needs of the public. Accordingly, exclusive commercialization licenses granted for NIH/ADAHMA intellectual property rights may require that this relationship be supported by reasonable evidence."

[43] U.S. Congress, Committee on Small Business, Subcommittee on Regulation, Business Opportunities, and Energy, *Exclusive Agreements Between Federal Agencies and Bristol-Myers Squibb Co. for Drug Development: Is the Public Interest Protected?* Hearings, July 29, 1991, Serial No. 102-35; HHS-OIG, Technology Transfer and the Public Interest: Cooperative Research and Development Agreements at NIH, OEI-01-92-01100, Washington, DC, November 1993; James Love, "Pricing of Drugs Developed with Public Funds, Comments Presented to the Second NIH CRADA Forum, September 8, 1994; James P. Love, "Health Registration Data Exclusivity, Biomedical Research, and Restrictions on the Introduction of Generic Drugs," statement to Subcommittee on Labor, Health and Human Services and Education and Related Agencies Committee on Appropriations U.S. Senate, October 21, 1997.

In 2000, the House of Representatives considered an amendment by Rep. Sanders prohibiting the use of NIH funding to grant exclusive or partially exclusive patent licenses under Bayh-Dole except in accordance with the Bayh-Dole Act provision, 35 U.S.C. section 209, requiring that a federally owned invention and its benefits be made available to the public "on reasonable terms."[44] It was, in essence, an amendment that called on NIH simply to enforce existing law.[45] The House debate on the amendment returned repeatedly to the Bayh-Dole requirement that medicines made with federal research dollars be sold on "reasonable terms."[46] Rep. Sanders told his colleagues:

> Our amendment requires that the NIH abide by current law and ensure that a company that receives federally owned research or a federally owned drug provide that product to the American public on reasonable terms. This is not a new issue ...
>
> While a reasonable pricing clause is not the only device that will protect the investment that American taxpayers have made in numerous profitable drugs, this amendment makes clear that Congress will not stand by while NIH turns over valuable research without some evaluation that the price charged to consumers will be reasonable as is required by current law.

This amendment requiring NIH to enforce "reasonable terms" requirements with respect to pharmaceutical makers passed the House last year by a vote of 313-109.

Opponents to the exercise of march-in rights can be expected to argue just what some industry representatives asserted in opposing the inclusion of the march-in rights provision in the original Bayh-Dole legislation: That the assertion of Bayh-Dole rights would, henceforth, discourage businesses from licensing, developing, and creating products based on, federally funded research. One is tempted to respond that industry representatives who want to make this claim, after march-in rights have been asserted by a federal agency, should be required to put their money where their mouth is, and refrain from entering into agreements where any federal research money is involved. Such enterprises would quickly realize the folly in rejecting still-profitable contracts and allowing willing competitors to scoop them up.

If the Government acted to apply a brake to runaway profits now, companies might see the wisdom in cutting prices for particular products to reflect better such factors as the ratio between the federal contribution to research and development and the company's own contribution; costs; risk; and the public interest. But there would still be the potential to make healthy, attractive profits. And thus there would still be incentive to participate with the federal Government in funding research, and to patent and license products in which the Government played a role.

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[44] See 146 Cong.Rec. H4291-93; 35 U.S.C. sections 209(c)(1)(A) (license granted "only if ... the interests of the Federal Government and the public will best be served by the proposed license, in view of the applicant's intentions, plans and ability to bring the invention to practical application or otherwise promote the invention's utilization by the public") and 201(f) (defining "practical application" to include the "reasonable terms" requirement).

[45] Arno & Davis, at 666-67.

[46] 146 Cong.Rec. at H4291-93.

Indeed, in asserting march-in rights in appropriate cases, the Government could actually spur private industry to increase its contribution to research and development on efforts in which the federal Government also has provided or is providing support. The reason why is plain: If the Government makes clear that the relative contributions of Government and the contractor are a factor in determining, for purposes of Bayh-Dole, whether the contractor is making the product available on "reasonable terms," then the more the contractor contributes to research, the weaker the potential argument for anyone claiming that the contractor's price is unreasonable.

At least some industry representatives shared this view at the time Congress considered the Bayh-Dole legislation. H.F. Manbeck, general patent counsel at General Electric, said during hearings on the bill, "I am in agreement ... that march-in rights will not hurt the affected contractor and not act as a disincentive to the innovation process. Absolutely."[47]

And one recent scholarly analysis agreed that "companies will not refuse to invest in federally funded research if a funding agency exercises march-in rights."[48] Why? Because the Bayh-Dole license transfers remain a good bargain for industry:

> For federally funded technology a balance must be struck between permitting licensees to commercialize their technology and disrupting this development by compelling patent owners to license their technology to third parties. Granted, this forced licensing will arguably generate some uncertainty in the licensing of federally funded research. However, companies will not turn their backs on this cost-effective resource of federally-subsidized university technology.

And, also, because the grant of march-in rights "when necessary" is critical to maintaining public support for this bargain.[49] In other words, if the Government declines to thoroughly review the evidence and act in the face of evidence of drugs sold at high monopoly prices, it would weaken the public's confidence in the fairness and efficiency of the Bayh-Dole Act regime and the overall regime governing the creation and sale of critical medicines. The public may conclude that there no circumstances under which a Bayh-Dole beneficiary company will be scrutinized for charging unwarranted prices. In that light, the public, and then perhaps the public's representatives in Congress, may decide that Bayh-Dole bargain, as so redefined, is not such a good deal for the taxpayers after all. That could create momentum for repealing laws that give the fruits of public research to private industry. In the long run, industry would be better served by the Government taking action now on behalf of fair prices for consumers and a fair return for taxpayers.

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[47] Government Patent Policy, Hearings Before the Subcommittee on Science, Research and Technology of the House Committee on Science and Technology, 96th Cong., 1st Sess., 1979, at 157 (statement of H.F. Manbeck)

[48] Eberble, March-In Rights, 3 Marq.Intell.Prop.L.Rev. at 178.

[49] Eberble, March-In Rights, 3 Marq.Intell.Prop.L.Rev. at 173-74.

Just as evaluating prices for reasonableness is an appropriate government function in certain circumstances, the granting of a license to a responsible party, where a Bayh-Dole contractor has not met its responsibilities, is comparable to government action in related contexts. Courts have ordered compulsory licenses, at reasonable royalty rates, as a remedy for antitrust violations. See United States v. Glaxo Group Ltd., 410 U.S. 52, 64 (1973) ("Mandatory selling on specified terms and compulsory patent licensing at reasonable charges are recognized antitrust remedies). United States law provides for the grant of compulsory licenses under certain conditions in a range of situations: with respect to copyrights, for secondary transmissions by cable television systems[50], for making and distributing phonorecords of certain musical works[51], and for performance of sound recordings via digital audio transmissions[52]; with respect to patents, for certain air pollution prevention inventions[53] and for inventions related to nuclear energy.[54]

III. Conclusion

The 1980 Bayh-Dole bill struck a bargain between Government, research institutions, industry, taxpayers and consumers, aimed at spurring research and bringing new inventions to the market for the benefit of all. The bargain was amended by the Reagan Administration in 1983 to extend the benefits of Bayh-Dole licensing to large corporations. Now it is time for the bargain to be enforced. It is time to correct an imbalance that has led to unjust enrichment and unwarranted hardship.

Two NIH officials recently concluded that the "greatest value" of the march-in rights provision of Bayh-Dole likely is its "in terrorem effect," its use "as the proverbial Sword of Damocles, suspended over the federally-funded invention licensing process...."[55] But this deterrent value has been diminished over time.

If the Government maintains its record of never exercising march-in rights, then government contractors will understand that there are few if any foreseeable circumstances in which such march-in rights ever will be granted. They will understand that they can obtain on the cheap tremendous benefits from taxpayer-funded research and then, without risk of sanction, turn around and charge the same taxpayers highly-inflated monopoly prices, even for medicines critical to combating fatal diseases. They will understand that devoting great resources to research is only the second-best strategy for reaping big profits; the better one being to let federally-funded research labs carry the research load and expense and then to charge a patent-holder's monopoly price anyway.

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[50] 17 U.S.C. section 111.
[51] 17 U.S.C. section 115.
[52] 17 U.S.C. section 114(f); see Recording Indus. Ass'n of Am. v. Librarian of Congress, 176 F.3d 528 (D.C.Cir. 1999).
[53] 42 U.S.C. section 7608.
[54] 42 U.S.C. section 2183.
[55] McGary and Levey, 14 Berkeley Tech.L.J. at 1116.

Continued government inaction will confirm once and for all the worst fears of Bayh-Dole's harshest critics back in 1980: that, as Senator Long then put it, the bill was a massive "giveaway," a law "deleterious to the public interest," a regime under which Americans are "forced to subsidize a private monopoly twice: first for the research and development and then through monopoly prices."[56]

By contrast, if the Government finally acts to exercise march-in rights in appropriate circumstances, it could produce a critical change with respect to medicines and medical technologies created with federal funding. Patent holders and licensees might begin adjusting their prices to better reflect their actual contributions to research. This could produce substantial cost savings for insurers, governments, and patients, and allow more resources to go to other health care costs -- and, in the case of the global AIDS crisis, also to those overseas suffering from this disease. If industry concluded it could no longer enjoy an almost totally free ride on federal research dollars, and that larger profits depended on making a greater contribution to research and development, that should encourage industry to devote greater, not fewer, resources to R&D. And there will remain strong profits and thus tremendous incentive for industry to continue marketing patented products made mostly with federal research and development money.

[56] Hearings Before the Subcommittee on Monopoly & Anticompetitive Activities of the Senate Select Committee on Small Business, 95th Cong. At 233 (1977) (statement of Sen. Long); Patent Policy: Joint Hearing Before the Senate Committee on Commerce, Science and Transportation and the Senate Committee on the Judiciary, 96th Cong. 463-65 (statement of Sen. Long).

Statement of James Love
President, Essential Inventions, Inc.
NIH Meeting on Norvir/Ritonavir March-In Request
May 25, 2004

Introduction

Essential Inventions has asked the Department of Health and Human Services (DHHS) to exercise its march-in rights in six patents held by Abbott Laboratories that are used in the manufacture and sale of ritonavir, a drug used to treat AIDS. Essential Inventions also has a separate petition asking DHHS to exercise march-in rights in the Columbia University patent on Xalatan, a drug used for the treatment of glaucoma. These petitions ask the government to protect the public, under the particular provisions set out in the Bayh-Dole Act.

Policy Basis for Norvir March-In Request

In December 2003, Abbott Laboratories increased the price of ritonavir by 400 percent. The price increase was not uniform. Some US public sector programs will not face the 400 percent price increase. No foreign consumers will face the 400 percent price increase. Abbott did not increase the price of Kaletra, an Abbott fixed dose combination product that combines ritonavir and lopinavir. As a consequence of the discriminatory price increase, US employers/insurers/consumers who buy ritonavir with private sector insurance will pay five to ten times more than employers/insurers/consumers in other high-income countries. US insurers will place pressure on patients to switch to the Kaletra fixed dose combination. Non-Abbott drug developers will be effectively excluded as a first line treatment on most formularies, reducing potential markets and undermining incentives for R&D.

The 400 percent price increase for a treatment for a deadly disease comes eight years after Ritonavir was introduced into the US market, having already generated billions of dollars in revenue to Abbott (for Norvir, the standalone product, and Kaletra, the co-formulated fixed dose combination). Patients living with AIDS, and employers and insurers that pay for AIDS treatments, are all concerned that the very aggressive price hike by Abbott will encourage other companies to sharply increase prices for AIDS drugs.

Table 1 Retail Price of Norvir in Six Countries *(Monthly: sixty 100 milligram tabs)*	
Australia	$ 52.04
Belgium	$ 58.91
Canada	$ 58.97
Germany	$ 111.91
Italy	$ 132.00
USA (CVS, Washington, DC)	$ 642.90

Table 2 Retail Price of Norvir Boost, Before and After Price Increase Annual average wholesale cost			
Boehringer-Ingelheim/Tipranavir	Before	$ 3,129	
400 milligrams/day	After	$16,644	
	Difference		$12.515
Merck/Crixivan	Before	$1,564	
200 milligrams/day	After	$7,822	
	Difference		$6,258
Abbott/Kaletra			
200 milligrams/day	Difference		$0

The fundamental questions posted by the Norvir march-in request are the following:

Is it appropriate for Abbott to increase the price of ritonavir, a government funded invention, by 400 percent in one day, after the company has already earned billions on the drug? Is it appropriate for Abbott to price ritonavir, a government-funded invention, 5 to 10 times higher in the United States than in other high-income countries? It is appropriate for Abbott to price ritonavir, a government-funded invention, 5 times higher when the drug is used in combination with non-Abbott owned protease inhibitors, than the price when ritonavir is used in connection with Abbott's own protease inhibitor lopinavir.

If DHHS determines that the answer to any of these three questions is no, it should grant the march-in request.

Legal Basis for March-In

In the terms of the Act, the first ground for the march-in is that the "action is necessary because the contractor or assignee has not taken, or is not expected to take within a

reasonable time, effective steps to achieve practical application of the subject invention."[1] The Act defines "practical application" as the utilizing of the invention in such a way "that its benefits are to the extent permitted by law or government regulations available to the public on reasonable terms."[2]

Abbott is not making the product available to the public on "reasonable terms." It is not reasonable to raise the price of an essential life saving drug by 400 percent. It is not reasonable to price an essential life saving drug 5 to 10 times more in the United States than in Europe, Canada or other high-income countries. It is not reasonable to charge 5 times more just because ritonavir is used with a competitor's protease inhibitor.

These acts are not reasonable. They are outrageous pricing abuses.

The second ground is that the "action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees."[3] There is evidence in the record that the price increases for ritonavir is creating hardships on persons living with AIDS. There is also evidence that the recent price increase is having a harmful impact on the pipeline for new AIDS drugs, by reducing the expected market share for Abbott's competitors. Indeed, if Abbott charges different prices for ritonavir depending upon which drugs it is used with, and discriminates against its competitors, it is unlikely that there will be significant new investment in AIDS drugs that require ritonavir as a boosting agent. This is the most serious threat to the health and safety needs of persons living with AIDS.

The NIH has received letters in opposition to this petition that assert that the Bayh-Dole march-in provisions were not intended to address abuses of patent rights that concern the pricing of drugs.[4] It is difficult to imagine how the term making "available to the public on reasonable terms" would exclude prices. Professor Jerome Reichman of Duke University Law School has looked at this issue for us, and will present in a separate statement his views on how the term "available to the public on reasonable terms" should be interpreted.

Any fair reading of the legislative history of the Bayh-Dole Act and also the pre-Bayh-Dole Act debates over the patenting of federally funded inventions reveal longstanding concerns over the potential for abuses stemming from monopoly pricing of inventions.[5]

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[1] 35 U.S.C. § 203(a)(1).
[2] 35 U.S.C. § 201(f).
[3] 35 U.S.C. § 203(a)(2). `
[4] Joseph P. Allen, President National Technology Transfer Center, letter to Mark Rohrbaugh, March 31, 2004. Norman J. Latker, letter to Mark Rohrbaugh, April 14, 2004.
[5] American Association for the Advancement of Science (AAAS), *The Protection by Patents of Scientific Discoveries: Report of the Committee on Patents, Copyrights, and Trademarks.* New York: Science Press, 1934; Robert Weissman, "Public Finance, Private Gain: The Emerging University-Business-Government Alliance and the New U.S. Technological Order," Undergraduate thesis, Harvard University, 1989; Peter S. Arno & Michael H. Davis, "Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed upon Patents Derived in Whole or in Part from Federally Funded Research," 75 *Tulane L. Rev*. 631, 640, 656 (2000); David C. Mowery, Richard Nelson,

As described in some detail in the attached memo prepared by David Halperin, the legislative approval of the Bayh-Dole was clearly tied to the existence of the march-in provision as a general safeguard to protect the public from abusive pricing of federally funded inventions, including medicines.[6]

We do not claim the NIH is required to exercise federal march-in rights on every federally funded patent, or even for many federally funded patents. Nor is the NIH obligated to exercise its royalty free rights in the patents. The federal government has broad discretion to act, but also broad discretion to not act. The NIH has never used a march-in petition to grant licenses to patents on drugs. But even the possibility of a march-in proceeding may have influenced licensing practices in the past, not only for drugs, but for the licensing of patents on stem cell lines or other research tools.

Whatever the NIH does in this proceeding will influence the terms under which future products are made available to the public. If the NIH decides, for example, that government funded inventions should not be priced higher in the United States than in other high income countries, it will be a straightforward rule that patent owners can both understand and easily follow. Likewise, the NIH could adopt policy guidance on other practices that should be avoided, such as the Abbott effort to charge far more for a drug if used with a competitor's product, or decisions to sharply increase prices on highly profitable products.

On the other hand, if the NIH denies the petition, the opposite signal will be sent to patent owners. The facts in the Abbott case are so extreme that a "sky is the limit" or "anything goes" precedent will have been sent. This will likely lead to even more aggressive pricing on federally funded inventions, and perhaps even for medicines in general.

Government Role in Development of Ritonavir.

Ritonavir was initially developed on a US government grant to Abbott. The NIH not only provided Abbott with approximately $3.5 million to finance Abbott's discovery and development of ritonavir, but the NIH also undertook its own research on ritonavir, employing Dr. John Erickson, a former Abbott researcher who played an instrumental role in obtaining the initial NIH grant to Abbott. Abbott acknowledges US government rights in six of the key patents for ritonavir.

Abbott claims that the US contribution to the development of ritonavir was small compared to Abbott's. Abbott deliberately under-estimates the economic value of NIH contributions in the early stages of development, and ignores the continued US government investment in research on ritonavir.

To fairly evaluate that the economic value of the $3.5 million grant to Abbott, one must recognize the risky nature of the public investment. The odds of success for investments

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Bhaven N. Sampat and Arvids A. Ziedonis, *Ivory Tower and Industrial Innovation: University-Industry Technology Transfer Before and After the Bayh-Dole Act,* Stanford Business Books, 2004.

[6] David Halperin, "the Bayh-Dole Act and March-In Rights," 2001.

in pre-clinical research are low. Most NIH funded grants to develop AIDS drugs are unsuccessful. Only a few such grants lead to a commercial product. The pharmaceutical industry itself frequently emphasizes that risk must be considered when calculating investment costs. Often we are told that every compound has only a 1 in 5,000 chance of commercial success. This is more a polemic than an actual estimate, but consider for a moment if this were the true risk. The risk-adjusted value of the US government investment would then be $3.5 million multiplied by 5,000, or $17.5 billion. And this does not even include the adjustments for inflation and the cost of capital that industry economists typically include in cost estimates. There is no good estimate of the actual risks in the initial investment stage, but in any reasonable analysis it would be significant. Joseph DiMasi and his colleagues have estimated the cost of pre-clinical research, adjusted for risk and capital costs, to be approximately $335 million.[7] This is a good starting point for thinking about the value of the initial NIH investment in ritonavir.

Abbott claims to have spent hundreds of millions on the development of ritonavir, but this is a "trust us" number. We have almost no details from Abbott. The initial FDA approval of ritonavir was based upon clinical trials that involved 1,583 patients. This is less than 30 percent of the number of patients the DiMasi study says are average for new drug approvals. The trials were also relatively short, and the FDA approval time for Norvir was extremely short -- only 70 days.[8] When trials and FDA approval times are shorter, company costs are generally lower -- certainly in terms of the cost of capital. These objective data are evidence that Abbott's costs for clinical development were below average.

Subsequent to FDA approval, the NIH continued to pour money into ritonavir R&D. The NIH has sponsored a large number of post market clinical trials involving ritonavir, and has given out dozens of grants.

Abbott's role has also been important. Ritonavir has been a successful collaboration between the NIH and Abbott. It has also been a highly profitable collaboration for Abbott, as reflected both in its sales of Norvir and the sales of ritonavir as a component of Kaletra. Ritonavir has generated billions of dollars for Abbott. And the US government has received zero royalties from ritonavir.

Patent Landscape for Ritonavir

Ritonavir is sold in different formulations and presentations. For each presentation, Abbott has registered differed patents in the *FDA Orange Book*. If the NIH grants licenses to Abbott's six ritonavir patents to Essential Inventions, we will consider our options for providing generic versions of ritonavir. We have asked several patent lawyers and experts to review the patent landscape for ritonavir to determine if it is possible to produce and market a generic version of ritonavir if we are successful in obtaining the

[7] *Joseph A. DiMasi, Ronald W. Hansen, Henry G. Grabowski, "The price of innovation: new estimates of drug development costs,"* Journal of Health Economics 22 (2003) 151–185.
[8] The request for FDA marketing approval was December 21, 1995. The FDA approval for ritonavir was March 1, 1996.

march-in licenses. We believe this is feasible. Our priority is for the 100 milligram tablet. The following is an excerpt from an analysis by the Daniel Ravicher of the Public Patent Foundation on the capsule formation of ritonavir:[9]

> PUBPAT has undertaken a review of the patents pertaining to Abbott Laboratories' ritonavir drug products. In total, there are 5 patents listed by Abbott in the Orange Book for its approved ritonavir capsule product. Of those 5, the Ritonavir Petition would, if granted, provide access to 4, leaving only one patent, U.S. Patent No. 6,232,333 ("'333 patent"), as a potential barrier to making an effective generic ritonavir capsule product. Table 1 below sets forth the Orange Book patent listing for Abbott's ritonavir capsule product and also indicates which of those patents are subject to the Ritonavir Petition.

Patent No.	Listed for Abbott's Ritonavir Capsule	Subject to the Ritonavir Petition
5,541,206	YES	YES
5,635,523	YES	YES
5,648,497	YES	YES
5,846,987	YES	YES
6,232,333	YES	NO

Table 1: Orange Book Listed Patents for Abbott's Ritonavir Capsule

> The '333 patent, unlike each of the other 4 patents listed for Abbott's ritonavir capsule, does not claim the active ingredient, ritonavir, itself. Rather, it merely claims a pharmaceutical composition containing ritonavir. Upon initial review, we have serious doubts about the validity of the '333 patent and its applicability to an effective generic ritonavir product. One issue regarding the '333 patent's validity is that its Abstract and Specification purport to teach an invention providing "improved bioavailability." Yet, no such limitation is present in any of the '333 patent's claims. Such a missing limitation means that the scope of the claims is much broader than what the patent otherwise purports to cover. This breadth of the claims increases the likelihood that they are invalid.
>
> Regardless, the existence of the '333 patent in no way detracts from the importance or utility of the Ritonavir Petition. Access to the technology claimed in the 4 other patents that pertain to ritonavir is absolutely necessary to making an effective ritonavir capsule product available to the American public on fair terms. Further, a potential producer of a generic ritonavir product is much more likely to challenge the '333 patent if it

[9] April 29, 2004. Daniel Ravicher letter to Mark Rohrbaugh, "Analysis of Patents Relevant to the Ritonavir Petition."

stands alone as the sole patent at issue than if the other 4 patents must also be dealt with. This is especially true since the '333 patent has such glaring validity issues and may be much more easily designed around than the other 4 patents since it does not cover the active ingredient ritonavir itself.

Proposed Remedy Includes Novel R&D Mandate

The march-in remedy proposed by Essential Inventions includes a novel proposal for the creation of an R&D Fund for AIDS treatments, funded by generic suppliers of ritonavir. Essential Inventions has proposed a mandatory R&D contribution of $.004 per milligram (typically $292 per year per patient), but the NIH could choose any figure. This R&D mandate would be in addition to the payment of reasonable royalties to Abbott. The structure of the R&D Fund management would be left to the NIH, but it could include either public or private sector management of the R&D fund, and different approaches to managing the intellectual property rights of the Fund. The proposal is modeled after an R&D mandate that the NIH imposed on Bristol-Myers in the early 1980's in connection with the Bristol-Myers marketing of cisplatin, a US government funded cancer drug. It is important to Essential Inventions that the exercise of the march-in right does not undermine investments in R&D, and the mandate that generic producers contribute to the R&D Fund is a mechanism to ensure that R&D levels are increased to socially desirable levels.

Concluding Comments

In the 24 years since the Bayh-Dole Act has passed, it has attracted a broad base of support among policy makers and researchers. The Act is also subject to criticism over a wide range of issues, including the tensions between sharing information and claiming property rights in research, and concerns over unjust pricing of some government-funded technologies. It is important that the bargain struck in the Bayh-Dole Act be considered fair to taxpayers.

The Norvir march-in case will be an important precedent, no matter what the outcome. For those who defend the policy of giving patent rights to grant recipients and contractors, and allowing patent owners much flexibility in using exclusive rights, there is an important issue. Is it sustainable in the long run to treat the taxpayers as if their only interest in the patents is to ensure that products are commercialized, regardless of the terms? The failure to use the march-in clause, ever, for any set of facts, will create the impression that the Act has been captured by those who profit from the commercialization of the taxpayer funded research. In the long run, this may undermine support for the broader policy of giving grant recipients title of US government funded research.

DRAFT #1, SUNDAY, MAY 23, 2004

TESTIMONY BEFORE NIH PUBLIC HEARING ON

MARCH-IN RIGHTS UNDER THE BAYH-DOLE ACT

Washington, D.C., May 25, 2004

Statement of Jerome H. Reichman
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Statement of Jerome H. Reichman

I am Jerome H. Reichman, the Bunyan S. Womble Professor of Law at Duke University School of Law, in Durham, North Carolina. I have recently written a three-part, book length study, entitled *Nonvoluntary Licensing of Patented Inventions: The Law and Practice of Canada and the United States*, for the United Nations Conference on Trade and Development (UNCTAD), in Geneva, Switzerland.[1] Because of my expertise on compulsory licensing in domestic and foreign law, I have been asked to comment on the meaning of certain provisions in the Bayh-Dole Act that require patented products resulting from federally funded research to be made "available to the public on reasonable terms."[2]

In general, the compulsory licenses that States may impose on foreigners' patented inventions under current international law—that is, under the Paris Convention for the Protection of Industrial Property of 1883 and the WTO Agreement on Trade-Related Aspects of Intellectual Property of 1994 (TRIPS Agreement)[3]—fall into five categories. These are:

1. Antitrust violations
2. Abuses of the patentee's exclusive rights
3. Compulsory licenses to promote some overriding public interest
4. Government use of patents
5. Dependent patents, i.e., licenses that allow an improver to use a dominant patent so as to avoid blocking technological progress.[4]

Most developed countries have enacted statutes enabling government authorities to authorize third-party private uses of patented inventions when breaking the inventor's legal monopoly is deemed necessary to correct an abuse of the patentee's exclusive rights or to promote some overriding public interest.[5] The line between "abuse" and "public

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[1] J. H. REICHMAN WITH CATHERINE HASENZAHL, NON-VOLUNTARY LICENSING OF PATENTED INVENTIONS, PART I—HISTORICAL PERSPECTIVE, LEGAL FRAMEWORK UNDER TRIPS AND AN OVERVIEW OF THE PRACTICE IN CANADA AND THE UNITED STATES (UNCTAD/ICTSD, September 2002) [hereinafter HISTORICAL PERSPECTIVE]; PART II—THE CANADIAN EXPERIENCE (UNCTAD/ICTSD, October 2002) [hereinafter THE CANADIAN EXPERIENCE]; PART III—THE LAW AND PRACTICE OF THE UNITED STATES (UNCTAD/ICTSD, forthcoming 2004) [hereinafter LAW AND PRACTICE OF THE UNITED STATES].

[2] 18 USC §§200, 201(f), 203(1)(a).

[3] [cites]

[4] See TRIPS Agreement, *supra* note 3, art. 31; REICHMAN WITH HASENZAHL, HISTORICAL PERSPECTIVE, *supra* note 1.

[5] See REICHMAN WITH HASENZAHL, LAW AND PRACTICE OF THE UNITED STATES, *supra* note 1 [cites at fn 497]

interest" is seldom sharply delineated, and in many instances statutory definitions of abuse invoke the public interest as an additional criterion for intervention. Typical grounds for triggering these compulsory licenses are the "need to ensure adequacy of supply" and "to regulate the availability of products deemed vital to security, *public health*, or environmental protection."[6]

The United States Congress has consistently declined to enact any general compulsory licensing provision of the kind adopted by other countries. In this country, compulsory licenses are available for antitrust violations and for government use of patents, while courts may decline to enforce patents in infringement actions under common-law doctrines of misuse. Beyond these limited circumstances, the availability of a nonvoluntary license for abuse or on public interest grounds in the United States depends primarily on specialized enabling statutes or on specialized clauses incorporated into specific statutes.[7]

The Bayh-Dole Act's requirement that patented products be made available "to the public on reasonable terms" is one of the clearest examples of such a specialized enabling clause. It may be compared with a Canadian statute that authorized compulsory licenses for acts of abuse, which occur, *inter alia*, "if the demand for the patented article in Canada is not being met to an adequate extent and on reasonable terms."[8]

The legislative history of the Bayh-Dole Act confirms that qualified experts viewed the relevant provisions as authorizing a compulsory license either for abuse or on public interest grounds.[9] For example, Harry. F. Manbeck, then General Patent Counsel for General Electric [and later a Commissioner of Patents] stated that "[I]f [a contractor] fails to supply the market adequately at a fair price, then there is reason for requiring it to license both the background patents and the patents stemming from the contract work."[10] U.S. Comptroller General Staats expressed DOE's views that "march-in rights *to protect the public's interest* were developed to take care of and address … [a] contractor's *windfall profits* … and detrimental effects to competition…"[11]

The reason for express legislative concerns about abuse and the public interest in the Bayh-Dole context are clear from the record. Under normal conditions, the patentee assumes the full risk of his or her research and development expenditures, and in U.S. law, there are relatively few constraints on the licensing practices by means of which the patentee tries to recoup that investment and turn a profit. Under Bayh-Dole, however, the government will have funded a significant part of the patentee's R&D costs and thus attenuated the risk. While there was a consensus that releasing the research product to

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[6] [cites at fn 498].
[7] *Id*. [cite 503]
[8] See REICHMAN WITH HASENZAHL, THE CANADIAN EXPERIENCE, *supra* note 1, at 20-22 (discussing §65(2) of Canada's Patent Act of 1985).
[9] See generally Halperin, at ___.
[10] [cite Halperin, n. 21] (emphasis supplied).
[11] [cite id., n. 22]

private industry would augment applications and benefit economic growth generally, the march-in provisions were added to ensure that patentees' did not abuse their position by making the products available to the public on unreasonable terms that could lead to "windfall profits, [the] suppression of technology, and … detrimental effects to competition."[12]

A State's ability to impose compulsory licenses to regulate abuses of a foreign patentee's exclusive rights under domestic law has been regulated by article 5A of the Paris Convention for more than 75 years, and these provisions were incorporated into the TRIPS Agreement of 1994. The large body of state practice in implementing these norms over time was succinctly and authoritatively summarized by Bodenhausen in 1967, as follows:

> [W]hen national legislation is aiming at preventing *the abuses which might result from the exercise of the exclusive rights conferred by the patents*, the rules given in paragraphs (3) and (4) [of article 5A, Paris Convention] are mandatory for the member states…
>
> [E]xamples of such abuses may exist in cases where the owner of the patent, although working the patent in the country concerned, refuses to grant licenses on reasonable terms and thereby hampers industrial development, or does not supply the national market with sufficient quantities of the patented product, or *demands excessive prices, for such products*. The member states are free to define these, and other abuses.[13]

This international practice is consonant with the legislative history of the march-in right under Bayh-Dole, as appears, for example, from Harry Manbeck's reference to a contractor's failure "to supply the market adequately at a fair price," quoted above. In his and other's views, march-in rights were thus "part of the answer to the so-called windfall situation."[14]

Apart from the legislative history, which is consistent with international practice, it cannot logically be doubted that the language in the Bayh-Dole Act requiring patented products to be made available to the public on reasonable terms encompasses the patentee's pricing strategy. All unreasonable terms and conditions that rise to the level of actionable abuses have as their object the power, directly or indirectly, to increase the licensor's prices beyond the level that competition would otherwise ensure and thus to enhance profits. When patentees impose "field of use" or other licensing restrictions, when they engage in illegal tying, or as in the case at hand, they adopt a marketing

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[12] Staat, Halperin n. 23; see generally Halperin; Arno & Davis.

[13] G. H. C. BODENHAUSEN, GUIDE TO THE APPLICATION OF THE PARIS CONVENTION FOR THE PROTECTION OF INDUSTRIAL PROPERTY AS REVISED AT STOCKHOLM IN 1967 70-71 (1968) (emphasis supplied).

[14] Cite at Halperin nn. 21, 23.

strategy consistent with the practice known as "monopoly leveraging,"[15] they are not conducting scientific or economic experiments for the sake of increasing academic knowledge. They pay their lawyers to devise contractual conditions that will enable them to raise prices and make more money.

In this connection, one should recall that individual members of the public do not typically negotiate with their pharmacies when they purchase medicine. They buy the product and pay the price that market conditions permit the pharmacist to charge. These conditions, in turn, result from the contracts stipulated between patent holders as licensors and their various licensees. When the Bayh-Dole Act affirms that the resulting products must be made available to the public on reasonable terms, it can only mean that the underlying licensing agreements should not undersupply the market, unduly distort competition, or otherwise leverage the procurement of active ingredients in ways that boost the price to unreasonable "windfall" levels that many users cannot afford.

While the Bayh-Dole march-in provisions thus clearly contemplate practices that produce excessive prices—what Manbeck and others called "windfall profits"—and would make no sense if they did not, I hasten to add that the Act in no way implies a regime of price controls, like that adopted in Canada and many EU countries. Indeed, loose assertions about "price controls" merely create confusion and divert attention away from the real issues bearing on the patentee's specific marketing strategies.

Statutes that seek to prevent abuses or otherwise to protect the public interest, like the march-in provisions of the Bayh-Dole Act, normally leave patentees free to adopt the marketing strategies they deem suitable. They do not require regulatory approval of prices, as would be the case under, say, Canada's regulatory agency, the Patented Medicines Prices Review Board (PMPRB).[16] By the same token, the marketing strategies that the patentee actually adopts, and their impact on the availability of the relevant products to the consumers on reasonable terms, is always open to public scrutiny and challenge on objective grounds of abuse. In the Bayh-Dole context, this would necessarily require attention to the taxpayers' interests as well as those of the patentee, including the ability of purchasers to afford critical, life-saving medicines and not be charged prices that "create … hardship for the overall public or for individual members of the public."[17]

In the case at hand, there is objective evidence that Abbott has imposed a 400% price increase in order to steer consumers away from competing products that would otherwise be made available to the public at much lower prices. There is further evidence that this strategy imposes hardship on patients that would particularly benefit from the lower priced products. At least one leading expert in the field believes that Abbott's strategy may turn out to violate prescriptions against one form of abuse known as monopoly

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[15] Interview with Professor Arti Rai, Duke University School of Law.
[16] See REICHMAN WITH HASENZAHL, THE CANADIAN EXPERIENCE, *supra* note 1, at 43-44.
[17] Halperin, at 13.

leveraging.[18]

These are questions of fact and law that require investigation and due deliberation.[19] Although the practices under review appear questionable to me, it is not my task to anticipate the conclusions that the NIH may reach. I am here to testify that, under the march-in provisions of the Bayh-Dole Act as they were adopted, the NIH does have a solemn obligation to undertake this enquiry in good faith, with a view to determining whether the products of federally funded research are in fact being made available to the public under reasonable terms and conditions.

[18] Image Technical Services, Inc. V. Eastman Kodak Co., 125 F.3d 1195 (9th Cir. 1997).

[19] See, e.g., Arti K. Rai and Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROBS. 289, 294 (2003).

NATIONAL INSTITUTES OF HEALTH
OFFICE OF THE DIRECTOR

In the Case of

NORVIR®

Manufactured by

ABBOTT LABORATORIES, INC.

Introduction

The NIH received letters from members of Congress and the public requesting that the Government exercise its march-in rights under the Bayh Dole Act (Act), 35 U.S.C. §§ 200-212, in connection with one or more patents owned by Abbott Laboratories, Inc. (Abbott). The letters expressed concern over the price of Norvir®, which is covered by the patents and marketed by Abbott for the treatment of patients with HIV/AIDS.

The march-in provision of the Act, 35 U.S.C. § 203, implemented by 37 C.F.R. § 401.6, authorizes the Government, in certain specified circumstances, to require the funding recipient or its exclusive licensee to license a Federally-funded invention to a responsible applicant or applicants on reasonable terms, or to grant such a license itself.

After careful analysis of the Bayh-Dole Act and considering all the facts in this case as well as comments received, the National Institutes of Health (NIH) has determined that it will not initiate a march-in proceeding as it does not believe that such a proceeding is warranted based on the available information and the statutory and regulatory framework.

Background on the Invention

From 1988 through 1993, ritonavir was developed at Abbott Laboratories partly through the use of Federal funds and falls within the claims of a number of patents owned by Abbott. [1] In 1996, ritonavir (sold under the tradename "Norvir®") was approved by the FDA for marketing.

Other U.S. and foreign patents may exist which cover certain aspects of the marketed compound including specific formulations or delivery techniques, and may not be subject inventions within the meaning of the term as defined in 35 U.S.C. § 201(e).[2] These inventions would not be

[1]These patents are: U.S. Patent Nos. 5,541,206,. 5,635,523, 5,648,497, 5,674,882, 5,846,987, and 5,886,036.

[2]The term "subject invention" means any invention of the funding recipient conceived or first actually reduced to practice in the performance of work under a funding agreement.

subject to the Government's march-in authority.

Statutory and Regulatory Background

The stated policy and objective of the Bayh-Dole Act is:

> to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise without unduly encumbering future research and discovery; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.

Act at § 200. Toward this goal, the Act addresses not only rules governing the licensing of Government-owned inventions, but also addresses the rights of Federal contractors[3] to elect title to inventions made with Federal funding.

In giving contractors the right to elect title to inventions made with Federal funding, the Act also includes various safeguards on the public investment in the research. For example, the Federal agency retains 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. See 35 U.S.C. § 202(c)(4). In addition, the Act includes march-in rights which provide a Federal agency with the authority, in certain very limited and specified circumstances, to make sure that a federally funded invention is made available to the public. The march-in provisions are set out in Section 203(a), which states that:

> With respect to any subject invention in which a small business firm or nonprofit organization has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee or exclusive licensee of a subject invention to grant a

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[3] Section 201(c) defines the term "contractor" as any person, small business firm, or nonprofit organization that is a party to a funding agreement. Executive Order 12591 expanded this definition to include large businesses.

nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such -

(1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;

(2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;

(3) action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or

(4) action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204.

The Department of Commerce regulations implementing the Act and specifying the procedures that govern the exercise of march in proceedings are set forth at 37 C.F.R. § 401.6. The regulations provide that whenever an agency receives information that it believes might warrant the exercise of march-in rights, it may initiate a march-in proceeding after notification of the contractor and a request to the contractor for informal written or oral comments.

Public Comments

The NIH held a public meeting on May 25, 2004 at which comments were presented by advocates for and against the use of the Government's march-in authority in connection with Norvir®. The speakers presented differing perspectives regarding the interpretation and intention of the march-in provisions, the reasons for the increase in the price of ritonavir, and the anti-competitive effect of that price increase.

The NIH also has received written comments from a variety of groups and individuals representing universities, the AIDS community, pharmaceutical interests, drafters of the Bayh-Dole Act, and other interested parties. These comments along with those submitted at the public meeting are available on the NIH Office of Technology Transfer website at http://www.ott.nih.gov/policy/meeting/may25.htm.

The NIH is aware that members of Congress and the public have asked the Federal Trade Commission (FTC) to investigate the potential anti-competitive effects of the increase in the

price of Norvir®. The NIH agrees that the FTC is the appropriate agency to address this issue.

After carefully considering all the information provided and otherwise made available, the NIH does not believe the initiation of a march-in proceeding is warranted.

Discussion

The NIH is the steward of medical and behavioral research for the nation. Its mission is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability. Each year, a wealth of scientific discoveries emanates from the NIH intramural laboratories and from extramural activities under grants and contracts. Bringing these discoveries from "the bench to the bedside" requires drug and product development, scale-up, clinical testing, and finally marketing and distribution. Success in accomplishing this colossal task and fulfilling our primary mission of improving public health requires the participation of industry partners.

The NIH supports fundamental research that may lead to the development of pharmaceutical products. Occasionally, the NIH funds a technology that ultimately is incorporated into a commercial product or process for making a commercial product. It is important to the NIH that pharmaceutical companies commercialize new health care products and processes incorporating NIH-funded technology thereby making the technology available to the public. A central purpose of the Bayh-Dole Act involves the development and commercialization of such products out of federally-funded research.

Section 203(a) of the Act provides in part that march-in rights may be exercised by the funding Federal agency based on any of four conditions: (1) when "practical application" of the subject invention has not been achieved or is not expected to be achieved in a reasonable time, (2) when the action is necessary to alleviate health or safety needs, (3) when action is necessary to meet requirements for public use specified by Federal regulation that the contractor has failed to meet or (4) when the U.S. industry preference of Section 204 of the Act has not been met. The third and fourth conditions are not relevant to this discussion[4].

Practical Application of the Subject Inventions

A composition or product, such as Norvir®, that has achieved practical application is defined in Section 201(f) to mean that it is manufactured "under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms."

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[4]The last two conditions are clearly not relevant. Subparagraph (3) narrowly applies to "public use" specified by Federal regulations, but there are no regulations that apply in this case. Subparagraph (4) is not relevant because Abbott manufactures Norvir® in the United States.

In 1997, the NIH reviewed a march-in request from CellPro, Inc. that asserted Baxter Healthcare Corporation (Baxter) had failed to take effective steps to achieve practical application of the subject inventions. NIH determined that Baxter "met the statutory and regulatory standard for practical application" as evidenced by its "manufacture, practice, and operation" of the invention and the invention's "availability to and use by the public…." Accordingly, the NIH determined not to initiate march-in proceedings.[5]

Similarly, the record in this instance demonstrates that Abbott has met the standard for achieving practical application of the applicable patents by its manufacture, practice, and operation of ritonavir and the drug's availability and use by the public.

Ritonavir has been on the market and available to patients with HIV/ADDS since 1996, when it was introduced and sold under the tradename Norvir® as both a standalone protease inhibitor and a booster to increase the effectiveness of protease inhibitors marketed by other companies. Thus, the invention has reached practical application because it is being utilized and has been made widely available for use by patients with HIV/AIDS for at least eight years.

Health or Safety Needs

Norvir® has been approved by the Food and Drug Administration as safe and effective and is being widely prescribed by physicians for its approved indications. No evidence has been presented that march-in could alleviate any health or safety needs that are not reasonably satisfied by Abbott. Rather, the argument advanced is that the product should be available at a lower price, which is addressed below. Thus, the NIH concludes that Abbott has met the statutory and regulatory standard for health or safety needs.

Drug Pricing

Finally, the issue of the cost or pricing of drugs that include inventive technologies made using Federal funds is one which has attracted the attention of Congress in several contexts that are much broader than the one at hand.[6] In addition, because the market dynamics for all products developed pursuant to licensing rights under the Bayh-Dole Act could be altered if prices on such products were directed in any way by NIH, the NIH agrees with the public testimony that suggested that the extraordinary remedy of march-in is not an appropriate means of controlling

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[5]The determination also evaluated the health or safety need prong and found that Baxter had "taken appropriate steps to reasonably satisfy this need." The other two prongs were held to be "clearly not relevant."

[6]In addition, NIH addressed "The NIH 'Reasonable Pricing' Clause Experience" in its report to Congress, "A Plan to Ensure Taxpayers' Interests are Protected," July 2001, available at http://www.nih.gov/news/070101wyden.htm.

prices. The issue of drug pricing has global implications and, thus, is appropriately left for Congress to address legislatively.

Conclusion

Norvir® has been available for use by patients with HIV/AIDS since 1996 and is being actively marketed by Abbott and prescribed by physicians primarily as a booster drug. Accordingly, this drug has reached practical application and met health or safety needs as required by the Bayh-Dole Act. The NIH believes that the issue of drug pricing is one that would be more appropriately addressed by Congress, as it considers these matters in a larger context. The NIH also maintains that the FTC is the appropriate agency to address the question of whether Abbott has engaged in anti-competitive behavior.

The NIH is cognizant of the care with which Congress crafted the march-in language and understands that it has the responsibility to exercise its march-in authority deliberately and with great care. As such, the NIH has determined that it does not have information that leads it to believe that the exercise of march-in rights might be warranted in this case within the meaning of 35 U.S.C. § 203.

Elias A. Zerhouni, M.D.
Director, NIH

Introductory Remarks by Dr. Mark Rohrbaugh

List-of-Speakers

Written Comments Received:

Senator Birch Bayh

Robert Huff, Editor GMHC Treatment Issues

Norman J. Latker, former Patent Counsel, HEW

John Erickson, President & CSO Sequoia Pharmaceuticals

Dan Ravicher, Executive Director, Public Patent Foundation

C. Peter Magrath et al, NASULGC, AAU and ACE

Carl E. Gulbrandsen, Managing Director WARF

Katharina Phillips, Council on Governmental Relations

Patricia Harsche Weeks, Immediate Past President AUTM

Joseph P. Allen, President NTTC

Heather L. Mason, V.P. Pharmaceutical Specialty Optns., Abbott Labs

Benjamin Young, OHHP

Lynda Dee, Co-Chair AIDS Treatment Activists Coalition

Julie Britton Haden, West Virginia Coalition for People with HIV/AIDS

Rhonda Connard & Amanda Lowther, Covenant House

Michael Weinstein, President AIDS Healthcare Foundation

Stephan E. Lawton, V.P. & General Counsel, BIO

David D. Ho, The Aaron Diamond AIDS Research Center

David Gollaher, California Health Care Institute

David Miller President iBioTM

David Halperin Attorney Counselor

James Love Pres. Essential Inventions Inc.

Jerome Reichman Duke Univ.

NATIONAL INSTITUTES OF HEALTH
OFFICE OF THE DIRECTOR

In the Case of

Xalatan®

Manufactured by

PFIZER, INC.

Introduction

The NIH received letters from the public requesting that the Government exercise its march-in rights under the Bayh-Dole Act (Act), 35 U.S.C. §§ 200-212, in connection with one or more patents owned by Pfizer, Inc. (Pfizer). The letters expressed concern that the price of Xalatan® is higher in the United States than in Canada or Europe. Xalatan® is covered by licenses and patents and marketed by Pfizer for the treatment of patients with glaucoma.

The march-in provision of the Act, 35 U.S.C. § 203, implemented by 37 C.F.R. § 401.6, authorizes the Government, in certain specified circumstances, to require the funding recipient or its exclusive licensee to license a federally funded invention to a responsible applicant or applicants on reasonable terms, or to grant such a license itself.

After careful analysis of the Bayh-Dole Act and considering all the facts in this case as well as comments received, the National Institutes of Health (NIH) has determined that it will not initiate a march-in proceeding as it does not believe that such a proceeding is warranted based on the available information and the statutory and regulatory framework.

Background on the Invention

The basic concept that prostaglandins could be used to reduce intraocular pressure in treating ocular hypertension and glaucoma was developed at Columbia University (Columbia) under NIH-funded grants in the 1970s and early 1980s. Latanoprost, developed several years later in a collaborative effort between Columbia and Pharmacia Corporation, falls within the claims of U.S. Patent No. 4,599,353 that expires on July 28, 2006. Latanoprost was originally exclusively licensed to Pharmacia Corporation that, in 2003, merged with Pfizer. In 1996, latanoprost (sold under the tradename Xalatan®) was approved by the Food and Drug Administration (FDA) for marketing as a second-line treatment. In 2002, it received FDA approval as a first-line treatment for glaucoma.

Pfizer holds at least three other U.S. patents[1] that cover certain aspects of the marketed compounds and methods and are not subject inventions within the meaning of the term as defined in 35 U.S.C. § 201(e).[2] These inventions would not be subject to the Government's march-in authority.

Statutory and Regulatory Background

The stated policy and objective of the Bayh-Dole Act are:

> to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise without unduly encumbering future research and discovery; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.

Act at § 200. Toward this goal, the Act addresses not only rules governing the licensing of Government-owned inventions, but also addresses the rights of Federal contractors[3] to elect title to inventions made with Federal funding.

In giving contractors the right to elect title to inventions made with Federal funding, the Act also includes various safeguards on the public investment in the research. For example, the Federal agency retains 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. See 35 U.S.C. § 202(c)(4). In addition, the Act includes march-in rights which provide a Federal agency

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[1]These patents include U.S. Patent Nos. 5,296,504 and 5,422,368, due to expire in 2011, and 6,429,226, due to expire in 2009. None of these patents involve any federal funding.

[2]The term "subject invention" means any invention of the funding recipient conceived or first actually reduced to practice in the performance of work under a funding agreement.

[3] Section 201(c) defines the term "contractor" as any person, small business firm, or nonprofit organization that is a party to a funding agreement. Executive Order 12591 expanded this definition to include large businesses.

with the authority, in certain very limited and specified circumstances, to make sure that a federally funded invention is made available to the public. The march-in provisions are set out in Section 203(a), which states that:

> With respect to any subject invention in which a small business firm or nonprofit organization has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such -
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> > (1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;
> >
> > (2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;
> >
> > (3) action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
> >
> > (4) action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204.

The Department of Commerce regulations implementing the Act and specifying the procedures that govern the exercise of march-in proceedings are set forth at 37 C.F.R. § 401.6. The regulations provide that whenever an agency receives information that it believes might warrant the exercise of march-in rights, it may initiate a march-in proceeding after notification of the contractor and a request to the contractor for informal written or oral comments.

Public Comments

The NIH has received written comments from a variety of groups and individuals representing universities, the patient community, drafters of the Bayh-Dole Act, and other interested parties.

After carefully considering all the information provided and otherwise made available, the NIH does not believe the initiation of a march-in proceeding is warranted.

Discussion

The NIH is the steward of medical and behavioral research for the Nation. Its mission is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability. Each year, a wealth of scientific discoveries emanates from the NIH intramural laboratories and from extramural activities under grants and contracts. Bringing these discoveries from "the bench to the bedside" requires drug and product development, scale-up, clinical testing, and finally marketing and distribution. Success in accomplishing this colossal task and fulfilling our primary mission of improving public health requires the participation of industry partners.

The NIH supports fundamental research that may lead to the development of pharmaceutical products. Occasionally, the NIH funds a technology that ultimately is incorporated into a commercial product or process for making a commercial product. It is important to the NIH that pharmaceutical companies commercialize new health care products and processes incorporating NIH-funded technology thereby making the technology available to the public. A central purpose of the Bayh-Dole Act involves the development and commercialization of such products out of federally funded research.

Section 203(a) of the Act provides in part that march-in rights may be exercised by the funding Federal agency based on any of four conditions: (1) when "practical application" of the subject invention has not been achieved or is not expected to be achieved in a reasonable time, (2) when the action is necessary to alleviate health or safety needs, (3) when action is necessary to meet requirements for public use specified by Federal regulation that the contractor has failed to meet or (4) when the U.S. industry preference of Section 204 of the Act has not been met. The third and fourth conditions are not relevant to this discussion[4].

Practical Application of the Subject Inventions

A composition or product, such as Xalatan®, that has achieved practical application is defined in Section 201(f) to mean that it is manufactured "under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms."

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[4]The last two conditions are clearly not relevant. Subparagraph (3) narrowly applies to "public use" specified by Federal regulations, but there are no regulations that apply in this case. Subparagraph (4) is not relevant because Pfizer substantially manufactures Xalatan® in the United States.

In 1997, the NIH reviewed a march-in request from CellPro, Inc., that asserted Baxter Healthcare Corporation (Baxter) had failed to take effective steps to achieve practical application of the subject inventions. NIH determined that Baxter "met the statutory and regulatory standard for practical application" as evidenced by its "manufacture, practice, and operation" of the invention and the invention's "availability to and use by the public . . . ." Accordingly, the NIH determined not to initiate march-in proceedings.[5]

In August 2004, the NIH issued its March-In Position Paper in the Case of Norvir® that is available on the NIH Office of Technology Transfer Web site. In that case, NIH determined that it did not have information that led it to believe that the exercise of march-in rights might be warranted because the drug had been available since 1996 and was being actively marketed by the company and prescribed by physicians. Accordingly, the drug had reached practical application and met health or safety needs as required by the Bayh-Dole Act.[6] Furthermore, the position paper held that the issue of drug pricing was properly left to Congress to address.

Similar to the other two cases, the record in this instance demonstrates that Pfizer has met the standard for achieving practical application of the applicable patents by its manufacture, practice, and operation of latanoprost and the drug's availability and use by the public.

Latanoprost has been on the market and available to glaucoma patients since 1996, when it was introduced and sold under the tradename Xalatan®. Thus, the invention has reached practical application because it is being utilized and has been made widely available for use by glaucoma patients for at least eight years.

Health or Safety Needs

Xalatan® has been approved by the Food and Drug Administration as safe and effective and is being widely prescribed by physicians as both a first-line and second-line treatment. No evidence has been presented that march-in could alleviate any health or safety needs that are not reasonably satisfied by Pfizer. Rather, the argument advanced is that the product should be available at the same price as that charged in other countries, which is addressed below. Thus, the NIH concludes that Pfizer has met the statutory and regulatory standard for health or safety needs.

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[5]The determination also evaluated the health or safety need prong and found that Baxter had "taken appropriate steps to reasonably satisfy this need." The other two prongs were held to be "clearly not relevant."

[6]The other two prongs were held to be "clearly not relevant."

Drug Pricing

Finally, the issue of the cost or pricing of drugs that include inventive technologies made using Federal funds is one which has attracted the attention of Congress in several contexts that are much broader than the one at hand.[7] In addition, because the market dynamics for all products developed pursuant to licensing rights under the Bayh-Dole Act could be altered if prices on such products were directed in any way by the NIH, the NIH believes that the extraordinary remedy of march-in is not an appropriate means of controlling prices. The issue of whether drugs should be sold in the United States for the same price as they are sold in Canada and Europe has global implications and, thus, is appropriately left for Congress to address legislatively.

Conclusion

Xalatan® has been available for use by glaucoma patients since 1996 and is being actively marketed by Pfizer and prescribed by physicians as both a first-line and second-line treatment. Accordingly, this drug has reached practical application and met health or safety needs as required by the Bayh-Dole Act. The NIH believes that the issue of whether drug pricing should be consistent across the spectrum of developing countries is one that would be more appropriately addressed by Congress, as it considers these matters in a larger context.

The NIH is cognizant of the care with which Congress crafted the march-in language and understands that it has the responsibility to exercise its march-in authority deliberately and with great care. As such, the NIH has determined that it does not have information that leads it to believe that the exercise of march-in rights might be warranted in this case within the meaning of 35 U.S.C. § 203.

SEP 1 7 2004

Elias A. Zerhouni, M.D.
Director, NIH

[7]In addition, NIH addressed the role of NIH in the pricing of drugs in reports to Congress including "A Plan to Ensure Taxpayers' Interests are Protected," July 2001, available at http://www.nih.gov/news/070101wyden.htm and "Affordability of Inventions and Products," July 2004 available at http://ott.od.nih.gov/NewPages/211856ottrept.pdf.

NATIONAL INSTITUTES OF HEALTH
OFFICE OF THE DIRECTOR

DETERMINATION IN THE CASE OF FABRAZYME® MANUFACTURED BY GENZYME CORPORATION

Introduction

Dr. C. Allen Black, Jr. submitted a request ("the Request") on behalf of his clients ("Requestors"), dated August 2, 2010, to Secretary Sebelius, Department of Health and Human Services ("HHS"), asking the Government to exercise its march-in rights under the Bayh Dole Act, 35 U.S. §§ 202-212 (the "Act"). The Request concerned certain patents owned by the Mount Sinai School of Medicine ("Mount Sinai") that are based on inventions funded by the National Institutes of Health ("NIH") and exclusively licensed by Mount Sinai to the Genzyme Corporation ("Genzyme"). Specifically, Requestors have asked HHS to grant an open license to United States Patent Nos. 5,356,804 ("the '804 patent") and 5,580,757 ("the '757 patent") to permit the manufacture of Fabrazyme® (agalsidase beta), a form of alpha-galactosidase A, to treat Fabry Disease.[1] Fabrazyme® is in critically short supply due to Genzyme's manufacturing difficulties which are currently being monitored by and are under a Consent Decree with the U.S. Food and Drug Administration ("FDA"). The Requestors also seek an open license to the cell line producing Fabrazyme® and any technical know-how developed in conjunction with producing Fabrazyme® that would expedite the production and reduce duplication of manufacturing and product development efforts by a third party. Support of the Request has been received from other patients and interested parties.

Determination

Based upon the information currently available, NIH has determined that a march-in proceeding under 35 U.S.C. § 203(a)(2) is not warranted at the present time because any licensing plan that might result from such a proceeding would not, in our judgment, address the problem identified by the Requestors. A march-in proceeding resulting in the grant of patent use rights to a third party will not increase the supply of Fabrazyme® in the short term because years of clinical studies and regulatory approval would be required before another manufacturer's product could become available to meet patients' needs in the United States. NIH has no information that a company is expecting imminent FDA approval of a competing version of an agalsidase beta product. Secondarily, the '804 patent is not an obstacle for a company to conduct clinical trials in the United States in furtherance of regulatory approval for a competing drug, because such clinical trials are exempt from infringement under the Hatch-Waxman statutory safe harbor provision. (35 U.S.C. § 271(e)) Finally, Genzyme has indicated that it expects the production of Fabrazyme® to be back to full supply levels in the first half of

[1] Information about Fabry disease is available at http://www.ninds.nih.gov/disorders/fabrys/fabrys.htm.

2011. Genzyme appears to be working diligently and in good faith to address the Fabrazyme® shortage.

Notwithstanding the foregoing, NIH will continue to carefully monitor the shortage of Fabrazyme® and will re-evaluate this determination immediately upon receiving any information that suggests progress toward restoring the supply of Fabrazyme® to meet patient demand is not proceeding as represented.

Further, in the unlikely event that NIH receives information that a third party has a viable plan to obtain FDA approval to market agalsidase beta during the period in which Genzyme is not able to meet patient demand for Fabrazyme®, and, that third party requires commercial rights to the '804 patent in order to proceed with its plan, NIH will immediately re-consider its decision to exercise its march-in authority. Toward this end, NIH has asked Mount Sinai to: (1) provide monthly reports on the status of Genzyme's progress toward addressing the supply shortage of Fabrazyme® until such time as U.S. Fabry patients' needs have been met; (2) provide a copy of Genzyme's reports on the allotment of Fabrazyme to Fabry patients; and, (3) notify NIH within two business days after receiving any request from a third party for a license to the '804 patent to market agalsidase beta during the Fabrazyme® shortage.

The Requestors have also asked NIH to include in any license to the patent "the cell line producing Fabrazyme® and any technical know-how developed in conjunction with producing the drug." The march-in provision is, however, only directed to Bayh-Dole Act subject inventions and not to tangible materials or unpatented technical know-how. NIH's determination decision is directed solely to use of its march-in authority to the subject invention.

Statutory Background and Criteria

The stated policy and objective of the Bayh Dole Act is:

> [T]o use the patent system to promote the utilization of inventions arising from federally supported research or development; . . . to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; . . . . (35 U. S.C. § 200)

Toward this goal, the Bayh-Dole Act provides a Federal agency with march-in rights authority in certain limited circumstances, to ensure that a federally funded invention is available to the public. More specifically:

> With respect to any subject invention in which a small business firm or nonprofit organization has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require

the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such—

(1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;
(2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;
(3) action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
(4) action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204. (35 U.S.C. § 203(a))

With respect to the use of march-in, the regulations state at 37 C.F.R. § 401.6(b):

> Whenever an agency receives information that it believes might warrant the exercise of march-in rights, before initiating any march-in proceeding, it shall notify the contractor in writing of the information and request informal written or oral comments from the contractor as well as information relevant to the matter.

Based on the available information, a Federal agency can either initiate march-in procedures set forth at 37 C.F.R. § 401.6(c) or notify the contractor that it will not pursue march in rights.[2] Consistent with 35 U.S.C. § 203(a) with respect to any subject invention, a Federal agency is authorized to:

> require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself.

The NIH has the delegated authority to make the march-in determination in this case. NIH has received information from the Requestors, Genzyme, Mount Sinai, letters from patients who suffer from Fabry disease, and letters from other concerned members of the public, as well as other pertinent materials obtained by the NIH from public sources.

[2] See 37 C.F.R. § 401.6(b).

The Subject Invention

The patents in question are the '804 patent and the '757 patent. The '804 patent relates to the production of enzymatically active alpha-galactosidase A from a recombinant mammalian cell line. The '757 patent is similar but makes use of a fusion protein that must be cleaved before it is enzymatically active. This latter technology is not used in the manufacture of Fabrazyme®. Therefore, only the '804 patent is relevant to this determination.

Mount Sinai filed a patent application for the '804 patent on October 24, 1990. The patent issued on October 18, 1994 and, with term extensions, expires on September 27, 2015. Mount Sinai elected title to this invention and issued the Government a confirmatory license on September 13, 1991 as required by 37 C.F.R. § 401.14 (f)(1). There is no dispute that the '804 patent is a subject invention under 35 U.S.C. § 201(e) and 37 C.F.R. § 404.14 (a)(2).

Meeting Health or Safety Needs

The central inquiries in this case are whether there is an existing health need of Fabry patients associated with the exclusive licensing by Mount Sinai of the '804 patent to Genzyme and whether NIH, by exercising its march-in authority, could alleviate that problem. We have found the following information relevant:

(1) Until mid-June 2009, Genzyme produced sufficient quantities of Fabrazyme® to meet the needs of patients;

(2) In mid-June 2009, Genzyme interrupted its production of Fabrazyme® at its Allston, Massachusetts facility due to a viral contamination and further interrupted its production of Fabrazyme® due to a power outage;

(3) In May 2010, Genzyme entered into a Consent Decree with the FDA related to the production of Fabrazyme® and other products produced by Genzyme at its Allston plant; and

(4) Due to Genzyme's production difficulties at its Allston facility, Fabry patients, as of the date of this determination, are not able to obtain sufficient quantities of Fabrazyme®.

The Requestors state that, since Genzyme began rationing the dosages of Fabrazyme, they and other patients with Fabry disease "have suffered a return of symptoms including neuropathy, proteinuria, digestive disorders, heart disease, renal disease, morbidity, and increased risk of premature death."

In late October 2010, the European Medicines Agency (EMA), a European regulatory authority, issued a report to doctors urging that any Fabry patients on low doses of Fabrazyme® who are suffering adverse effects should receive full doses. The EMA reported that it initiated the review because of a trend of increased reports of adverse events correlating directly with the Fabrazyme® supply problems. These reports revealed a pattern suggesting that the decrease in the dose of Fabrazyme caused the Fabry disease to progress. The EMA observed that not everyone on a reduced dose suffered symptoms. Accordingly the EMA's report stated that continued low doses of Fabrazyme are acceptable for those patients whose condition remains stable.[3]

Based on the current information, the patients' required supply of Fabrazyme® cannot be met due to Genzyme's current manufacturing difficulties.

Commercial Development of Biological Products

The process for bringing a biological product to market for use in humans requires substantial time, effort, and resources, irrespective of any patent rights. Any new product must proceed through the complete FDA Investigational New Drug ("IND") and Biologic License Application ("BLA") approval processes. These approval processes include, among other things, the following generalized steps:

(a) arranging appropriate safeguards, as required by 21 C.F.R. Parts 50, 54, and 56;
(b) arranging a supply of clinical-grade materials suited for clinical research, as required under 21 C.F.R. Parts 210, 211, 600, and 606;
(c) gathering all of the necessary preclinical (in vitro and in vivo) data to support the start of clinical research;
(d) filing the IND and waiting thirty (30) days to permit the FDA to impose a hold on clinical research, pursuant to 21 C.F.R. Part 312;
(e) conducting enough clinical studies (at least two of which the FDA requires to be pivotal) to establish parameters for human pharmacokinetics, efficacy, dosing, and safety; and
(f) filing the BLA pursuant to 21 C.F.R. Part 601.

Once the BLA has been filed, the FDA's internal goal is to complete the review within ten months or within six months if the application has priority status.[4] However, the process may be indefinitely longer if the initial review does not result in an approval.

Even for a company seeking to expand production of its own, existing product by constructing a second facility, the FDA still requires that the company demonstrate the lack of "adverse effect

[3] http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2010/10/WC500098370.pdf.

[4] FDA Performance Report to the President and Congress for the Prescription Drug User Fee Act, FY 2009 at 9-10 (http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/PDUFA/UCM228022.pdf).

on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product,"[5] through whatever testing the FDA deems necessary – including a new round of clinical trials.[6] If a second company wants to make a similar, competing product, the competitor must file its own IND and BLA, just as if the competitor were the original innovator.

Genzyme's Development, Manufacture, and Sale of Fabrazyme®

Following Mount Sinai's grant of an exclusive license to Genzyme for the '804 patent, Genzyme made substantial investments in the development of Fabrazyme®. This effort included developing a recombinant cell line that produces the human enzyme alpha-galactosidase A under clinical conditions, and then conducting Phase I, II, III, and IV clinical studies with its enzyme product. Genzyme began marketing the drug Fabrazyme® in the European Union in 2001 and in the United States after it received FDA approval on April 24, 2003.[7] Genzyme is the only company that has been granted FDA approval in the United States to manufacture and sell an alpha-galactosidase A product. Fabrazyme® is the only approved therapeutic for Fabry disease in the United States.

On May 24, 2010, the FDA and Genzyme entered into a Consent Decree in a proceeding before the United States District Court for the District of Massachusetts to correct manufacturing quality violations at the company's Allston, Massachusetts manufacturing facility. Under this Consent Decree, Genzyme agreed, among other things, to adhere to an FDA approved timeline for making facility improvements to comply fully with current good manufacturing practice, periodic inspections by the FDA, and employment of an independent expert to inspect the Allston plant and issue recommendations. In addition, the Consent Decree provides a deadline for Genzyme to transfer its operations for filling drug vials from its Allston facility to other manufacturing sites but allows it to continue "to manufacture, process, test, pack, label, hold, and distribute . . . Fabrazyme®."

Prior to Genzyme's production difficulties it began constructing a new manufacturing facility in Framingham, Massachusetts, in order to expand the production of Fabrazyme®. According to Genzyme, this new plant will provide substantial additional capacity to support the anticipated increasing need for Fabrazyme®. Genzyme expects that its new Framingham manufacturing facility will be approved by the end of 2011.

Genzyme indicated to NIH that because Fabrazyme® inventories were not sufficient to avoid shortages during the period of suspended production and recovery, Genzyme immediately began working with regulatory authorities, physicians, and patient organization groups to carefully manage product supply with the goal of minimizing the impact of the shortage on the

[5] 21 C.F.R. § 601.12(b)(1).

[6] See generally 21 C.F.R. § 601.12.

[7] Reported on the FDA website, the FDA granted Orphan Drug Product status to Fabrazyme® on January 19, 1988; the market exclusivity associated with Orphan status expired April 24, 2010.

health of patients. Genzyme has further indicated that available Fabrazyme® has been and continues to be distributed equitably to all regions and without regard to charitable status.

Genzyme also stated that it has been allocating 38% of its available supply of Fabrazyme® to patients in the United States based on the U.S. percentage of Fabrazyme® usage prior to its supply interruption in mid-2009. Further, Genzyme expects to have the full supply of Fabrazyme® available in the first half of 2011.

In an August 20, 2010 letter to the Fabry community, Genzyme offered all patients currently treated with Fabrazyme® one full dose in September 2010 and one full dose in October 2010. More recently, Genzyme, in a letter to the Fabry community dated October 25, 2010, reported that: (1) patients currently treated with Fabrazyme who were infused biweekly prior to the shortage would receive two full doses in November 2010; and, (2) there was not a sufficient supply to support a dose increase for any patient nor would the drug be available for new patients to begin treatment in November. Genzyme advised that it is providing regular updates to its best estimate of Fabrazyme supply. Because it is working with a limited inventory, however, Genzyme further noted that even minor changes to its current manufacturing plan can impact the drug's availability and that it is committed to informing the Fabry community of shipping delays.

Commercial Development of Treatments for Fabry Disease

In considering this Request, we considered the '804 patent with respect to the development of alternative treatments of Fabrazyme. At least five other companies worldwide are known to be engaged in commercial development directed to alternative treatments for Fabry disease. At this time, based on the information available, we are encouraged that the worldwide supply of drugs or biologics for Fabry patients will increase in the medium- and long-term.

First, Shire plc, a UK company, obtained authorization to market its product Replagal® (agalsidase alpha), a form of alpha-galatosidase A, in the European Union in 2001. It is now available in forty-five countries but is not yet approved in the United States.[8] In the United States, Shire filed a BLA with the FDA in December 2009. By February 2010, however, Shire withdrew its BLA filing, replaced it with a rolling submission, and at the suggestion of the FDA, requested and received fast-track designation.[9] As of June 2010, enrollment was closed in its clinical studies. Shire has announced that it will actively manage emergency requests and will continue to provide the drug to U.S. patients who have been enrolled in the treatment IND and who obtained the drug for emergency use.[10] On August 3, 2010, Shire withdrew its BLA for Replagal® in order to consider updating its submission with additional clinical data.[11]

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[8] Source: Shire webpage (see http://www.shire.com/shireplc/en/products/rare/fabrydisease/REPLAGAL).
[9] Source: Shire webpage (see http://www.shire.com/shireplc/en/investors/investorsnews/irshirenews?id=329).
[10] Source: Letter from Fabry Support & Information Group to Fabry community (Jul. 9, 2010) (see: http://www.fabry.org/fsig.nsf/PDFs/PDFs10/$File/FDA_Approval_Letter.pdf).
[11] Source: Shire Half-Year Report for the six months ended June 30, 2010 at 5 (see: http://www.shire.com/shireplc/en/investors/reports).

Shire represents that it currently supplies Replagal® to over 2,300 Fabry disease patients and anticipates being able to continue to accommodate additional Fabry patients in 2010 while carefully monitoring supply and demand.[12] Shire further states that it "will be in a position to make Replagal® available to at least 300 additional patients in 2011, phased throughout the year, based on current manufacturing capacity."[13] Finally, Shire has said that approval of a new manufacturing facility in Lexington, Massachusetts will allow treatment of several hundred more Fabry patients.[14]

The '804 patent is not a barrier to the availability of Replagal® in the United States as the drug has been held not to infringe the '804 patent.[15] Further, Genzyme has encouraged patients to switch to Replagal® during the supply shortage of Fabrazyme®. However, since Mount Sinai's European patent equivalent to the '804 patent (EP 1 942 189) was granted on April 14, 2010, Mount Sinai has initiated infringement actions in Germany and Sweden against Shire for its sale of Replagal®.[16] Infringement actions can be coupled with a demand for an injunction to halt use of a patented invention. In this case, a reduction in the supply of Replagal® during a period of shortage of Fabrazyme would increase demand for Fabrazyme® in Europe and further limit the doses available to individual patients in the US and Europe. Mount Sinai has assured us that it will not pursue an injunction against the marketing and sale of Replegal® during any period of an existing or future shortage of Fabrazyme®. We expect Mount Sinai and Shire to make the welfare of the patients their first priority as they resolve resolve their differences.
Second, Amicus Therapeutics, a US company, is developing Amigal® (migalastat HCl), an oral small molecule "chaperone" medication to treat Fabry disease, which has reached Phase II and Phase III clinical trials.[17] Both Mount Sinai and Genzyme have reported that Amicus would not require a license under the '804 patent, as its product is a small molecule, and the '804 patent is directed to recombinant protein production. Recently Amicus and GlaxoSmithKline announced an agreement to develop and commercialize Amigal®, including advancing clinical studies and exploring co-administration of Amigal® with enzyme replacement therapy to treat Fabry disease.[18]

Three other companies have publicly reported pre-clinical development of alternative drugs to treat Fabry disease. Isu Abxis, a Korean company, reports that its ISU 303 drug is in clinical development.[19] Protalix, based in Israel, reports that it is engaged in pre-clinical development

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[12] Source: Q3 2010 Shire plc Press Release at 4 (Oct. 29, 2010) (see: http://www.shire.com/shireplc/en/investors/investorsnews/irshirenews?id=421).
[13] Id.
[14] Id.
[15] Genzyme Corp. v. Transkaryotic Therapies, Inc., 346 F. 3rd 1094 (Fed. Cir. 2003).
[16] Source: Source: Shire Half-Year Report for the six months ended June 30, 2010 at 5 (see: http://www.shire.com/shireplc/en/investors/reports).
[17] Source: Amicus webpage (see: http://www.amicustherapeutics.com/clinicaltrials/at1001.asp).
[18] GSK Press Release (Oct. 29, 2010) (see: http://www.gsk.com/media/pressreleases/2010/2010_pressrelease_10118.htm).
[19] Source: Abxis webpage (see: http://www.abxis.com/eng/index.asp).

of a Fabry drug, PRX-102.[20] Finally, JCR Pharmaceuticals Co., Ltd., based in Japan, has reportedly partnered with GlaxoSmithKline to co-develop its JR-051.[21] As of November 24, 2010, no clinical trials of these drugs have been reported.[22]

With respect to ISU 303, PRX-102 and JR-051, Mount Sinai and Genzyme have stated that none of the companies developing such products currently need a license to make, use or sell their products in the United States because any pre-clinical or clinical development activities in the United States would enjoy the protection of the Hatch-Waxman safe harbor, 35 U.S.C. § 271(e)(1). More specifically, the information available shows that no supplier of an alternative enzyme replacement therapy has approached Mount Sinai or Genzyme to seek a license to supply such a therapy during the duration of the shortage.

Conclusion

NIH has determined that the information currently available does not warrant a march-in proceeding under 35 U.S.C. § 203(a)(2) because, no remedy that is available under the march-in provision would address the problems identified by the requestors due to the shortage of Fabrazyme®. The license that Requestors have sought, were it to be granted, is unlikely to increase the supply of alpha-galactosidase A during the term of the '804 patent because years of clinical studies would be required before an alternative source could be approved by the FDA.

Moreover, NIH has not received any information that suggests a qualified third party is ready to supply an alpha-galactosidase A-based therapy.

On the other hand, Genzyme has expressed its commitment to provide a full supply of Fabrazyme® in the first half of 2011.

NIH is concerned about the urgent health needs of Fabry patients who are unable to obtain the recommended dosage of Fabrazyme® during this interim supply shortage and will continue to monitor the issues related to Fabry patient's access to Fabrazyme®.

[20] Source: Protalix webpage (see: http://www.protalix.com).
[21] Source: JCR Pharmaceuticals webpage (see: http://jcrpharm.jp/en).
[22] Source: ClinicalTrials.gov (see: http://www.clinicaltrials.gov).

We have asked Mount Sinai to: (1) provide monthly reports on the status of Genzyme's progress toward addressing the supply shortage of Fabrazyme® until such time as U.S. Fabry patients' needs have been met; (2) provide monthly reports on Genzyme's allotment of Fabrazyme® to Fabry patients; and, (3) notify NIH within forty-eight hours after receiving any request from a third party for a license to the '804 patent in order to market agalsidase during the Fabrazyme® shortage.

If at any time new information becomes available that could change our determination, we will evaluate it as quickly as possible to determine whether our decision should be modified.

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health

12/1/10

Date

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard
Rockville, MD 20852

February 13, 2013

Sent by Electronic Mail and US Mail

Dr. C. Allen Black
1579 Montgomery Road
Allison Park, Pennsylvania 15101

Subject: 2010 Request to HHS to Exercise its Bayh-Dole March-In Authority on U.S. Patent No. 5,356,804

Dear Dr. Black:

In a letter dated August 2, 2010, you requested on behalf of your clients that NIH use its march-in authority on U.S. Patent No. 5,356,804, a "Subject Invention" made using NIH funds and owned by The Mount Sinai School of Medicine ("Mount Sinai"). The patent is licensed exclusively to Genzyme Corporation ("Genzyme") for the production of Fabrazyme® (agalsidase beta). On December 6, 2010, NIH informed you of its decision not to proceed with march-in under 35 U.S. C. § 203(a)(2) because any licensing plan that might result from such a proceeding would not, in the judgment of NIH, address the problem you identified (see www.ott.nih.gov/policy/March-In-Fabrazyme.pdf). Notwithstanding this decision, NIH stated it would re-evaluate the need for march-in if a third party expressed interest in manufacturing agalsidase beta or if progress towards restoring the supply of Fabrazyme® to meet patient demand was not proceeding as represented by Genyzme. Due to the seriousness of Fabry patients' need to obtain their full prescribed dose of Fabrazyme®, NIH required Mount Sinai to report on the status of Fabrazyme® availability. To that end, both Mount Sinai and Genzyme reported each month to the NIH: (1) the status of Genzyme's progress toward addressing the supply shortage of Fabrazyme® until such time as U.S. Fabry patients' needs had been met; and (2) Genzyme's reports on the allotment of Fabrazyme® to Fabry patients. These parties were also required to notify NIH within two business days after having received any request from a third party for a license to Mount Sinai's Subject Invention to market agalsidase beta during the Fabrazyme® shortage.

From January 2011 through December 2012, both Mount Sinai and Genzyme provided monthly reports responsive to the above criteria. Neither Mount Sinai nor Genzyme informed NIH that they had received a request from a third party to license the Subject Invention, and at no point did a third party contact NIH with such a request. The December 2012 report from Genzyme stated that: (1) U.S. Fabry patients remain on full dose regimens, (2) Genzyme continues to accommodate new patients with full dosing and without placing them on a waiting list; and (3) Genzyme is able to provide full doses of Fabrazyme® to patients transitioning to Fabrazyme® as

a result of the Shire PLC's decision to withdraw its FDA Biologics License Application for Replagal®.

Based on Mount Sinai's and the Genzyme's representations in their respective December 2012 reports and the ability of U.S. Fabry patients to obtain full doses of Fabrazyme®, NIH has closed the above march-in case.

Sincerely,

/s/

Mark L. Rohrbaugh, Ph.D., J.D.
Director, Office of Technology Transfer

MLR:sf

NATIONAL INSTITUTES OF HEALTH OFFICE OF THE DIRECTOR DETERMINATION IN THE CASE OF NORVIR® MANUFACTURED BY ABBVIE

On October 25, 2012, the National Institutes of Health (NIH) received a request on behalf of Knowledge Ecology International, the American Medical Students Association, the U.S. Public Interest Research Group, and the Universities Allied for Essential Medicines (all referred to collectively as "Requestors") asking the NIH to exercise its Bayh-Dole Act march-in rights under 35 U.S.C. § 203 and to take other agency actions on six patents that are owned and used in the manufacture of AbbVie's[1] drug ritonavir and marketed as Norvir® ("Request").

The Requestors and AbbVie provided additional information for six questions that the NIH requested information on concerning the use of and access to Norvir® (Attachment 1). The NIH carefully considered available information, including all the information provided in the Request, the responses to the questions, information provided by AbbVie, as well as publicly available information directed to the reasonable use of and access to Norvir®. For the reasons provided below, the NIH declines to initiate a march-in investigation.

Patent Landscape for Ritonavir

The six patents at issue, U.S. Patent Nos. 5,541,206, 5,635,523, 5,648,497, 5,674,882, 5,946,987, and 5,886,036, claim inventions directed to the treatment of patients with HIV/AIDS and made by AbbVie with funding by the NIH ("Subject Patents"). These Subject Patents have expiration dates between December 29, 2012, and July 15, 2014. In addition, the Food and Drug Administration ("FDA") granted AbbVie six-months of pediatric exclusivity beginning at the expiration of each patent. AbbVie owns an additional 11 patents that were not made with Government-funding and thus are not subject to Bayh-Dole and the rights reserved for the Government, such as march-in and the Government's use license. The Subject Patents and the additional AbbVie patents are used in the manufacture of three different formulations of Norvir® (tablet, soft gel capsule, and oral solution), according to the FDA's Electronic Orange Book. Of the listed patents specified in the FDA's Orange Book for which the Government has no rights, the patents for the soft gel Norvir® tablet expire by November 22, 2020; for the Norvir® tablet by February 25, 2025; and for the oral solution of Norvir® by December 26, 2016.[2] As such, the NIH understands that the earliest the FDA could approve any generic version of Norvir® oral solution is after December 26, 2016, absent any other actions by AbbVie or another company. Additionally, if AbbVie initiates litigation under the Hatch-Waxman Act and does not prevail, a generic company could possibly receive FDA approval. Currently, there are at least three generic manufacturers, Roxane Laboratories, Inc., Hetero USA, Inc., and Mylan, Inc., seeking

[1] As of January 1, 2013, AbbVie is a new independent biopharmaceutical company composed of Abbott's former proprietary pharmaceutical business, including Norvir®. The six Norvir® patents in question are now owned by AbbVie, as are all of the other patents used for the manufacture of Norvir®. Even though the Request names Abbott Laboratories and Abbott Laboratories participated in the 2003 request for march-in, AbbVie is the current owner of the subject patents and is referred to throughout this determination.

[2] These dates include the FDA's six-month extensions.

early approval of a generic version of a Norvir® formulation through the filing of an Abbreviated New Drug Application (ANDA) for which AbbVie has instituted patent infringement actions under the Hatch-Waxman Act framework. These proceedings are expected to determine the validity and/or infringement of the Subject Patents and the 11 AbbVie patents by proposed generic formulations.

Summary of 2004 NIH March-In Request on Ritonavir

The Subject Patents were first reviewed in response to a 2004 march-in request that asserted a significant price increase initiated by Abbott in 2003 for Norvir® raised issues of practical application, pricing, and health and safety needs. In 2004, after holding a public meeting and receiving written comments, the NIH determined that "it [did] not have information that leads it to believe that the exercise of march-in rights might be warranted . . . within the meaning of 35 U.S.C. § 203." See In the case of Norvir, Manufactured by Abbott Laboratories, Inc. at page 6 (July 29, 2004) ("2004 Norvir® Position Paper").

The current Request relates to the pricing of Norvir® and the same three issues considered and decided in 2004, which were also addressed more generally in the Determination in the Case of Petition of Cell Pro, Inc. (1997), and in the Position Paper in the Case of Xalatan® (2004). (See http://www.ott.nih.gov/policies-reports). Additionally, the Requestors ask that the NIH use its Government use license and/or use the Government's march-in rights to adopt "two general policy rules regarding the commercialization of federally-funded inventions, and apply those rules in the case of six patents claimed for the manufacture and sale of the drug ritonavir under the federal government's authority to grant licenses to third parties in cases of abuses of patent rights."

Statutory Authority and Criteria

The stated policy and objective of the Bayh Dole Act is:

> [T]o use the patent system to promote the utilization of inventions arising from federally supported research or development; . . . to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government, and protect the public against nonuse or unreasonable use of inventions; . . . . (35 U. S.C. § 200).

Toward this goal, the Bayh-Dole Act provides a Federal agency with march-in authority in certain limited circumstances, to ensure that a federally funded invention is available to the public. More specifically:

> With respect to any subject invention in which a small business firm or nonprofit organization has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee, or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible

applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such—

(1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;
(2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;
(3) action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
(4) action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204. (35 U.S.C. § 203(a))

With respect to the use of march-in, the regulations state at 37 C.F.R. § 401.6(b):

> Whenever an agency receives information that it believes might warrant the exercise of march-in rights, before initiating any march-in proceeding, it shall notify the contractor in writing of the information and request informal written or oral comments from the contractor as well as information relevant to the matter.

Based on the available information, a Federal agency can either initiate march-in procedures set forth at 37 C.F.R. § 401.6(c) or notify the contractor that it will not pursue march in rights.[3] Consistent with 35 U.S.C. § 203(a) with respect to any subject invention, a Federal agency is authorized to:

> require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself.

Analysis of the Bayh-Dole Criteria and the Request for NIH to use its March-In Authority for Ritonavir

(1) ***35 U.S. C. § 203 (a)(1) "action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use."***

[3] See 37 C.F.R. § 401.6(b).

The Request asserts that AbbVie failed to achieve practical application of Norvir® because of its high, differential pricing structure between publicly funded and private sector health care plans. As set forth in the NIH's prior march-in determinations, including the NIH 2004 determination for Norvir®, practical application is evidenced by the "manufacture, practice, and operation" of the invention and the invention's "availability to and use by the public . . . ." (2004 Norvir® Position Paper). Norvir® has now been on the market as an FDA approved drug since 1995. As in 2004, Norvir® is used primarily as a booster to increase the effectiveness of protease inhibitors. According to the FDA approved labels, Norvir® is used as a co-administered drug with five other protease inhibitors on the market. The Requestors have provided no information, and no information was identified to suggest, that ritonavir is in short supply either as a standalone drug, co-formulated with AbbVie's lopinavir labeled as Kaletra®, or co-administered with other HIV anti-retroviral medications owned by competing pharmaceutical companies.

In addition, the Request states that on November 18, 2011, Matrix Laboratories received FDA approval for a co-formulated product of ritonavir and atazanavir. The FDA approval was granted as part of the United States President's Emergency Plan for AIDS Relief (PEPFAR) as a co-formulated drug for sale only in Africa and Least Developed Countries. While not available as a co-formulated product in the United States, Europe, or other developed countries, atazanavir is marketed by Bristol Myers Squibb as Reyataz® and can be co-administered with ritonavir. Finally, the Requestors acknowledge that the FDA on August 27, 2012, approved "the Gilead drug, cobicistat, ("COBI"), a protease inhibitor similar to ritonavir...." COBI, as reported in the Request, "is part of a four drug fixed dose combination." The Requestors note that as a result, "a competing 'boosting' drug now exists in cobicistat...." The Requestors also state that even though COBI has received FDA approval, "it must still be evaluated for effectiveness and appropriateness across larger populations than those who participated in clinical trials."

AbbVie's record of manufacture and ritonavir's availability and use around the world demonstrate that AbbVie has achieved practical application of the Subject Patents as required under Bayh-Dole.

(2) *35 U.S. C. § 203 (a)(2) "action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or other licensees*

A second consideration under Bayh-Dole is whether march-in is warranted to alleviate health or safety needs which are not reasonably satisfied by the contractor (35 U.S.C. § 203(a)(2)). Under this prong, the Requestors assert that AbbVie's prices for the private sector health care plans negatively affect public health, correlating Norvir® prices to poor compliance and deferred or interrupted treatment. As noted above, Norvir® is available as a single drug as well as in co-administration or co-formulation with other anti-retroviral drugs. The price for Norvir® has not increased since 2003. In addition, AbbVie states that Norvir® is provided free under its Patient Assistance Program, regardless of income, to those patients who have been prescribed the drug and have no prescription drug insurance coverage. AbbVie states that it provides access to Norvir® at no cost or at reduced prices for eligible patients. (See http://abbvie.com/responsibility/patients-first/patient-assistance-programs.html)

0Responding to a similar argument in 2004, the NIH determined that "Norvir® has been approved by the FDA as safe and effective and is being widely prescribed by physicians for its approved indications." What has changed since 2004 is the availability of new formulations and combination therapies using ritonavir. No new information was provided or identified to suggest AbbVie has failed to "reasonably satisfy" the health and safety need standard of the Bayh-Dole march-in statute.

> **(3) *35 U.S. C. § 203 (a)(3) "actions is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees"***

The third assertion is that action by the NIH is necessary to meet requirements for public use specified by Federal regulations, and such requirements are not reasonably satisfied by the contractor as required under 35 U.S.C. § 203(a)(3). In support, the Request cites the implementing regulations and requirements of the American with Disabilities Act (ADA) and the Patient Protection and Affordable Care Act (PPACA). This Bayh-Dole criterion is applicable when a statute or regulation, e.g., a safety or standards regulation, specifically requires the use of a patented technology, and the patent owner is not willing to grant licenses to third parties required to use it in their products. The cited statutes and implementing regulations do not specify a requirement for public use of Norvir® but rather deal with more general access and insurance issues. The NIH concludes that, these statutes do not apply as a basis for consideration of march-in because the ADA and PPACA do not specifically require the use of ritonavir.

Additional Government Actions Requested for the Rights to use the Subject Patents

> **(1) *Request for use of the Government's use license.***

The Requestors alternatively ask the NIH to utilize its non-exclusive, nontransferable, irrevocable, paid up license to "practice or have practiced for or on behalf of the United States [the] subject invention throughout the world," also referred to as a confirmatory or Government-use license. The statutory basis to use the Government use license is found at 35 U.S.C. §202(c)(4) and states, in part, that a federal funding agency has a nonexclusive license to practice or have practiced for or on behalf of the United States any subject invention throughout the world.[4] The NIH has authority to act directly or by contract to "secure, develop and maintain, distribute, and support the development and maintenance of resources needed for research."[5] As such, the NIH is a research institution not a drug manufacturer. Even if the NIH were to exercise

[4] 25 U.S.C. § 202 recites: With respect to any invention in which the contractor elects rights, the Federal agency shall 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 agreements relating to weapons development and production.

[5] 42 U.S.C. § 284(b)(1)(F).

its Government license for the patents based on Government funded inventions, it would not address the majority of the patents listed for the drug formulations that are not Government-owned. Finally, there is already a statutory mechanism, the Hatch-Waxman Act, to address barriers to generic entry by permitting companies to begin developing generic versions of brand name drugs prior to the expiration of patents. In such circumstances, the generic could be ready to be considered for FDA approval upon the expiration of exclusivity for the brand name drug. As discussed above, Hatch-Waxman proceedings have been instituted for at least three generic companies. The use of the Government's use license in this case is not warranted.

(2) *Request for NIH to Issue Rules Related to Pricing Disparities between the United States and other Developed Counties.*

The Requestors proposed two rules under which the NIH would grant contracts or open licenses for NIH-funded inventions. Rule 1 would establish a rebuttable assumption that U.S. prices of a drug arising from an NIH-funded invention are not reasonable where the U.S. prices for a drug are higher than seven of the ten largest countries, as measured by gross national product (GNP), among the countries determined by the World Bank to be high income or where the U.S. prices are 10 percent higher than reference countries. Absent rebuttal of the presumption, the rule would then permit the Secretary of Health and Human Services ("HHS") to award contracts or grant licenses to competitors to supply the drug to the U.S. consumer. Rule 2 would require the Secretary of HHS to grant licenses to third parties to use the NIH-funded inventions, "subject to the payment of a reasonable royalty and appropriate field of use, if a product based on those patented inventions:

(a) Is a drug, drug formulation, delivery mechanism, medical device, diagnostic or similar invention, and
(b) Is used or is potentially useful to prevent, treat, or diagnose medical conditions or diseases involving humans, and
(c) Its co-formulation, co-administration, or concomitant use with a second product is necessary to effect significant health benefits from the second product, and
(d) The patent holder has refused a reasonable offer for a license."

Under the Requestor's Rule 1, the comparison of prices for drugs that are available in the United States would be to prices of the same drugs that are available in high income countries around the world such as Norway, Italy, France, Canada, Australia, the Netherlands, New Zealand, and the United Kingdom. It is not appropriate to assess the price of one drug out of the context of a country's entire health care delivery and drug pricing/reimbursement system. Moreover, the United States does not have a delivery system like any of these other country comparators.

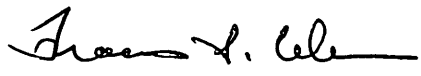
With respect to Requestors' Rules 1 and 2, the statutory authority for the NIH to consider using its march-in authority, as set out above, is directed to "any subject invention" if one of the four Bayh-Dole march-in criteria are met. We do not think that the AbbVie pricing policies and pricing disparities between the United States and other countries trigger any of the four Bayh-Dole march-in criteria.

Conclusion

The NIH is sensitive to the impact of the pricing of drugs and their availability to patients. As in 2004, when similar pricing and availability issues were raised and discussed at public hearings, the NIH's role in the present case is limited to compliance with the Bayh-Dole Act, including its march-in criteria, outlined and discussed in detail (above).

Drug pricing and patient access are broad and challenging issues in the United States. The NIH continues to agree with the public testimony in 2004 that the extraordinary remedy of march-in is not an appropriate means of controlling prices of drugs broadly available to physicians and patients.

In conclusion, as set forth in this determination, the information and justification provided in the Request, as well as publicly available information, do not support re-consideration of the NIH determination to decline to initiate a march-in proceeding for the Subject Patents used by AbbVie in the production of Norvir® and other combination products. As stated in previous march-in considerations, the general issue of drug pricing is appropriately addressed through legislative and other remedies, not through the use of the NIH's march-in authorities. The exercise of the Government's use license to the Subject Patents is not appropriate in this case. Finally, the NIH declines to set the rules proposed by the Requestors directing the initiation of such proceedings based on certain price disparities between the United States and other developed countries.



Francis S. Collins, M.D., Ph.D.
Director, NIH

11/1/13

Date

NATIONAL INSTITUTES OF HEALTH (NIH) QUESTIONS ON MARCH-IN REQUEST FOR RITNOVIR

FOR REQUESTERS

KNOWLEDGE ECONOLOGY INTERNATIONAL, THE AMERICAN MEDICAL STUDENTS ASSOCIATION, THE U.S. PUBLIC INTEREST RESEARCH GROUP and THE UNIVERSITIES ALLIED FOR ESSENTIAL MEDICINES

In considering the march-in request on six subject inventions identified in the march-in request for ritonavir, the NIH has the following six questions.

1. Are you aware of any supply availability issues with respect to ritonavir, alone or as part of a combination drug that were not included in your march-in request? _____Yes _____No

   If yes, please provide supporting information.

2. Are you aware of any patents not identified in your march-in request that are necessary for the administration of ritonavir? _____Yes _____No

   If yes, please provide supporting information.

3. Apart from the asserted status that all of the identified patents are directed to a subject invention, please explain your rationale for each patent's inclusion in your request.

4. In your march-in request you assert that march-in action by the NIH is necessary under the implementing regulations and requirements of the American with Disabilities Act (ADA) and the Patient Protection and Affordable Care Act (PPACA). Please identify the specific implementing regulations and requirements for the ADA and the PPACA that are directed to ritonavir.

5. Was the differentiation in pricing for ritonavir that was provided in the march-in request for ritonavir by itself or for ritonavir in combination with other drugs?

6. Is there any supplemental information that you would like to submit to the NIH that was not included in your original march-in request? _____Yes _____No

   If yes, please provide your supplemental information.

INFORMATION PAPER—SUPPLEMENT & DISCUSSION
March-in Rights Request by KEI to NIH and DoD Pertaining to Xtandi®

APPENDIX D
Interim Response to KEI, February 24, 2016
And
Copies of electronic OTSG and USAMRMC Taskers directing a response to the KEI request be prepared on behalf of the Secretary of Defense
And
Request of Knowledge Ecology International (KEI) and The Union for Affordable Cancer Treatment (UACT) for the government to exercise march-in rights

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DEPARTMENT OF THE ARMY
OFFICE OF THE SURGEON GENERAL
7700 ARLINGTON BOULEVARD
FALLS CHURCH, VA 22042-5140

REPLY TO
ATTENTION OF

FEB 24 2016

Office of The Surgeon General

Mr. Andrew S. Goldman
Knowledge Ecology International
1621 Connecticut Avenue, Suite 500
Washington, DC 20009

Dear Mr. Goldman:

I have been asked to respond on behalf of the Secretary of Defense Ashton Carter to your January 14, 2016 letter concerning your request for the United States Federal Government to exercise its march-in rights pursuant to 35 U.S.C. § 203 to patented inventions made by the University of California with funding from the National Institutes of Health (NIH) and the Department of Defense (DoD).

The United States Army Medical Research and Materiel Command is working to address the important issues raised in your letter. Since this request was concurrently made to multiple federal agencies, we are coordinating a formal response between both the Department of Health and Human Services/NIH and the DoD. We anticipate a final decision no later than June 1, 2016, and will provide you a follow-on response at that time.

The point of contact for this letter is Major Nancy Heath, (301) 619-7111, or email nancy.o.heath.mil@mail.mil.

Sincerely,

Uldric L. Fiore, Jr.
Chief of Staff

Arwine, Elizabeth A CIV USARMY MEDCOM USAMRMC (US)

From: Rogers, Sandra J CIV USARMY MEDCOM USAMRMC (US)
Sent: Tuesday, February 09, 2016 5:24 PM
To: Brinkley, Carlton C COL USARMY MEDCOM CDMRP (US); Buchanan, Julie B CIV USARMY MEDCOM CDMRP (US); Salzer, Wanda L Col USAF USARMY MEDCOM CDMRP (US); Smith, Shayla M CTR USARMY MEDCOM CDMRP (US); Blount, Michael T CIV USARMY MEDCOM USAMRAA (US); Garver, E Kim MRS CIV USARMY MEDCOM USAMRAA (US); Gonzalez, Leah E CIV USARMY MEDCOM USAMRAA (US); Hovermale, Laurie E CIV USARMY MEDCOM USAMRAA (US); Keen, Charity L CIV USARMY MEDCOM USAMRAA (US); Martin, Brian E CIV USARMY MEDCOM USAMRAA (US)
Cc: Lopezduke, Alejandro COL USARMY MEDCOM USAMRMC (US); Donahue, Sarah L CIV USARMY MEDCOM USAMRMC (US); Smith, Christina L CIV USARMY MEDCOM USAMRMC (US); Heath, Nancy O MAJ USARMY MEDCOM USAMRMC (US)
Subject: MRMC TASKER 1602042//OSD RED TOP: U.S. Federal Government Use its Rights in Patents for the Prostate Cancer Drug (Enzalutamide) (UNCLASSIFIED)
Attachments: 1602181909_1602181909.pdf

Importance: High

Classification: UNCLASSIFIED
Caveats: NONE

MRMC TASKING

Control No.: 1602042 HQDA Number: 160218909 Unit: HQ-MRMC FOIA/Congress/Privacy:

Date Received: 09-FEB-16
Suspense Date: 16 FEB-16
Org Susp Date:

Tasking Office: MCMR-SGS
Action Office: MCMR-CD
POC: Col Salzer

(X) Immediate Action () Reply Direct () Prepare Reply () Signature of:

SUBJECT: OSD RED TOP: Request the U.S. Federal Government Use its Rights in Patents for the Prostate Cancer Drug (Enzalutamide)

PURPOSE: Request for Information

ACCOUNTABLE OFFICE: MCMR-CD
LEAD: CDMRP
ASSIST: USAMRAA

COORDINATING INSTRUCTIONS:

Prepare a GO/SES level response on behalf of the Secretary of Defense (SD). First sentence of your response should read, "I have been asked to respond on behalf of Secretary of Defense Ashton Carter to your January 14, 2016 letter concerning. . ."

Response is due to OTSG NLT 17 Feb, but needs review by CoS prior to submission. OTSG will send to General Counsel (legal review) and return to MRMC for signature.

Arwine, Elizabeth A CIV USARMY MEDCOM USAMRMC (US)

From: Davis, Shedrick C (Shed) CIV USARMY HQDA OTSG (US)
Sent: Tuesday, February 09, 2016 2:12 PM
To: Layo, Gennaro Villareiz CPT USARMY MEDCOM HQ (US); USARMY NCR HQDA OTSG Mailbox MEDCOM OPS CENTER; Lopezduke, Alejandro COL USARMY MEDCOM USAMRMC (US); Donahue, Sarah L CIV USARMY MEDCOM USAMRMC (US); Heath, Nancy O MAJ USARMY MEDCOM USAMRMC (US); Rogers, Sandra J CIV USARMY MEDCOM USAMRMC (US); Smith, Christina L CIV USARMY MEDCOM USAMRMC (US)
Cc: USARMY NCR HQDA OTSG List OTSG SGS
Subject: 1602181909: OSD RED TOP: Request the U.S. Federal Government Use its Rights in Patents for the Prostate Cancer Drug (Enzalutamide) (UNCLASSIFIED)
Attachments: 1602181909_1602181909.pdf

Importance: High

Follow Up Flag: Follow up
Due By: Wednesday, February 17, 2016 11:00 AM
Flag Status: Flagged

Classification: UNCLASSIFIED
Caveats: NONE

Team G-33,

Please task MRMC to prepare a GO/SES level response on behalf of the Secretary of Defense (SD). First sentence of your response should read, "I have been asked to respond on behalf of Secretary of Defense Ashton Carter to your January 14, 2016 letter concerning. . ."

By 17 Feb 16, submit the draft document (Word format) to the OTSG SGS, usarmy.ncr.hqda-otsg.list.otsg-sgs@mail.mil, who will obtain the requisite Office of the General Counsel (legal) review, and return it to MRMC for signature and dispatch.

Provide a copy of the signed response to the OTSG SGS, to close this task.

//////////////
The task information reads:

Attached correspondence, addressed to the Secretary of Defense (SD), is assigned to OTSG for Direct Reply on behalf of the SD. First sentence of your response should read, "I have been asked to respond on behalf of Secretary of Defense Ashton Carter to your January 14, 2016 letter concerning. . ." Your proposed response must be coordinated with OGC (POC: Ms. Joyce Maple, SACO, 693-3018) and with other Army Staff Agencies as appropriate, and must be signed at a level no lower than General Officer or SES. Provide a copy of your signed/dated response to the ECC Tasking Official.

If you are unable to meet the suspense and require an extension, then you must prepare an interim reply for your Principal's or Principal Deputy's signature. First sentence of your interim reply should read, "I have been asked to provide an interim reply on behalf of the Secretary of Defense to your January 14, 2016 letter concerning. . ." The interim reply must include the reason for the delay and when a final reply is anticipated. Mail the original and provide a copy to the ECC Tasking Official who will then prepare and submit an SD Form 391 (Request for Extension) to OSD Correspondence Management Division.

//////////////

Army Strong!

Shed

Serving to Heal.....Honored to Serve

Shedrick C. Davis | Deputy Secretary of the General Staff, Office of The Surgeon General | 7700 Arlington Blvd | Suite 4SW112 | Falls Church, VA 22042 | Office: 703-681-6572| Blackberry: 703-919-8472 | NIPR e-mail: shedrick.c.davis.civ@mail.mil | SIPR e-mail: usarmy.ncr.hqda-otsg.mbx.medcom-operations-center@mail.smil.mil

Classification: UNCLASSIFIED
Caveats: NONE

If you are unable to meet the suspense and require an extension, then you must prepare an interim reply for your Principal's or Principal Deputy's signature. First sentence of your interim reply should read, "I have been asked to provide an interim reply on behalf of the Secretary of Defense to your January 14, 2016 letter concerning. . ." The interim reply must include the reason for the delay and when a final reply is anticipated. Mail the original and provide a copy to the ECC Tasking Official who will then prepare and submit an SD Form 391 (Request for Extension) to OSD Correspondence Management Division.

TASKING POC: MAJ Nancy Heath 301 619-7111 or nancy.o.heath.mil@mail.mil.

v/r
Sandra

Sandra J. Rogers
Staff Action Officer

US Army Medical Research and Materiel Command
ATTN: MCMR-SG
810 Schreider Street
Fort Detrick, MD 21702-5012

Office - 301.619.7118
Fax - 301.619.2982
Email - sandra.j.rogers28.civ@mail.mil

-----Original Message-----
From: Davis, Shedrick C (Shed) CIV USARMY HQDA OTSG (US)
Sent: Tuesday, February 09, 2016 2:12 PM
To: Layo, Gennaro Villareiz CPT USARMY MEDCOM HQ (US); USARMY NCR HQDA OTSG Mailbox MEDCOM OPS CENTER; Lopezduke, Alejandro COL USARMY MEDCOM USAMRMC (US); Donahue, Sarah L CIV USARMY MEDCOM USAMRMC (US); Heath, Nancy O MAJ USARMY MEDCOM USAMRMC (US); Rogers, Sandra J CIV USARMY MEDCOM USAMRMC (US); Smith, Christina L CIV USARMY MEDCOM USAMRMC (US)
Cc: USARMY NCR HQDA OTSG List OTSG SGS
Subject: 1602181909: OSD RED TOP: Request the U.S. Federal Government Use its Rights in Patents for the Prostate Cancer Drug (Enzalutamide) (UNCLASSIFIED)
Importance: High

Classification: UNCLASSIFIED
Caveats: NONE

Team G-33,

Fri 2/5/2016 3:28 PM

Service Account, CRM Setup <donotreply.crmsetup@mail.mil>

SA - Request Type: General Incoming, OSD000609-16, CMD Tasking, OPR: SA, Suspense Date: 02/26/16

To USARMY Pentagon HQDA OAA Mailbox CAPB BR of EXEC COMMS and CONTROL

Action Item

Notification Type: New ACTION task has been assigned

Importance: High

Control Number: **OSD000609-16**
Action ID: CMD000924-16
Tasker ID: CATMS20012016CADNFB
From: **KNOWLEDGE ECOLOGY INTERNATIONAL**
To: **SECDEF**
Task Subject: USE RIGHTS FOR THE PROSTATE CANCER DRUG ENZALUTAMIDE

Request Type: General Incoming
Date of Receipt: 01/20/16
OPR: SA
Response Type: RD-Reply Direct
OCRs: UPR-ASD-HA
CCs: ExecSec UPR DHA-PI ES-DSD
Task Instructions: NONE
Task Suspense Date: 02/26/16
Distribution: RLB ES UPR

KEI
KNOWLEDGE ECOLOGY INTERNATIONAL

UACT
UNION FOR AFFORDABLE CANCER TREATMENT

January 14, 2016

The Honorable Sylvia Mary Mathews Burwell
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201
Via: Sylvia.Burwell@hhs.gov

Francis Collins, M.D., Ph.D.
Director
National Institutes of Health
9000 Rockville Pike
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The Honorable Ashton Carter
Secretary
Department of Defense
1400 Defense Pentagon
Washington, D.C. 20301-1400
Via: ashton.b.carter.civ@mail.mil; whs.pentagon.esd.mbx.cmd-correspondence@mail.mil

Dear Secretaries Burwell and Carter and Director Collins:

Introduction

Knowledge Ecology International is a non-profit organization with offices in Washington, DC and Geneva, Switzerland. The Union for Affordable Cancer Treatment (UACT) is a non-profit cancer patient group. More about each group is available on their respective web pages: http://keionline.org and http://cancerunion.org.

This letter is a request that the U.S. federal government use its rights in patents for the prostate cancer drug (enzalutamide), marketed under the brand name of Xtandi by Japan-based Astellas

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Pharma. This is a product that has an average wholesale price (AWP) of $129,269 per year,[1] and which is far more expensive in the United States than in other countries.

Specifically, we ask the Department of Health and Human Services (DHHS), National Institutes of Health (NIH), and/or the Department of Defense (DoD) to use its royalty-free rights in the relevant patents, or to grant this request for march-in rights. The relevant patents include, but are not limited to, the three patents listed in the FDA Orange Book for Xtandi (7709517, 8183274, and 9126941), all of which were granted to the Regents of the University of California, a public institution. All three inventions were made with the support of the United States government under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129.

The statutory basis for the request includes 35 U.S.C. § 202(c)(4), for the royalty-free rights in the patents, and 35 U.S.C. § 203(a)(1-3), noting that the term "practical application" of an invention in 35 U.S.C. § 203(a)(1) is defined by 35 U.S.C. § 201(f) to require that the benefits of an invention are "available to the public on reasonable terms." It is our contention that the pricing of Xtandi is excessive and discriminatory as regards U.S. citizens.

Xtandi is an expensive drug everywhere, indeed so expensive that access is extremely limited in many countries. But, based upon our research, the prices in the United States are far higher than any other country in the world, despite the fact that the critical research benefited from U.S. taxpayer funded grants from the NIH and DoD.

More generally, we ask the U.S. federal government to adopt the policy that the federal government will use its royalty free rights, or grant licenses under federal march-in rights, when prices in the United States are excessive, and/or higher than they are in high income foreign countries, and to apply that policy in this case for patents on enzalutamide.

Such an approach would be in accord with the policy and objective of the Bayh-Dole Act as stated in 35 U.S.C. § 200, to "protect the public against nonuse ***and*** the unreasonable use of inventions..." [emphasis added].

The analysis in this document includes the following topics and tables.

1. Prices for Xtandi are much higher in the United States than in other high income countries,
2. The high prices for Xtandi create hardships on U.S. patients,
3. The cost of Xtandi to Medicare,
4. Astellas and Medivation projections of Xtandi sales,
5. The role of the U.S. government in funding research on Xtandi,
6. Enzalutamide is an important cancer drug,

[1] $88.48 per 40 mg unit, four times a day, 365.25 days per year.

7. The University of California at Los Angeles (UCLA) interest in the patents,
8. Orange Book patent claims for Xtandi,
9. Non-patent exclusivity,
10. Generic supply,
11. Xtandi R&D investments through the 2012 approval for the lead indication,
12. Clinical trials on enzalutamide, including trials subsequent to 2012 NDA,
13. Licensing terms, including reasonable royalty,
14. Funding of research to further develop enzalutamide,
15. Standard for determining the Xtandi prices are unreasonable.
16. Conclusion

Tables:

1. Prices for Xtandi are much higher in the United States than in other high income countries.

Xtandi is sold in 40 mg capsules or tablets, and is prescribed for daily use for as long as the drug continues to be effective and tolerated. The typical dose of Xtandi for the treatment of prostate cancer is 4 x 40 mg per day.

The U.S. average wholesale price (AWP), according to *Redbook* data published April 2015, was $88.48 per 40 milligram capsule, which amounts to $353.92 per day, or $129,269.28 per year (365.25 day year). The average price for Medicare in 2014 was $69.41 per capsule,[2] or $101,408.01 for a full year's treatment.

Astellas Pharma, a Japanese-owned drug company, is exploiting the weak response of the United States to excessive pricing of drugs, and is charging U.S. consumers and third-party payers roughly two to four times as much as the prices in other high income countries. For example, in Norway, a country with a per capita income of $103,630 in 2014, the price is $32.43 per 40 mg capsule, just 47 percent of the US Medicare price, and 39 percent of the Redbook AWP for the U.S. private sector.

In Australia, the price is $23.46 per capsule, roughly one third of the U.S. Medicare price. In Quebec, Canada, the price is $20.12 per capsule, just 29 percent of the U.S. Medicare price, and 24 percent of the U.S. AWP.

Astellas Pharma, the company that holds the rights to market Xtandi, is a member of the Japan-based Mitsubishi UFJ Financial Group (MUFJ) keiretsu. Note that in Japan, the price per 40 mg unit of this UCLA-invented drug is $26.37, less than one-third of the U.S. AWP.

In our opinion, it is unreasonable, and indeed outrageous, that prices are higher in the United States than in foreign countries, for a drug invented at UCLA using federal government grants.

[2] See Centers for Medicare and Medicaid Services Medicare Drug Spending Dashboard, available at: https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Dashboard/Medicare-Drug-Spending/Drug_Spending_Dashboard.html

Table 1.1: Prices for Xtandi 40mg capsule/tabs, in the United States and 13 high income countries.

Country	Price per unit, national currency	EX Rate (Jan. 6, 2016)	Price per unit, USD	Percent of 2015 AWP	2014, GNI Per Capita, Atlas Method, USD
USA, April 2015 AWP	88.48 USD	1	$88.48	100%	$55,200
USA, 2014 Medicare	69.41 USD	1	$69.41	78%	$55,200
Australia	33.04 AUD	0.71	$23.46	27%	$64,540
Belgium	29.15 EUR	1.08	$31.48	36%	$47,260
Canada, Quebec	28.35 CAN	0.71	$20.12	23%	$51,630
France	24.75 EUR	1.08	$26.73	30%	$42,960
Germany, pubic insurance	34.19 EUR	1.08	$36.93	42%	$47,640
Italy, procurement price	24.08 EUR	1.08	$26.01	29%	$34,270
Japan	3,138.80 Yen	0.0084	$26.37	30%	$42,000
The Netherlands	29.15 EUR	1.08	$31.48	36%	$51,890
Norway	294.78 NOK	0.11	$32.43	37%	$103,630
Spain	29.98 EUR	1.08	$32.38	37%	$29,440
Sweden	224.705 SEK	.12	$26.96	30%	$61,610
Switzerland	35.82 CHF	0.99	$35.46	40%	$88,120*
UK	24.42 GBP	1.46	$35.65	40%	$43,430

*Only 2013 was available for Switzerland.

2. The high prices for Xtandi create hardships on U.S. patients.

Recent clinical studies indicate that treatment delays may be harmful to patients. While the drug is relatively new, clinicians are now recommending that doctors prescribe Xtandi before prescribing other drugs that target the same androgen axis, to prevent the development of drug resistance.

Since 2014, the FDA has expanded the use of Xtandi to first line treatment for metastatic castration-resistant prostate cancer (mCRPC) based on the phase III PREVAIL clinical trial. Currently Xtandi (FDA approved, 2012), Zytiga (FDA approved, 2011), and Taxotere (FDA approved, 2004) are the top three prescribed drugs in first line metastatic CRPC treatment.[3] However, using Taxotere before Xtandi has been shown to decrease the effectiveness of Xtandi

[3] Flaig TW *et al.* Treatment evolution for metastatic castration-resistant prostate cancer with recent introduction of novel agents: retrospective analysis of real-world data.Cancer Med. 2015 Dec 29.

by a median overall survival of 15.8 months.[4] Zytiga and Xtandi are both oral therapeutics that target the androgen signaling axis, and although prospective head-to-head comparison clinical trials are still ongoing, retrospective analysis data have indicated that there is a clear clinical cross-resistance between the two drugs.[5] In fact, in a study conducted by Schrader *et al.*, it was reported that 48.6% of patients who previously took Zytiga and Taxotere were completely resistant to Xtandi.[6] Based on the susceptibilities of individual patients, oncologists may want to prescribe Xtandi over Zytiga for its toxicity profile or to patients who cannot tolerate low-dose steroids.[6] If insurance companies were to restrict the use of Xtandi in favor of Zytiga or Taxotere, it would likely prove detrimental to the survival of those patients.

As a direct result of the high price charged by Astellas, U.S. insurance companies and other third party payers have predictably restricted access to Xtandi. Insurers discourage prescribers by requiring restrictive prior authorizations that prevent use of Xtandi before a patient has failed other treatments. UnitedHealthcare, for example, noted in a memorandum that "Supply limits and/or Step Therapy may be in place."[7]

Table 2.1 shows information from insurance formularies from across the United States, including whether prior authorization is required and what tier the insurer has placed the drug on in their formulary. Higher tiers generally indicate higher copays and restricted access, and insurers generally use 3- or 5-tier systems. (See the next section for a discussion of Medicare spending on Xtandi.)

Table 2.1: Prior authorization requirements and formulary tiers for seven insurers providing reimbursements for Xtandi/enzalutamide.

Payer	Formulary	Tier	Prior Authorization
Rocky Mountain Health Plans	Good Health Formulary[8]	3	Yes
Kaiser Permanente	Exchange Formulary[9]	4	No
Aetna	Three Tier Open Individual Formulary[10]	3	Yes: step therapy
Cigna	Prescription Drug List[11]	5	Yes

[4] Crawford ED *et al.* Treating Patients with Metastatic Castration Resistant Prostate Cancer: A Comprehensive Review of Available Therapies. J Urol. 2015 Dec;194(6):1537-47.
[5] Zhang T. *et al.* Enzalutamide versus abiraterone acetate for the treatment of men with metastatic castration-resistantprostate cancer. Expert Opin Pharmacother. 2015 Mar;16(4):473-85.
[6] Schrader AJ *et al.* Enzalutamide in castration-resistant prostate cancer patients progressing after docetaxel and abiraterone. Eur Urol. 2014 Jan;65(1):30-6.
[7] https://goo.gl/PFtBkf
[8] http://www.rmhp.org/docs/default-source/resources/good_health_formulary.pdf?sfvrsn=10
[9] https://healthy.kaiserpermanente.org/static/health/pdfs/formulary/mid/mid_exchange_formulary.pdf
[10] https://goo.gl/Z31uvf
[11] http://www.cigna.com/individuals-families/prescription-drug-list?consumerID=cigna&indicator=IFP

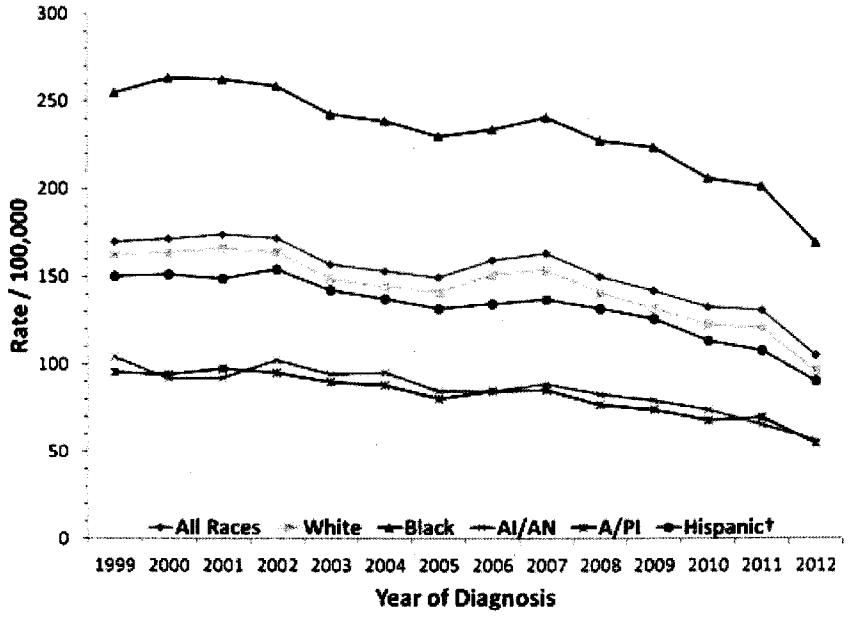
BlueCross BlueShield	Federal Employee Program[12]	4	Yes
Montana Health CO-OP	2015 CoventryOne Prescription Drug List[13]	4	Yes
Anthem BlueCross	Select Drug List 4-Tier Formulary[14]	4	Yes

There is also a racial disparity in the incidence, mortality, and treatment of prostate cancer. NIH and DoD should be concerned that the high price of Xtandi may be contributing to systemic racial discrimination in medical care in the United States. Data collected by the Centers for Disease Control shows that African American men have higher incidence and mortality rates than all other populations. Around two times more African American men have prostate cancer than white men (graph 2.1), and around 2.5 times more African American men die from the disease compared to white men (graph 2.2).[15] In addition, African American men are more likely to have a more aggressive form of prostate cancer. Researchers believe that this racial disparity is the result of sociobiological factors that affect people of African descent.

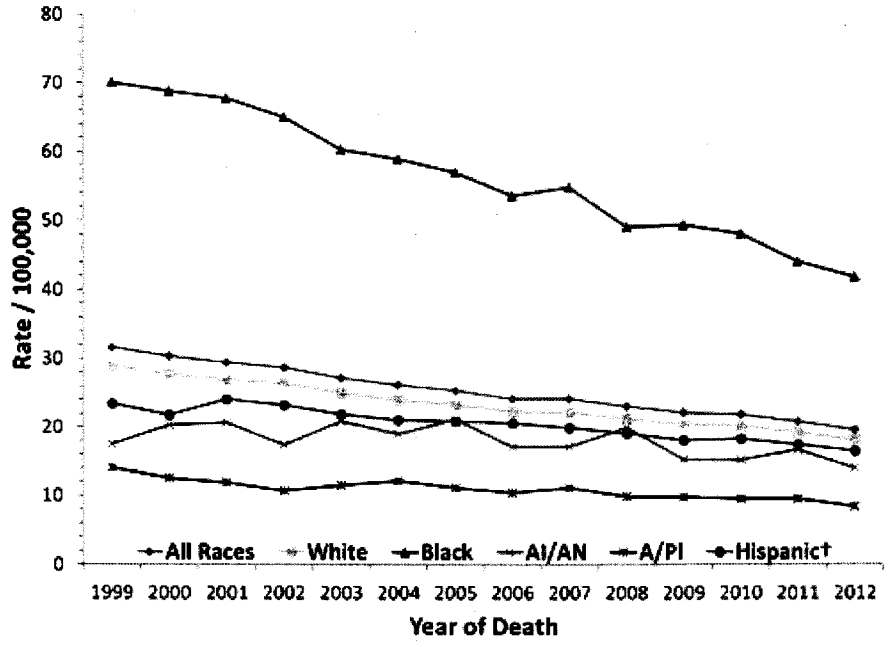
Beyond sociobiological effects on incidence, mortality, and severity of prostate cancer, African American men face systemic discrimination that affects their access to and quality of treatment. One recent study has found that African-American men on Medicare being treated for nonmetastatic prostate cancer experienced treatment delays, and had more postoperative emergency room visits and readmissions compared to white men.[16] "This might be a form of institutional discrimination based on socioeconomic status resulting in racially disparate outcomes," wrote Dr. Otis Brawley, chief medical officer of the American Cancer Society, commenting on that study.[17]

[12] https://media.fepblue.org/-/media/PDFs/Brochures/FEP_AbbreviatedFormulary_100715.pdf
[13] http://www.mhc.coop/wp-content/uploads/docs/MHC-Covered-Drugs.pdf
[14] https://fm.formularynavigator.com/MemberPages/pdf/2016CASelectHIX_7006_Full_1576.pdf
[15] See CDC, "Prostate Cancer Rates by Race and Ethnicity," available at http://www.cdc.gov/cancer/prostate/statistics/race.htm.
[16] Schmid M et al. Racial differences in the surgical care of Medicare beneficiaries with localized prostate cancer. JAMA Onc. 2015 Oct. doi:10.1001/jamaoncol.2015.3384
[17] Brawley OW. The meaning of race in prostate cancer treatment. JAMA Onc. 2015 Oct. doi:10.1001/jamaoncol.2015.3615

Graph 2.1: "Prostate Cancer Incidence Rates by Race and Ethnicity, U.S., 1999–2012"[18]



Graph 2.2: "Prostate Cancer Death Rates by Race and Ethnicity, U.S., 1999–2012"[19]



[18] See CDC, "Prostate Cancer Rates by Race and Ethnicity," available at http://www.cdc.gov/cancer/prostate/statistics/race.htm, which contains additional notes on the data/methodologies used to create graphs 1 and 2 in this letter.
[19] See CDC, "Prostate Cancer Rates by Race and Ethnicity," available at http://www.cdc.gov/cancer/prostate/statistics/race.htm.

Veterans who served in Vietnam and the Korean demilitarized zone, who may have been exposed to Agent Orange, are also at higher risk for more aggressive forms of prostate cancer, according to a study conducted by the Department of Veterans Affairs and Oregon Health and Science University.[20]

3. The cost of Xtandi to Medicare.

According to the Centers for Medicare and Medicaid Services, total Medicare spending on Xtandi grew dramatically from under $35 million in 2012 to nearly $447 million in 2014. The increase in outlays from 2013 to 2014 was 93 percent. Part of that growth was due to a 9 percent price increase from 2012 to 2014, a period in which the Consumer Price Index (CPI) grew a mere 3 percent. There was also a steep increase in the number of patients, from 2,143 in 2012, to 7,329 in 2013, and 11,800 in 2014.

Table 3.1: Xtandi/Enzalutamide/Medicare Part D, 2012 to 2014

Year	Total Spending	Beneficiary Cost Share	Beneficiary Count	Total Annual Spending Per User	Avg Cost Per Unit	Claim Count
2012	$34,898,755.93	$2,359,870.77	2,143	$16,285.00	$63.72	4,519
2013	$231,503,731.19	$13,276,790.11	7,329	$31,587.36	$64.85	29,572
2014	$447,311,084.46	$24,567,059.52	11,800	$37,907.72	$69.41	53,980

For prostate cancer, the average age at diagnosis is 66 years. At present, approximately 14 percent of the population is 65 or over, but in five years this will increase to 16 percent, and by 2030 is expected to exceed 19 percent. As the population continues to age, we can reasonably predict that Medicare expenditures on Xtandi will continue to climb.

4. Astellas and Medivation projections of Xtandi sales.

According to the Astellas 2015 annual report,[21] the United States market will represent 61.16 percent of all global sales of Xtandi, for the fiscal year ending March 31, 2016. Note that in the U.S., sales of Xtandi increased 77 percent from FY2013 (April 1, 2013 to March 31, 2014) to FY2014 (April 1, 2014 to March 31, 2015), and are projected to increase 51 percent from FY2014 to FY2015. This is a steep increase in use for a costly drug.

[20] Ansbaugh N et al. Agent Orange as a risk factor for high-grade prostate cancer. Cancer. 2013 Jul; 119(13):2399-2404. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4090241/.
[21] Astellas Annual Report 2015, available at https://www.astellas.com/en/ir/library/pdf/2015AR_en_1007-2.pdf.

Table 4.1: Actual and projected Xtandi sales, FY2013 to FY2015[22]

Country/Region	FY2013	FY2014	FY2015 (projected)
Japan		$125,147,037	$193,179,990
U.S.	$441,000,000	$779,000,000	$1,180,000,000
Percent Change in Sales, U.S.		77%	51%
Other Americas	$8,000,000	$24,000,000	$35,000,000
Europe, Middle East, and Africa	$75,255,950	$259,095,485	$505,289,950
Asia/Oceania		$5,039,478	$15,958,347
Global	$524,255,950	$1,192,282,001	$1,929,428,288
Percent U.S. Sales to Global	84%	65%	61%

Astellas developed Xtandi in collaboration with Medivation. The Medivation 2015 SEC 10-K filing reports actual Xtandi sales in the United States for calendar years 2012 to 2014.

Medicare's share of sales have increased sharply since 2012. In 2014 they accounted for 66 percent of Xtandi's overall U.S. sales, and 42 percent of global sales. The United States is the largest spender on Xtandi, and most of that money is coming from taxpayers and the insurance payments of aging Americans.

Table 4.2: Actual Xtandi sales, U.S., 2012 to 2014[23]

Calendar Year	2012	2013	2014
Xtandi U.S. Sales	$71,504,000	$392,415,000	$679,805,000
Percent Change in U.S. Sales		449%[24]	73%
Xtandi Non-U.S. Sales		$52,800,000[25]	$381,100,000
Medicare Total Spending	$34,898,755.93	$231,503,731.19	$447,311,084.46
Medicare Share of U.S. Sales	49%	59%	66%
Medicare Share of Global Sales	49%	52%	42%

[22] Astellas defines its fiscal year as April 1 to March 31, beginning in the year indicated. Monetary amounts were converted to USD from regional currencies, as necessary.
[23] Medivation 2015 Form 10-K, available at http://files.shareholder.com/downloads/MDV/1291225255x0xS1193125-15-62576/1011835/filing.pdf.
[24] Note: Xtandi was approved on August 12, 2012, which accounts for low sales.
[25] Note: Xtandi was first approved outside the U.S. in June 2013, which accounts for low sales.

5. The role of the U.S. government in funding research on Xtandi.

As noted above, all three patents in the Orange Book for Xtandi disclose the fact that the inventions were made with the support of the United States government under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129.

In addition to the grants listed in these three patents, the development of this drug benefited from additional research subsidies from the federal government and charitable foundations, including grants for clinical testing of the drug. For example, a 2009 paper in *Science* reporting on the development of MDV3100 (the development name for enzalutamide)[26] acknowledged funding from the Prostate Cancer Foundation, the National Cancer Institute, the DOD PC051382 Prostate Cancer Research Program Clinical Consortium Award, and support from the Charles H. Revson Foundation. Likewise, a 2010 paper in *the Lancet* reporting on a critical Phase 1-2 trial acknowledges the financial support of Medivation, but also the Prostate Cancer Foundation, National Cancer Institute, the Howard Hughes Medical Institute, Doris Duke Charitable Foundation, and Department of Defense Prostate Cancer Clinical Trials Consortium.[27]

6. Enzalutamide is an important cancer drug.

In the United States today there are nearly 3 million men suffering from prostate cancer, with over 220,000 new cases in 2015 alone, and 27,540 deaths. It is the third most common form of cancer in the U.S.

When patients are treated early and tumors are localized, the prognosis is often favorable. However, some patients will relapse, leading in nearly all cases to castration resistant prostate cancer (CRPC). At the CRPC stage, the disease is no longer responsive to androgen deprivation therapy (ADT), thus limiting the available treatment options with a greater disease burden. Access to Xtandi/enzalutamide, a non-steroidal second generation androgen receptor agonist, becomes critical to extending the life of the patient, and allowing patients to live an improved quality of life.

There are currently six treatments being used to treat CRPC. Xtandi/enzalutamide has several advantages over the other treatments. Four of the treatments are invasive and require I.V. administration, leukapheresis, or the use of radiopharmaceuticals. Xtandi/enzalutamide and Zytiga are the only daily oral tablets. However Xtandi/enzalutamide's pill burden is lighter since

[26] Tran C *et al.* Development of a second-generation antiandrogen for treatment of advanced prostate cancer. Science. 2009. May. 8;324(5928):787-90.

[27] Scher HI *et al.* Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1-2 study, Lancet. 2010 Apr 24;375(9724):1437-46. doi: 10.1016/S0140-6736(10)60172-9.

it does not need to be taken in combination with prednisone. As such, Xtandi/enzalutamide is well tolerated and has more favorable toxicity profile.

Quality of life was also more frequently improved and median time to deterioration was significantly longer with Xtandi/enzalutamide compared to placebo, as reported by patients in functional assessment questionnaires administered during clinical trials.[28]

With recent and ongoing clinical trials reporting better prostate cancer control when Xtandi/enzalutamide is used in chemotherapy naive CRPC cases or in combination with other agents, it is expected that this drug will soon be prescribed to wider subset of patients.[29,30,31] In fact experts say that in the next 3 years all CRPC will progress to Xtandi or Zytiga.[32]

Xtandi/enzalutamide is also being tested for other types of cancer, including clinical trials for breast cancer (triple negative[33], her2+[34]), hepatocellular carcinoma[35], bladder cancer[36], ovarian or fallopian tube cancer,[37] pancreatic cancer[38] and Mantle Cell Lymphoma[39].

7. The University of California at Los Angeles (UCLA) interest in the patents

According to the Medivation's 2014 10-K report to the Securities and Exchange Commission (SEC), the University of California at Los Angeles (UCLA) licensed the patents for the drug to Medivation in exchange for an annual payment of $2.8 million, a 4 percent royalty on global net sales of the drug, and in addition a 10 percent share of Medivation's sublicensing income

[28] Rodriguez-Vida A *et al.* Enzalutamide for the treatment of metastatic castration-resistant prostate cancer.Drug Des Devel Ther. 2015 Jun 29;9

[29] Scher HI *et al.* Increased survival with enzalutamide in prostate cancer after chemotherapy. N Engl J Med. 2012 Sep.

[30] Loriot Y *et al.* Effect of enzalutamide on health-related quality of life, pain, and skeletal-related events in asymptomatic and minimally symptomatic, chemotherapy-naive patients with metastatic castration-resistant prostate cancer (PREVAIL): results from a randomised, phase 3 trial. Lancet Oncol. 2015 May.

[31] STRIDE results presented at 2015 American Society of Clinical Oncology annual meeting, Clinicaltirals.gov:NCT01981122.

[32] Zhang T. *et al.* Enzalutamide versus abiraterone acetate for the treatment of men with metastatic castration-resistantprostate cancer. Expert Opin Pharmacother. 2015 Mar;16(4):473-85.

[33] NCT01889238.

[34] NCT02091960.

[35] NCT02528643, NCT02642913. Hepatocellular carcinoma (HCC, also called malignant hepatoma) is the most common type of liver cancer, often secondary to a viral hepatitis infection (hepatitis B or C) or cirrhosis.

[36] NCT02605863, NCT02300610.

[37] NCT02300610.

[38] NCT02138383.

[39] NCT02489123. Mantle cell lymphoma (MCL) is a rare, B-cell NHL that most often affects men over the age of 60.

derived from the Astellas Collaboration Agreement.[40] The Astellas Collaboration Agreement has separate terms for U.S. and non-U.S. sales, as described below:

Medivation 2014 10-K

p.121:

(c) License Agreement with UCLA

Under an August 2005 license agreement with UCLA, the Company's subsidiary Medivation Prostate Therapeutics, Inc. holds an exclusive worldwide license under several UCLA patents and patent applications covering XTANDI and related compounds. Under the Astellas Collaboration Agreement, the Company granted Astellas a sublicense under the patent rights licensed to it by UCLA.

The Company is required to pay UCLA (a) an annual maintenance fee, (b) $2.8 million in aggregate milestone payments upon achievement of certain development and regulatory milestone events with respect to XTANDI (all of which has been paid as of December 31, 2014), (c) ten percent of all Sublicensing Income, as defined in the agreement, which the Company earns under the Astellas Collaboration Agreement, and (d) a four percent royalty on global net sales of XTANDI, as defined.

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(c) Collaboration Revenue

Collaboration revenue consists of three components: (a) collaboration revenue related to U.S. XTANDI sales; (b) collaboration revenue related to ex-U.S. XTANDI sales; and (c) collaboration revenue related to upfront and milestone payments.

[...]

Collaboration Revenue Related to U.S. XTANDI Sales

Under the Astellas Collaboration Agreement, Astellas records all U.S. XTANDI sales. The Company and Astellas share equally all pre-tax profits and losses from U.S. XTANDI sales. Subject to certain exceptions, the Company and Astellas also share equally all XTANDI development and commercialization costs attributable to the U.S. market, including cost of goods sold and the royalty on net sales payable to UCLA under the Company's license agreement with UCLA. The primary exceptions to the equal cost sharing are that each party is responsible for its own commercial FTE costs and that development costs supporting marketing approvals in both the United States and either Europe or Japan are borne one-third by the Company and two-thirds by Astellas. The Company recognizes collaboration revenue related to U.S. XTANDI sales in the period in

[40] UNITED STATES SECURITIES AND EXCHANGE COMMISSION, Form 10-K, For the Fiscal Year Ended December 31, 2014, http://www.sec.gov/Archives/edgar/data/1011835/000119312515062576/d850483d10k.htm

which such sales occur. Collaboration revenue related to U.S. XTANDI sales consists of the Company's share of pre-tax profits and losses from U.S. sales, plus reimbursement of the Company's share of reimbursable U.S. development and commercialization costs. The Company's collaboration revenue related to U.S. XTANDI sales in any given period is equal to 50% of U.S. XTANDI net sales as reported by Astellas for the applicable period.

[...]

Collaboration Revenue Related to Ex-U.S. XTANDI Sales

Under the Astellas Collaboration Agreement, Astellas records all ex-U.S. XTANDI sales. Astellas is responsible for all development and commercialization costs for XTANDI outside the United States, including cost of goods sold and the royalty on net sales payable to UCLA under the Company's license agreement with UCLA, and pays the Company a tiered royalty ranging from the low teens to the low twenties on net ex-U.S. XTANDI sales. The Company recognizes collaboration revenue related to ex-U.S. XTANDI sales in the period in which such sales occur. Collaboration revenue related to ex-U.S. XTANDI sales consists of royalties from Astellas on those sales.

[...]

Medivation came to acquire rights to Xtandi from UCLA through an agreement initiated by Dr. Charles L. Sawyers and Dr. Michael E. Jung, researchers at UCLA working on prostate cancer screening techniques and treatments. Dr. Sawyers is an oncologist who currently runs a lab at Memorial Sloan Kettering Cancer Center and serves on the Board of Directors for Novartis.[41] He was a key participant in the development of Gleevec and Sprycel, and is a recipient of the Lasker Award. Dr. Michael E. Jung is a Distinguished Professor of Chemistry at UCLA, where he runs a lab that conducts research on chemicals related to the treatment of cancer.

Dr. Sawyers approached Medivation through its founder, Dr. David Hung, a former colleague at the University of California, San Francisco. They settled on an agreement that required Dr. Sawyers and Dr. Jung to disclose all molecules related to their prostate cancer research that benefitted from Medivation funding. Dr. Sawyers served on Medivation's Scientific Advisory Board, as did Dr. Jung, receiving $20,000 and $400,000 worth of stocks, respectively.

In addition, Dr. Sawyers and Dr. Jung used the fruits of their research to found their own pharmaceutical firm, Aragon Pharmaceuticals, which they used as a vehicle to develop a drug with a very similar chemical structure to Xtandi. Medivation sued the doctors, Aragon, and UCLA, over the development of that drug.[42] According to SEC filings, Medivation and UCLA are now engaged in separate litigation over licensing payments on Xtandi.[43]

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[41] More on Dr. Sawyers is available here: http://www.bloomberg.com/research/stocks/private/person.asp?personId=12631592&privcapId=25460204.
[42] For an amended complaint, filed February 9, 2012, see here: https://goo.gl/p3Ipnm.
[43] Medivation 2015 10-K SEC filing, available here: http://files.shareholder.com/downloads/MDV/1291225255x0xS1193125-15-62576/1011835/filing.pdf.

8. Orange Book patent claims for Xtandi

As noted above, Astellas has listed three patents in the FDA Orange book for Xtandi sales. These include US patent number 7709517, for both a drug substance and drug product claim, and two additional patents, US patent numbers 8183274 and 9126941.

Table 8.1: Xtandi Patents

Patent Number	**7,709,517**	**8,183,274**	**9,126,941**
Title:	Diarylhydantoin compounds	Treatment of hyperproliferative disorders with diarylhydantoin	Treatment of hyperproliferative disorders with diarylhydantoin compounds
Publication date	May 4, 2010	May 22, 2012	Sep 8, 2015
Filing date	May 15, 2006	Feb 18, 2010	Apr 17, 2012
Priority Date	May 13, 2005	May 13, 2005	May 13, 2005
Inventors	Charles L. Sawyers, Michael E. Jung, Charlie D. Chen, Samedy Ouk, Derek Welsbie, Chris Tran, John Wongvipat, Dongwon Yoo	Charles L. Sawyers, Michael E. Jung, Charlie D. Chen, Samedy Ouk, Chris Tran, John Wongvipat	Charles L. Sawyers, Michael E. Jung, Charlie D. Chen, Samedy Ouk, Chris Tran, John Wongvipat
Original Assignee	The Regents Of The University Of California	The Regents Of The University Of California	The Regents Of The University Of California
Expiration date	Aug 13, 2027	May 15, 2026	May 15, 2026
FDA substance claim	Yes		
FDA product claim	Yes		
FDA use claim code		U - 1281; The treatment of patients with metastatic castration-resistant prostate cancer (CRPC) who have previously	U - 1588, The treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

		received docetaxel. U - 1588, The treatment of patients with metastatic castration-resistant prostate cancer (CRPC).	
Disclosure of US rights in the patent	This invention was made with United States Government support under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129. The Government has certain rights in the invention.	This invention was made with United States Government support under National Institutes of Health SPORE grant number 5 P50 CA092131 and Department of Defense (Army) grant number W81XWH-04-1-0129. The Government has certain rights in the invention.	This invention was made with Government support under Grant No. W81XWH-04-1-0129 awarded by the United States Army, Medical Research and Materiel Command; Grant No. CA092131 awarded by the National Institutes of Health. The Government has certain rights in this invention.

9. Non-patent exclusivity.

The FDA Orange Book lists two grants of non-patent exclusivity to Astellas for enzalutamide, both expiring in 2017. One was granted for enzalutamide as a new chemical entity, expiring August 31, 2017; the second was granted under code I-693 for "treatment of patients with metastatic castration-resistant prostate cancer (CRPC)", expiring September 10, 2017. These dates are sufficiently close that they should not be used to excuse non-action on this request, particularly since it may take several months for a generic supplier to prepare data for an Abbreviated New Drug Application (ANDA).

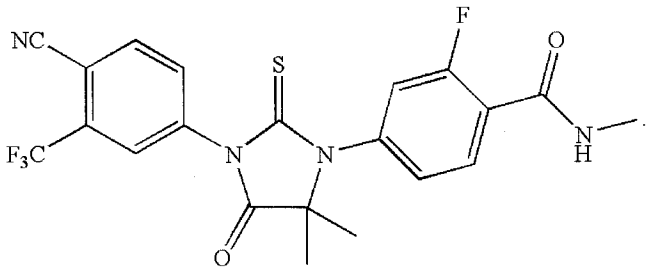
10. Generic supply

Enzalutamide is a small molecule drug that does not have a complex structure.

Enzalutamide is a synthetic, non-steroidal pure antiandrogen, originally named MDV3100, which has the formula $C_{21}H_{16}F_4N_4O_2S$, a molar mass of 464.44 g/mol and a chemical name of 4-(3-(4-Cyano-3-(trifluoromethyl)phenyl)-5,5-dimethyl-4-oxo-2-thioxoimidazolidin-1-yl)-2-fluoro-N-methylbenzamide. The chemical structure, illustrated in Figure 1, includes a thiohydantoin and two benzene groups.

Figure 10.1: Structure of MDV3100 (CAS number: 915087-33-1)

[RD162']



Petitioners have excellent relations with several generic drug manufacturers, and do not anticipate difficulties obtaining the necessary FDA approvals for generic versions of enzalutamide, once the federal government provides access to the patents, either by using the royalty-free right in the patents or granting this march-in request.

Note that the 2015 U.S. AWP for Xtandi of $88.48 per 40 mg capsule is equivalent to $2,212 per gram of active pharmaceutical ingredient.

Generic products with similar complexity for manufacturing can be obtained for under $10 per gram of API, retail,[44] and considerably less in bulk.

11. Xtandi R&D investments through the 2012 approval for the lead indication

Xtandi was approved as a treatment for prostate cancer in August 31, 2012, as a priority drug under the FDA Priority Review program. The application was by Astellas, and was approved by the FDA as NDA 203415.

The application for the NDA was supported by evidence from four clinical trials, including one Phase 1 trial with 140 patients enrolled, one Phase 1/2 trial with 27 patients enrolled, one Phase 2 trial with 60 patients enrolled, and one Phase 3 trial with 1,199 patients enrolled. Total enrollment for the 4 trials was 1,426 patients.

[44] For example, generic versions of the cancer drug imatinib.

Table 11.1: Trials Reported in FDA Medical Review for 2012 Approval for Xtandi

Study Number	NCT Number	Phase	Start- End Date	Enrolled (FDA Review)	Study Sponsor	Federal Funding
S-3100-1-01	NCT00510718	1	7/2007- 1/2010	140	Medivation	NCI, DoD[45]
CRPC-MDA-1	NCT01091103	2	2/2010- 7/2011	60	Medivation	NCI, DoD[46]
CRPC2	NCT00974311	3	9/2009- 9/2011	1199	Medivation	n/a
9785-CL-0111	NCT01284920	1/2	11/2010- 7/2012	27	Astellas Pharma	n/a

The two earliest trials (NCT00510718, NCT01091103) received subsidies from the National Cancer Institute and Department of Defense, in addition to funding from the Prostate Cancer Foundation and other non-profit institutions. After receiving favorable results from the trials subsidized by NCI and DoD, Medivation and Astellas funded two additional trails.

The size of the trials for Xtandi were typical of other cancer drugs approved from 2010 to 2014 for the lead indication as a New Molecular Entity, and much smaller than trials used to approve non-cancer drugs.

Table 11.2: Trial enrollment cited in in FDA medical reviews for lead indication of new drugs, 2010 to 2014

Average for all cancer drugs	1,316
Average for non-Cancer Drugs	4,733
Xtandi	1,426

Medivation reported their direct expenditures and cost-sharing payments from Astellas for collaboration on the development of Xtandi between 2005 and 2012, when the FDA granted Xtandi marketing approval. They defined direct costs as "clinical and preclinical study costs, cost of supplying drug substance and drug product for use in clinical and preclinical studies, contract research organization fees, and other contracted services pertaining to specific clinical and preclinical studies."[47] The number reported excludes indirect costs, which include "administrative and support costs."[48]

Astellas contributed to half of all direct costs for R&D conducted for U.S. drug approval, two-thirds of costs for R&D directed towards trials aimed at both U.S. and non-U.S. use of

[45] Scher, Howard I., et al. "Antitumour activity of MDV3100 in castration-resistant prostate cancer: a phase 1–2 study." *The Lancet* 375.9724 (2010): 1437-1446.
[46] Efstathiou, Eleni, et al. "Molecular characterization of enzalutamide-treated bone metastatic castration-resistant prostate cancer." *European urology* 67.1 (2015): 53-60.
[47] Medivation 2009 10-K SEC filing, available here: http://files.shareholder.com/downloads/MDV/1291225255x0xS1193125-10-57020/1011835/filing.pdf.
[48] Ibid. Indirect costs for all drugs combined are available in Medivation SEC filings.

Xtandi, and full development costs for commercialization outside the United States. Based upon the Medivation SEC filings, R&D outlays on Xtandi were $303 million through the end of the calendar year 2012.

Table 11.3: R&D expenditures on Xtandi, 2005-2012 (in thousands of USD)

SEC 10-K Year	2005	2006	2007	2008	2009	2010	2011	2012
Medivation Direct Costs	$261	$3,021	$2,619	$8,845	$27,046	$23,454	$42,3350	$67,086
Development cost-sharing payments from Astellas					$2,784	$34,125	$44,285	$47,473
Total	$261	$3,021	$2,619	$8,845	$29,830	$57,579	$86,620	$114,559
Cumulative Total								$303,334

Medivation reported outlays of an additional $285 million in calendar years 2013 and 2014, much of that money aimed at justifying broader use of Xtandi for prostate cancer, but also on testing the drug to treat other types of cancer.

Table 11.4: R&D expenditures on Xtandi, 2013 and 2014 (in thousands of USD)

SEC 10-K Year	2013	2014
Medivation Direct Costs	$73,076	$102,669
Development cost-sharing payments from Astella	$46,594	$63,479
Total	$119,670	$166,148
Cumulative Total		$285,818

The company outlays on R&D investments were significant, although it is worth noting that the early and most risky trials were small and subsidized by the United States government.

Note that through the end of 2014, representing a little more than two years of reimbursements, Medicare spent $704 million on Xtandi. Astellas expects a sharp increase in U.S. sales in 2015 and 2016, and the company revenues also include sales from non-Medicare patients in the United States and patients outside of the United States.

12. Clinical trials on enzalutamide, including trials subsequent to 2012 NDA.

Like many cancer drugs, the initial approval of the drug for the lead indication has lead to continued research to determine the best uses of the drugs, both for prostate cancer patients and to test the benefits of using enzalutamide to treat other types of cancer.

As of January 6, 2015, there were 129 trials listed in the ClinicialTrials.Gov database.

The funding of the trials is reported under the categories Industry, U.S. Fed., NIH, and Other, as well as combinations of those categories.

- 54 of the 129 trials were reported as funded by Industry alone.
- Another 31 trials were reported as funded by Industry and some other funder.
- The NIH or other U.S. Federal agencies were reported as funders in whole or in part of 18 trials.
- The category "Other" is quite important, accounting for 29 trials funded exclusively by Other, and another 42 where "Other" is among the funders.

Many of the trials funded by "Other" refer to universities and other non-profit research organizations that receive NIH or other federal agency research grants. "Other" also refers to funding from foreign governments and charities.

Table 12.1: Number of trials funded by Industry, NIH, other "U.S. Fed" and "Other," as reported in ClinicalTrials.Gov, January 6, 2016.

Funder	Number of Trials
"Industry" only	54
Mixed including "Industry"	31
"Other" only	29
Mixed including "Other"	42
NIH only	3
Mixed including NIH or other "U.S. Fed"	16

Table 12.2: Number of trials funded by Astellas and/or Medivation, as reported in ClinicalTrials.Gov, January 6, 2016.

Funder	Number of Trials
Astellas and/or Medivation as sponsor of industry only funded trials	39
Astellas and/or Medivation as sponsor of mixed funded trials	18

Among the trials funded in whole or in part by "Industry", the majority, 57, were funded by Astellas and/or Medivation, and of those only for 39 (30 percent of the 129) were they the sole funder of the trials.

Other companies, such as Lilly, Gilead, Roche, Bayer, Sanofi, and smaller companies, were involved in funding 28 trials.

13. Licensing terms, including reasonable royalty.

We are requesting the federal government grant an open license to any generic drug manufacturer.

The federal government has no obligation to pay royalties on the patents when and if it exercises its royalty free rights in the patents.

If the government orders the licensing of the patents under the federal march-in statutes, the terms of the license, including the royalty, have to be "reasonable under the circumstances."[49]

The issue of the appropriate royalty rate can be briefed and argued when and if the federal government is inclined to exercise march-in rights on the patent.

"Under the circumstances" would include many factors, such as that the facts motivating the granting of the march-in request are related to abuses of the patent rights, including in particular charging an excessive price and discriminating against U.S. consumers.

Rights in test data

Patents are granted for inventions, but as noted above, patents are not the only intellectual property rights associated with drug development.

The FDA provides additional intellectual property rights for investments in clinical trials, including five years of exclusive rights to rely upon data supporting the registration of a new chemical entity, and three years of rights in the data to support new indications on a drug.

The five years of test data exclusivity for Xtandi as a treatment for patients with metastatic castration-resistant prostate cancer (CRPC) will expire on September 10, 2017 in the United States, and later in many other countries. For example, the term of protection for test data is up to 8 years in Japan and Canada, and 11 years in the European Union.[50] The rights in test data are designed to protect and reward investments in clinical trials, and they operate separately from patent protection. The existence of the test data rights eliminates the need to consider investments in clinical trials when considering the royalty to the patent holder, because those investments are protected by this separate intellectual property right. As regards the

[49] 35 USC 203(a).

[50] Comparison of the Non-patent Drug Exclusivities Available in the United States, Canada, Europe and Japan. The International Economic Forum of the Americas. Serge Lapointe, Ph.D. June 14, 2012 http://forum-americas.org/sites/default/files/documents/20120614-lapointe-pres.pdf

investments in the U.S. market, it is likely that Astellas will have earned more than $5 billion from the U.S. market alone, through September 10, 2017, the date of the most relevant test data exclusivity in the United States ends. Astellas will have also earned billions more from sales outside of the United States, where most patients reside.

Average industry royalty rates

According to the IRS, in 2012, the average rate of aggregate royalties (for all patents, know-how, trademarks, etc.[51]), reported on corporate income tax returns for the pharmaceutical and medicine manufacturing sector (MINOR CODE 325410) was 6.95 percent.

14. Funding of research to further develop enzalutamide.

One possible argument against any policy that lowers drug prices or shortens the term of a monopoly is that society benefits from the incentive to invest in R&D to find new uses for a drug.

It is possible to address the objective of providing sustainable sources of R&D funding without having high prices or longer monopolies.

On at least two occasions in the past involving NIH funded cancer drugs, and more recently in connection with proposals to create or extend monopolies in various drafts of the 21st Century Cures Act, there have been proposals to have mandates for funding R&D.

In one case, involving a dispute over the term of the monopoly on the cancer drug cisplatin in the early 1980s, there was a proposal that generic firms be obligated to contribute to the costs of ongoing research to determine new uses for the drug, following generic entry. This proposal, made by a generic drug company seeking to end the cisplatin monopoly, led to a compromise whereby Bristol-Myers was allowed to extend the monopoly for five more years, but only after they lowered the price of cisplatin and contributed tens of millions of dollars to independent research through non-profit institutions, at the direction of the NIH. Later, BMS proposed something similar, in an unsuccessful effort to extend data exclusivity on the cancer drug Taxol. In early drafts of the the 21st Century Cures legislation, there were proposals to associate extensions of drug monopolies with obligations to provide money to the NIH, and to make other investments in R&D.

In this case involving Xtandi, the NIH could simultaneously end the Xtandi monopoly and require any generic drug company to make contributions toward follow-on research to explore new and/or better uses of enzalutamide. Such obligations could be a condition of any use of the federal government's royalty free right in the drug, or as a condition of obtaining a march-in license.

[51] The IRS does not provide a definition of royalties. See: https://www.irs.gov/pub/irs-tege/eotopicd89.pdf.

Note that there are benefits in having different parties participate in the testing of drugs, including those that do not have conflicts of interest as regards reporting possible negative impact of products, or allowing greater competition in designing better delivery mechanisms or new combination products. Also, in the case of Xtandi, more than half of the trials involving enzalutamide are already funded by entities other than Astellas.

15. Standard for determining that Xtandi prices are unreasonable.

In determining if the prices for Xtandi violate the statutory obligation to make products available to the public on reasonable terms and conditions, the NIH has broad discretion to consider a variety of factors, including the high price of the drug and the fact that the high price leads to restrictions on access and financial hardships on patients. However, in this case, we recommend the NIH address a narrower question, that can be answered clearly, given the robust evidence.

Do the Astellas prices for Xtandi discriminate against consumers in the United States? And, if so, the NIH should approve the March-In request, or use its royalty free rights in the patents, to prevent U.S. residents from paying more for a drug invented on federal grants than residents of other high income countries.

We have obtained prices for Xtandi in the United States and in 13 other high income countries, and this data allows the NIH to determine whether U.S. consumers are being asked to pay more for a drug invented on federal grants than Astellas charges in other high income countries.

One possible comparison to determine if the price is unreasonable is to consider the prices in other industrialized countries outside of the United States that have (1) per capita incomes of at least half that of the United States, (2) have the large economies as measured by the GDP, and (3) are members of the OECD, and to consider the U.S. price to be unreasonable, if the average wholesale price (AWP) in the U.S. is higher than the median price in the reference countries.

We propose using an odd number of countries. The 13 countries that have incomes at least 50 percent of the United States and which have the largest economies include Japan, Germany, France, the UK, Italy, Canada, Australia, Spain, the Netherlands, Switzerland, Sweden, Belgium and Norway.

We have prices for all 13 of the reference countries. None of the prices are higher than $36.93, and the April 2015 U.S. AWP was $88.48. It is not a close call: the U.S. prices are discriminatory and are unfair to U.S. residents. Note that the *highest* price of the 13 high income reference countries was less than half (42 percent) of the average wholesale price (AWP) in the United States, the median of the 13 prices reference prices we have obtained is just 36 percent of the US AWP, and the prices in Japan and Canada are 30 percent and 23 percent respectively of US AWP. As a percentage in 2014 per capita income, the U.S. prices are also

far higher than for any of the 13 high income countries. In eight countries, the annual cost of Xtandi is between 47 percent and 97 percent of annual per capita income. In four countries, the annual cost of Xtandi is between 111 percent and 161 percent of per capita income. In the United States, the annual cost of Xtandi is 234 percent of 2014 per capita income.

Table 15.1: US Average Wholesale Price, relative to prices in 13 reference countries

	2014 GDP	2014 annual Per Capita Income	price per 40 mg unit	Annual price (x 4x 365.25) as percent of 2014 per capita income
United States, Average Wholesale price April 2015	$17,419,000,000,000	$55,200	$88.48	234%
Japan	$4,601,461,206,885	$42,000	$26.37	92%
Germany	$3,868,291,231,824	$47,640	$36.93	113%
France	$2,829,192,039,172	$42,960	$26.73	91%
United Kingdom	$2,988,893,283,565	$43,430	$35.65	120%
Italy	$2,141,161,325,367	$34,270	$26.01	111%
Canada	$1,785,386,649,602	$51,630	$20.12	57%
Australia	$1,454,675,479,666	$64,540	$23.46	53%
Spain	$1,381,342,101,736	$29,440	$32.38	161%
Netherlands	$879,319,321,495	$51,890	$31.48	89%
Switzerland	$701,037,135,966	$88,120*	$35.46	59%
Sweden	$571,090,480,171	$61,610	$26.96	64%
Belgium	$531,546,586,179	$47,260	$31.48	97%
Norway	$499,817,138,323	$103,630	$33.09	47%
Median, reference countries			$31.48	91%
Unweighted average, reference countries			$29.70	89%

* For Switzerland, only 2013 per capita income was available.

One defense for the high U.S. price for Xtandi would be that the product could not have been developed at a lower price. But given the significant market for this drug, the federal subsidies in both the preclinical and clinical stages, and the fact that prostate cancer is the among the three most common types of cancer,[52] that defense can be rejected entirely, and certainly going forward, given the billions of dollars in revenue already earned by Astellas.

16. Conclusion

We are requesting the federal government take steps to address the discriminatory and unfair pricing of Xtandi/enzalutamide by Astellas. U.S. residents should not have to pay two to four

[52] American Cancer Society: Cancer Facts and Figures 2015. Atlanta, Ga: American Cancer Society, 2015.

times as much for a cancer drug than residents of other high income countries, particularly when the drug was invented with the support of federal grants and benefited from other federal research subsidies. The average wholesale price for Xtandi was $129,269 per year in 2015, and this was more than twice as high as the price in any other high income country in our 13 country survey, and four times as high as the price in Canada. U.S. taxpayers are generous when it comes to financing research programs at the NIH, the U.S. Department of Defense, and in other federal agencies. However, we should not allow the companies that commercialize this research to discriminate and use unfair prices that impose financial hardships on U.S. residents, create access barriers for cancer patients, and make our workforce less competitive in global markets.

There are many areas where current U.S. laws are inadequate to address excessive or unfair prices. This is not one of them. The Bayh-Dole Act was passed with the promise that the federal March-In rights or the federal government royalty-free rights in patents would be available to protect the public from the unreasonable use of patented inventions. This is such a case.

Please contact Andrew S. Goldman, counsel for Policy and Legal Affairs at KEI, about this request. He can be reached at andrew.goldman@keionline.org, or by telephone at +1.202.332.2670.

Sincerely,

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Manon Ress, Michael Davis and Ruth Lopert, on behalf of
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Senators Boxer, Brown, Grassley, King Leahy, McCain McCaskill Nelson Sanders, Schumer Sessions, and Wyden

Representatives Doggett, Schakowsky, Tom Price, Markwayne Mullin, the Congressional Prostate Cancer Task Force

INFORMATION PAPER—SUPPLEMENT & DISCUSSION
March-in Rights Request by KEI to NIH and DoD Pertaining to Xtandi®

APPENDIX E
Applicable law

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35 U.S.C. Section 200. Policy and objective.

It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise without unduly encumbering future research and discovery; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.

(Added Pub. L. 96–517, § 6(a), Dec. 12, 1980, 94 Stat. 3018; amended Pub. L. 106–404, § 5, Nov. 1, 2000, 114 Stat. 1745.)

35 U.S.C. Section 201. Definitions.

As used in this chapter—

(a) The term "Federal agency" means any executive agency as defined in section 105 of title 5, and the military departments as defined by section 102 of title 5.

(b) The term "funding agreement" means any contract, grant, or cooperative agreement entered into between any Federal agency, other than the Tennessee Valley Authority, and any contractor for the performance of experimental, developmental, or research work funded in whole or in part by the Federal Government. Such term includes any assignment, substitution of parties, or subcontract of any type entered into for the performance of experimental, developmental, or research work under a funding agreement as herein defined.

(c) The term "contractor" means any person, small business firm, or nonprofit organization that is a party to a funding agreement.

(d) The term “invention” means any invention or discovery which is or may be patentable or otherwise protectable under this title or any novel variety of plant which is or may be protectable under the Plant Variety Protection Act (7 U.S.C. 2321 et seq.).

(e) The term “subject invention” means any invention of the contractor conceived or first actually reduced to practice in the performance of work under a funding agreement: *Provided*, That in the case of a variety of plant, the date of determination (as defined in section 41(d) [1] of the Plant Variety Protection Act (7 U.S.C. 2401(d))) must also occur during the period of contract performance.

(f) The term “practical application” means to manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms.

(g) The term “made” when used in relation to any invention means the conception or first actual reduction to practice of such invention.

(h) The term “small business firm” means a small business concern as defined at section 2 of Public Law 85–536 (15 U.S.C. 632) and implementing regulations of the Administrator of the Small Business Administration.

(i) The term “nonprofit organization” means universities and other institutions of higher education or an organization of the type described in section 501(c)(3) of the Internal Revenue Code of 1986 (26 U.S.C. 501(c)) and exempt from taxation under section 501(a) of the Internal Revenue Code (26 U.S.C. 501(a)) or any nonprofit scientific or educational organization qualified under a State nonprofit organization statute.

(Added Pub. L. 96–517, § 6(a), Dec. 12, 1980, 94 Stat. 3019; amended Pub. L. 98–620, title V, § 501(1), (2), Nov. 8, 1984, 98 Stat. 3364; Pub. L. 99–514, § 2, Oct. 22, 1986, 100 Stat. 2095; Pub. L. 107–273, div. C, title III, § 13206(a)(12), Nov. 2, 2002, 116 Stat. 1904.)

35 U.S.C. Section 203. March-in rights.

(a) With respect to any subject invention in which a small business firm or nonprofit organization has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such—

(1) action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;

(2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;

(3) action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or

(4) action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204. (Section 204 pertains to the preference for United States industry).

(b) A determination pursuant to this section or section 202(b)(4) [1] shall not be subject to chapter 71 of title 41. An administrative appeals procedure shall be established by regulations promulgated in accordance with section 206. Additionally, any contractor, inventor, assignee, or exclusive licensee adversely affected by a determination under this section may, at any time within sixty days after the determination is issued, file a petition in the United States Court of Federal Claims, which shall have jurisdiction to determine the appeal on the record and to affirm, reverse, remand or modify, as appropriate, the determination of the Federal agency. In cases described in paragraphs (1) and (3) of subsection (a), the agency's determination shall be held in abeyance pending the exhaustion of appeals or petitions filed under the preceding sentence.

(Added Pub. L. 96–517, § 6(a), Dec. 12, 1980, 94 Stat. 3022; amended Pub. L. 98–620, title V, § 501(9), Nov. 8, 1984, 98 Stat. 3367; Pub. L. 102–572, title IX, § 902(b)(1), Oct. 29, 1992, 106 Stat. 4516; Pub. L. 107–273, div. C, title III, § 13206(a)(14), Nov. 2, 2002, 116 Stat. 1905; Pub. L. 111–350, § 5(i)(2), Jan. 4, 2011, 124 Stat. 3850.)

37 C.F.R. 401.6 Exercise of march-in rights.

(a) The following procedures shall govern the exercise of the march-in rights of the agencies set forth in 35 U.S.C. 203 and paragraph (j) of the clause at §401.14.

(b) Whenever an agency receives information that it believes might warrant the exercise of march-in rights, before initiating any march-in proceeding, it shall notify the contractor in writing of the information and request informal written or oral comments from the contractor as well as information relevant to the matter. In the absence of any comments from the contractor within 30 days, the agency may, at its discretion, proceed with the procedures below. If a comment is received within 30 days, or later if the agency has not initiated the procedures below, then the agency shall, within 60 days after it receives the comment, either initiate the procedures below or notify the contractor, in writing, that it will not pursue march-in rights on the basis of the available information.

(c) A march-in proceeding shall be initiated by the issuance of a written notice by the agency to the contractor and its assignee or exclusive licensee, as applicable and if known to the agency, stating that the agency is considering the exercise of march-in rights. The notice shall state the reasons for the proposed march-in in terms sufficient to put the contractor on notice of the facts upon which the action would be based and shall specify the field or fields of use in which the agency is considering requiring licensing. The notice shall advise the contractor (assignee or exclusive licensee) of its rights, as set forth in this section and in any supplemental agency regulations. The determination to exercise march-in rights shall be made by the head of the agency or his or her designee.

(d) Within 30 days after the receipt of the written notice of march-in, the contractor (assignee or exclusive licensee) may submit in person, in writing, or through a representative, information or argument in opposition to the proposed march-in, including any additional specific information which raises a genuine dispute over the material facts upon which the march-in is based. If the information presented raises a genuine dispute over the material facts, the head of the agency or designee shall undertake or refer the matter to another official for fact-finding.

(e) Fact-finding shall be conducted in accordance with the procedures established by the agency. Such procedures shall be as informal as practicable and be consistent with principles of fundamental fairness. The procedures should afford the contractor the opportunity to appear with counsel, submit documentary evidence, present witnesses and confront such persons as the agency may present. A transcribed record shall be made and shall be available at cost to the contractor upon request. The requirement for a transcribed record may be waived by mutual agreement of the contractor and the agency. Any portion of the march-in proceeding, including a fact-finding hearing that involves testimony or evidence relating to the utilization or efforts at obtaining utilization that are being made by the contractor, its assignee, or licensees shall be closed to the public, including potential licensees. In accordance with 35 U.S.C. 202(c)(5), agencies shall not disclose any such information obtained during a march-in proceeding to persons outside the government except when such release is authorized by the contractor (assignee or licensee).

(f) The official conducting the fact-finding shall prepare or adopt written findings of fact and transmit them to the head of the agency or designee promptly after the conclusion of the fact-finding proceeding along with a recommended determination. A copy of the findings of fact shall be sent to the contractor (assignee or exclusive licensee) by registered or certified mail. The contractor (assignee or exclusive licensee) and agency representatives will be given 30 days to submit written arguments to the head of the agency or designee; and, upon request by the contractor oral arguments will be held before the agency head or designee that will make the final determination.

(g) In cases in which fact-finding has been conducted, the head of the agency or designee shall base his or her determination on the facts found, together with any other information and written or oral arguments submitted by the contractor (assignee or exclusive licensee) and agency representatives, and any other information in the administrative record. The

consistency of the exercise of march-in rights with the policy and objectives of 35 U.S.C. 200 shall also be considered. In cases referred for fact-finding, the head of the agency or designee may reject only those facts that have been found to be clearly erroneous, but must explicitly state the rejection and indicate the basis for the contrary finding. Written notice of the determination whether march-in rights will be exercised shall be made by the head of the agency or designee and sent to the contractor (assignee of exclusive licensee) by certified or registered mail within 90 days after the completion of fact-finding or 90 days after oral arguments, whichever is later, or the proceedings will be deemed to have been terminated and thereafter no march-in based on the facts and reasons upon which the proceeding was initiated may be exercised.

(h) An agency may, at any time, terminate a march-in proceeding if it is satisfied that it does not wish to exercise march-in rights.

(i) The procedures of this part shall also apply to the exercise of march-in rights against inventors receiving title to subject inventions under 35 U.S.C. 202(d) and, for that purpose, the term “contractor” as used in this section shall be deemed to include the inventor.

(j) An agency determination unfavorable to the contractor (assignee or exclusive licensee) shall be held in abeyance pending the exhaustion of appeals or petitions filed under 35 U.S.C. 203(2).

(k) For purposes of this section the term *exclusive licensee* includes a partially exclusive licensee.

(l) Agencies are authorized to issue supplemental procedures not inconsistent with this part for the conduct of march-in proceedings.

INFORMATION PAPER—SUPPLEMENT & DISCUSSION
March-in Rights Request by KEI to NIH and DoD Pertaining to Xtandi®

APPENDIX F

National Economic Impacts from DoD License Agreements With U.S. Industry 2000-2014, Submitted by TechLink, Montana State University, and Business Research Division of Leeds School of Business, University of Colorado

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National Economic Impacts from DoD License Agreements With U.S. Industry

2000-2014

Submitted by:

TechLink
Montana State University, Bozeman

Business Research Division
Leeds School of Business
University of Colorado, Boulder

National Economic Impacts from DoD License Agreements with U.S. Industry

2000-2014

TechLink and University of Colorado Business Research Division

CONTENTS

National Economic Impacts from DoD License Agreements with U.S. Industry, 2000-2014

EXECUTIVE SUMMARY

This study quantifies the overall **contributions of Department of Defense (DoD) license agreements to the nation's economy and defense mission.** U.S. government agencies have a legislative mandate to transfer their patented inventions to industry. Patent license agreements are used to transfer these inventions. License agreements enable companies to develop and sell new products and services using these inventions.

In 2015, an independent research team undertook a yearlong study of the economic impacts from DoD license agreements with U.S. industry. The study's primary purpose was to determine the extent to which DoD license agreements active during the 2000-2014 period contributed to **new economic activity and job creation** in the United States. A secondary purpose was to estimate the extent to which these license agreements resulted in the **transition of new technology to U.S. military use.** This study was undertaken at the direction of the Air Force Technology Transfer Program and the Defense Laboratories Office within the Office of the Assistant Secretary of Defense for Research & Engineering.

The research team surveyed all 602 companies with DoD license agreements active during the 2000-2014 period. Companies were asked to divulge the total sales of new products and services and other economic outcomes directly related to their license agreements. They were also asked about related economic outcomes, including sales to the U.S. military, follow-on research and development contracts, sublicensing revenue, and sales by sublicensees and spin-out companies.

The response rate was very high—92 percent of the companies that the research team was able to contact participated in the study. The team was able to obtain full or partial information on the economic outcomes of 663 out of the 733 total DoD license agreements (90 percent). IMPLAN economic impact assessment software was used to estimate the economic impacts related to the sales and other economic outcomes from these agreements.

Study results are believed to significantly understate the actual economic impacts because of non-responding companies, the effects of inflation, and other factors analyzed in the report.

Major findings from the study included the following:

- **$20.4 billion in total sales** of new products and services resulting from the DoD license agreements
- **$3.4 billion** in sales of new products to the U.S. military
- **$48.8 billion in total economic output** nationwide
- **$1.6 billion** in new tax revenues (federal, state, and local)
- **182,985 full-time jobs** created or retained
- **12,199 full-time jobs** *per year* with an **average salary of $71,337**

PURPOSE OF STUDY

U.S. government agencies have a federal legislative mandate to transfer their inventions to the private sector in order to benefit the nation's economy.[1] Patent license agreements are used to transfer these inventions to industry. License agreements enable companies to develop and sell new products and services using these inventions.

This study was undertaken to estimate the contribution to the national economy of license agreements transferring Department of Defense (DoD) inventions to industry. The study's purpose was to determine the extent to which these license agreements have (1) contributed to new economic activity and job creation in the United States, and (2) resulted in the transition of new technology to U.S. military use. The period covered by the study was 2000-2014.[2]

The study was undertaken in two major phases. First, the research team surveyed all companies having active license agreements with DoD during the 2000-2014 period—a total of 602 companies with 733 different agreements. Companies contacted were asked to divulge the total sales of new products and services directly related to their DoD license agreements. Second, the research team used IMPLAN economic impact assessment software to estimate the total economic impacts related to these sales. IMPLAN is a leading program used by more than 1,500 organizations nationwide to model economic impacts. Analysis included estimates of economic output, value added, employment, labor income, and tax revenues.

RESEARCH TEAM

TechLink, a DoD-funded technology transfer center at Montana State University, conducted this economic impact study in collaboration with the Business Research Division (BRD) of the Leeds School of Business at the University of Colorado Boulder. Since 1999, TechLink has served as DoD's primary national "partnership intermediary," helping to develop technology transfer partnerships between DoD laboratories and U.S. industry nationwide. TechLink's primary focus is facilitating the transfer of patented inventions from DoD labs to U.S. companies through license agreements. TechLink currently brokers or facilitates approximately 60 percent of all DoD license agreements with industry. These license agreements enable companies to develop, manufacture, and sell new products and services using DoD inventions.[3] This benefits the national economy and also supports the U.S. defense mission.

[1] 15 U.S.C. 3701 and 3710, *inter alia*

[2] This study is an update of a previous study completed in 2013: *National Economic Impacts from DoD License Agreements with U.S. Industry, 2000-2011*, available at: http://techlinkcenter.org/articles/2013-report-economic-impact-dod-invention-licensing

[3] For more information, see *www.techlinkcenter.org*

The BRD has been analyzing local, state, and national economies for more than 95 years. It specializes in customized research and economic impact studies that help companies, associations, nonprofits, and government agencies make informed business and policy decisions.[4] The BRD has conducted economic impact studies for a wide range of clients, including the National Renewable Energy Laboratory, Xcel Energy, Western Union, the American Petroleum Institute, and CO-LABS, a consortium of federally funded scientific laboratories, universities, businesses, and local governments in Colorado.

With TechLink, the BRD has previously conducted two national economic impact studies focusing on DoD small business innovation research and technology transfer programs. The first study examined the economic impacts from all Air Force SBIR/STTR Phase II projects completed during the 2000-2013 period—a total Air Force investment of approximately $4 billion.[5] The second study focused on the economic impacts from all TechLink-facilitated technology transfer agreements active during the 2000-2014 period. This latter study was an update of previous studies conducted in 2009 and 2012. The current study is the sixth major economic impact study undertaken by TechLink.[6]

The principal authors of this study were Dr. Will Swearingen of TechLink and Brian Lewandowski of the BRD. Other key members of the research team were Phillip Luebke, Andrew Schoneberg, Chris Huvaere, and Kirkwood Donavin of TechLink, and Dr. Richard Wobbekind of the BRD.

[4] For more information, see *www.colorado.edu/leeds/centers/business-research-division*

[5] The Air Force SBIR/STTR Program economic impact study is available at: http://static.techlinkcenter.org/techlinkcenter.org/files/economic-impacts/USAF%20SBIR-STTR%20Economic%20Impact%20Study%20FY2015.pdf. SBIR and STTR are acronyms respectively for Small Business Innovation Research and Small Business Technology Transfer.

[6] All of these studies are available online at *http://techlinkcenter.org/economic-impacts*

METHODOLOGY

Data Gathering

To undertake this study, TechLink first assembled essential information on all DoD license agreements active during the 2000-2014 period. This information came from two different sources: (1) TechLink itself, for license agreements that it had brokered or facilitated between DoD labs and industry; and (2) DoD labs, for agreements they had established independently of TechLink assistance. A total of 733 license agreements were included in the study. TechLink provided information on 366 of these agreements and the DoD labs on the remaining 367 agreements. The study included license agreements from 65 different DoD laboratories.

The information gathered for each agreement included the name of the company that had licensed the DoD technology, contact information for the company's designated point person, the patent number(s) or a short description of the licensed technology, and the effective dates of the agreement.

Two TechLink economic research specialists used this information to contact each of the companies involved. A total of 602 companies were contacted by email and telephone about the outcomes of their 733 license agreements with DoD. The number of agreements exceeds the number of companies because a sizeable subset of companies (94, or 15 percent) had two or more license agreements with DoD. Of this group, 18 companies had three or more agreements, including one company with 13 different agreements.

602
companies surveyed

92%
of companies contacted provided information

663
license agreements with known results

Survey Questions

Companies were asked a series of questions that focused on the economic outcomes related to their license agreements with DoD. They were informed that all economic and financial information that they provided to TechLink would be kept entirely confidential and would only be aggregated with the information from other companies in the study, and not shared with any other entity, including DoD.

Questions asked included the following:

1. Did your company develop any new products or services based on the license agreement, including improvements to existing products or services?
2. What were the total cumulative sales of new or improved products or services related to this license agreement?
3. Of the total sales, what was the dollar value of sales to the U.S. military, either directly or through a prime contractor?
4. In addition to sales of products and services, did the agreement lead to any follow-on R&D contracts for further development of the licensed technology? If so, what was the dollar value of those contracts?[7]
5. Did you sublicense the technology to other companies? If so, what were the total royalties received from the sublicensees? What are the names of the licensees, so we can follow up to ask them about their sales?
6. Did you create a start-up or spin-out company to commercialize the licensed technology? If so, what is the name of the company, so we can follow up to ask them about their sales?
7. Did you receive any significant investment funding, such as venture capital or angel funding, directly related to the licensed technology?

Response Rate

The research team was able to obtain definitive information on the outcomes of 620 license agreements out of the 733 total. Partial economic information on an additional 43 licenses was gathered through non-survey methods, described below. In total, the research team obtained economic information on slightly over 90 percent of the DoD license agreements. Combined, these 663 licenses were used to estimate the economic impact of the DoD licensing program.

The company response rate was also very high. Only 50 of the 602 companies surveyed declined to participate in the study, either explicitly or by ignoring repeated telephone calls and email messages. Ninety-two (92) percent of the companies contacted agreed to provide sales and other economic information.

However, 32 companies could not be contacted because they had ceased to operate as corporate entities. They had either gone out of business, changed their names, or been acquired by other companies. With these companies added to those that declined to respond, the company response rate for the study was around 86 percent, still very high for these types of studies.

[7] Contracts for further development of a technology were treated as sales of R&D services and were included in the total sales.

The primary reasons for the study's high response rates were believed to be the following:

- Clear communication about the purpose and legitimacy of the study. Companies were informed that the study's purpose was to quantify the extent to which DoD-developed inventions licensed to industry were having a positive impact on the national economy and U.S. defense mission. Companies that questioned the legitimacy of the study were sent a letter from the Director of the Defense Laboratories Enterprise in the Office of the Assistant Secretary of Defense for Research & Engineering that explained the purpose, confidential nature, and importance of the study as well as TechLink's role in undertaking it.
- Strong assurance that company-specific information would be kept confidential. Companies were assured that the DoD was only interested in the overall economic impacts from its licensing agreements with industry—not in company-specific results. Most companies consider their sales figures to be confidential, proprietary, or business-sensitive. Without the assurance that all responses would be treated as confidential information, few companies would have been willing to divulge their sales information.
- Conciseness of the survey. The survey questions were few in number and relatively easy to answer. In many cases, the research team was able to secure the necessary information over the telephone on the first contact. More commonly, extensive follow-up by phone and email was required, often involving several different company personnel. However, the conciseness of the survey encouraged participation.
- Persistence by the TechLink economic research specialists. Some companies were contacted more than a dozen times by email or telephone in the attempt to get through to the right person and obtain the necessary information. This dogged persistence was a key factor behind the high response rate.

In several cases involving non-responding companies, the TechLink team was able to get at least partial sales information through secondary research. Internet searches of specific non-responding company names sometimes led to press releases and other announcements of contracts awarded to these companies—contracts typically for sales to the U.S. military. When these announcements were discovered, the research team undertook further research to determine whether the contracts involved products based on the technology licensed from DoD.

Web sites that document U.S. government contracts were useful when the licensed technologies were primarily commercialized for sales to the U.S. military or other U.S. government agencies. Government sites consulted included: (1) USAspending.gov, the website of the Office of Management and Budget (OMB), which provides searchable information on all federal contracts awarded (https://www.usaspending.gov); (2) DIBBS, the Defense Logistics Agency (DLA) Internet Bid Board System, which provides information on all DLA awards to industry (https://www.dibbs.bsm.dla.mil); and (3) the Federal Procurement Data System, a central repository of information on government-wide contracts maintained by the General Service Administration (https://www.fpds.gov).

Commercial sites consulted for U.S. government sales included: (1) Government Contracts Won, which lists awards to thousands of different defense contractors, large and small (www.governmentcontractswon.com); (2) BidLink, which enables searches of procurement history by the National Stock Numbers (NSNs) that are used to order specific military products (www.bidlink.net); and (3) PartsLogistics, which also allows government contracts to be searched by NSNs (www.partslogistics.com). Usually, searches of several of these sites were needed to piece together at least a partial history of the U.S. government sales by specific non-responding licensees of DoD inventions.[8]

In a few cases involving large publicly traded companies that declined to participate in the study, the research team was able to obtain highly accurate sales information on major products derived from DoD inventions by reviewing these companies' online annual reports. These cases comprised some of the largest sales in the study and were focused primarily on the civilian marketplace. In several cases involving non-responding defense contractors, a search of the annual DoD budgets was productive. These budgets, available online, provided often-detailed information on major acquisition contracts for defense-related products that were based on the licensed DoD inventions. Similarly, in several cases in which defense contractors had large contracts from foreign governments for defense-related products embodying the DoD inventions, the research team was able to find records of these sales in DoD reports to Congress.[9]

NAICS Code Assignments

TechLink next assigned each company to the appropriate North American Industry Classification System (NAICS) code for the product or service resulting from its license agreement. This was an essential step for analysis of the overall economic impacts. NAICS codes are one of the most important inputs to the economic impact model, IMPLAN (described below), because they are used to accurately determine the economic multipliers specific to the particular industrial activity.

NAICS is the U.S. federal government's standard industry classification system. It is a comprehensive production-oriented system that groups companies into industries based on the activities in which they are primarily engaged. NAICS recognizes 1,065 different industries in the United States and assigns a unique code to each industry. Some of the companies in this study with multiple license agreements were assigned to more than one NAICS code, depending on the associated product or service.

To identify the appropriate NAICS codes, multiple sources were referenced, including Hoover's (www.hoovers.com), the LexisNexis Academic web site (www.lexisnexis.com), a commercial NAICS-related website (www.naics.com) that provides a convenient system for looking up NAICS codes by industry sectors and subsectors, and the federal System for Award Management (www.sam.gov), which contains NAICS codes self-identified by the companies.

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[8] For example, see the following fiscal year 2016 budget justification from the Army: http://asafm.army.mil/9Documents/OfficeDocuments/Budget/budgetmaterials/fy16/rforms//vol2.pdf

[9] The U.S. Congress requires annual reports on all major "foreign military sales" and "direct commercial sales" of defense-related technology. These are found at the website of the Defense Procurement and Acquisition Policy (DPAP) Contract Policy and International Contracting (CPIC) Directorate: http://www.acq.osd.mil/dpap/cpic/cp/congressional_reports.html

For businesses not listed on these sites, the classification tree at the official U.S. government's NAICS code website (http://www.census.gov/eos/www/naics/) was compared to activity reported by the companies in their interviews with the TechLink team to arrive at the appropriate NAICS codes.

The TechLink research team entered company sales and other economic data and NAICS code information into the custom database developed for this study. The database greatly facilitated data entry from the economic research specialists gathering company information. Once the data were aggregated and carefully validated by the team, the database provided mechanisms for quickly querying and analyzing the data as well as generating a final dataset for economic impact modeling.

TechLink subsequently submitted the final dataset to the Business Research Division at the Leeds School of Business, University of Colorado Boulder. Among other information, this dataset included—for each license agreement—a code number to identify the agreement and conceal the company's name, the 6-digit NAICS code for the corresponding product or service, and the total sales figures.

For the purposes of this study, the following economic outcomes were regarded as "company sales" and, together, comprised the "total sales:" (1) all sales of new products and services directly related to the licensed DoD technologies, including both commercial and military sales; (2) follow-on R&D contracts to further develop these technologies for specific applications (defined as sales of R&D services); (3) royalties from sublicensing the licensed DoD technologies; (4) sublicensee sales of the licensed technologies; and (5) sales of products or services embodying the licensed technologies by start-up or spin-out companies.

Data Analysis

The BRD employed a widely used economic impact analysis software program, IMPLAN, to estimate the economic contribution effects of the total sales resulting from the DoD license agreements. More than 1,500 entities in academia, the private sector, and government use IMPLAN to model economic impacts. It is employed to determine economic impacts on regions ranging in size from zip code area to county, state, and national levels (www.implan.com).

IMPLAN draws on a mathematical input-output framework originally developed by Wassily Leontief, the 1973 Nobel laureate in economics, to study the flow of money through a regional economy. IMPLAN assumes fixed relationships between producers and their suppliers, based on demand, and that inter-industry relationships within a given region's economy largely determine how that economy responds to change. Increases in demand for a certain product or service causes a multiplier effect—a cascade of ripples through the economy. This increased demand affects the producer of the product, the producer's employees, the producer's suppliers, the supplier's employees, and others, ultimately generating a total impact on the economy that significantly exceeds the initial change in demand.

For example, Company X licenses a patented laser invention from the Air Force Research Laboratory. It then develops an improved barcode scanner using this technology, which it manufactures and sells nationwide. This requires Company X to hire factory workers, who spend their payroll checks on groceries and other goods. In addition, Company X has to purchase components and raw materials from other companies, which also employ workers who purchase groceries and other goods, and so on.

In this example, direct effects are the result of the sales of the new barcode scanner based on the Air Force technology. Indirect effects are the result of the inter-industry purchases of components and raw materials needed to manufacture the barcode scanner. Induced effects are the result of the household expenditures as workers spend their payroll checks on goods and services across a wide spectrum of the economy. Economic impacts are the sum of direct effects, indirect effects, and induced effects.

Multipliers are the ratio of the overall economic impact to the initial change and are typically derived from the following equation: (direct effect + indirect effect + induced effect) / direct effect. Multipliers are very specific to industry sectors and regions. IMPLAN uses NAICS codes to distinguish between 536 industry sectors recognized by the U.S. Department of Commerce. Each sector has a unique output multiplier because it has a different pattern of purchases from firms inside and outside of the U.S. economy. Each year, IMPLAN is updated using data collected by various federal government agencies.

In this study, the BRD applied the national-level IMPLAN model to the total sales figures reported by the companies surveyed. As previously indicated, these figures represented all sales of products and services related to the DoD license agreements active during the 2000-2014 period. Using IMPLAN, the BRD was able to estimate the sum of the direct, indirect, and induced effects of these sales. The overall purpose of this modeling exercise was to estimate the total economic contribution of these sales to the nation's economy, including total economic output, value added, employment, labor income, and tax revenues.

Data presented are for the year 2014 accounting period and expressed in 2014 dollars. The large majority of the company sales occurred prior to 2014 and some date back to the early 2000s. However, most of these sales are ongoing and there was a need to standardize the year. Use of 2014 as the reference year represents a conservative approach because it does not consider the relatively higher value of the earlier sales figures due to inflation (e.g., a dollar in 2000 was worth 37 percent more than a dollar in 2014).

RESULTS

Sales From DoD License Agreements

Nearly half of the DoD license agreements successfully resulted in commercialization, with many others still in the commercialization process. Companies reported that 353 of the 733 license agreements in the study (48 percent) had generated sales of products or services or other revenues. These agreements involved licensed technologies from 55 different DoD laboratories nationwide.

The data revealed that DoD license agreements generated **total cumulative sales** of slightly over **$20.4 billion**, or $20,442,227,211 (*see* Table 1).

As previously mentioned, the "total sales" category included all of the following sources of revenue from commercialization of the licensed DoD technologies:

- Sales of new products and services, including both commercial (civilian) sales and sales to the U.S. military
- Follow-on R&D contracts to further develop the DoD technologies for specific applications, which were defined as sales of R&D services
- Royalties from sublicensees of the licensed technologies
- Sublicensee sales of the licensed technologies, when this information could be obtained
- Sales by spin-out or start-up companies, when this information was available.

Table 1. Sales resulting from DoD license agreements, 2000-2014

	Total Companies	Total Agreements	Percent of Total Agreements	Total Sales
Included in Study	602	733	100	$20.4 Billion
Achieving Sales	294	353	48	$20.4 Billion
No Sales	262	310	42	--
No Response[10]	46	70	10	--

Source: Cumulative sales reported by companies to TechLink, Montana State University, during survey from January to September 2015.

[10] The "No Response" category excludes license agreements for which information was gathered from non-survey sources.

Companies reported that 310 license agreements (42 percent) had not generated sales or other revenues. This category included (1) newer agreements involving technologies that companies were still actively engaged in commercializing, and (2) agreements that, for many different reasons, had not resulted in commercialization and had been abandoned. A total of 113 agreements involved companies from which the research team was unable to obtain information. These companies either were unwilling to participate (72 agreements) or were uncontactable (41 agreements). As previously mentioned, for 43 of these agreements, information that was useful to this economic impact study was acquired through secondary, non-survey sources (leaving 70 agreements about which no information was acquired).

Table 2 shows the total cumulative sales from the DoD license agreements ($20,442,227,211), broken down by sales category. As this table shows, ***commercial (civilian) product and service sales*** totaled nearly $15.7 billion ($15,650,123,126) and accounted for 77 percent of the total sales. ***Military product and service sales*** were nearly $3.4 billion ($3,432,347,974) and constituted 17 percent of the total.

R&D contracts to further develop the licensed technologies accounted for around $869 million ($868,509,903). These contracts were considered sales of R&D services and came from both the government and private sectors. For example, a small biotech company that licensed some promising infectious disease antibodies from an Army medical lab may have received substantial funding from the National Institutes of Health to help develop a diagnostic test for the disease as well as funding from a major pharmaceutical company to develop a vaccine or therapeutic product. These R&D contracts accounted for around 4 percent of the total sales. The remaining 2 percent of the total sales consisted of ***royalties from sublicensees*** ($41,791,231), ***sales by sublicensees*** ($443,354,977), and ***sales by spin-out companies*** ($6,100,000).

Table 2. Sales from DoD license agreements, by sales category, 2000-2014

Sales Category	Total Sales *$ Millions*	Percent of Total
Commercial Product/Service Sales	$15,650	77
Military Product/Service Sales	$3,432	17
R&D Contracts	$869	4
Royalties from Sublicensees	$42	0.2
Sales by Sublicensees	$443	2
Sales by Spin-out Companies	$6	--
Total Combined Sales	$20,442	100

Source: Cumulative sales reported by companies to TechLink, Montana State University, during survey from January to September 2015.

Remarkably, a single license agreement accounted for approximately $14.1 billion of the sales from DoD license agreements—around 69 percent. This was a license for a respiratory syncytial virus (RSV) antibody from the Uniformed Services University of the Health Sciences (USUHS). The antibody is used in a top-selling drug, Synagis, to prevent serious lower respiratory tract disease in infants and young children. Without this top-selling drug, total sales were slightly over $6.3 billion.

Total sales from the single USUHS license agreement were nearly 16 times larger than those from the second most successful license agreement, which generated almost $900 million in sales. Only 14 agreements generated more than $100 million in sales; however, 61 agreements had sales of at least $10 million. Notably, 178 license agreements generated sales of at least $1 million—approximately 24 percent.

Including all 663 license agreements for which sales information was obtained, the average agreement generated around $31 million in sales. Excluding sales of Synagis, the average figure was around $8.7 million. Among just the 353 license agreements with sales, the average figure was nearly $20.6 million (not counting sales of Synagis). Among all agreements with sales, the median sales figure was approximately $1.5 million.

Military Sales

As noted, the survey found that sales to the U.S. military amounted to slightly over $3.4 billion, which was approximately 17 percent of the total sales. However, excluding Synagis, U.S. military sales accounted for nearly 54 percent of total sales. This high percentage is a very positive finding from the DoD perspective. It demonstrates that, via technology transfer, the DoD R&D system is achieving its objective of developing new technology to support the U.S. defense mission.

Some of the companies surveyed had primarily military sales. While companies do not need license agreements to manufacture products based on DoD-patented inventions for U.S. government use, they obtain licenses because they hope to make commercial or foreign military sales. It is ideal when there are both commercial and military markets for new technologies, because DoD benefits from production economies of scale that help reduce the cost of new defense-related products. In addition, having a commercial marketplace helps ensure the ongoing development of the new technologies and also sustains production in between the spikes of military demand. Frequently, the commercial market is substantially larger than the military market for dual-use civilian/military products.

Sales by Company Size

A notable survey finding concerned company size. A common assumption is that large corporations, particularly large defense contractors, are the primary DoD technology transfer partners. However, this study determined that large corporations (with 500 or more employees) accounted for only 17 percent of all licenses achieving sales from their DoD license agreements. Small businesses (per the U.S. Small Business Administration definition, those with fewer than 500 employees) accounted for 83 percent of the licenses with sales (*see* Table 3). Within the small business category, "medium-sized" companies, with between 100 and 499 employees, accounted for 9 percent of the licenses with sales; "small" companies, with 10 to 99 employees, for 31 percent; and "very small" companies, with fewer than 10 employees, for 42 percent.

However, because of the previously mentioned top-selling drug, the large corporation category accounted for 82 percent of the total sales related to the DoD license agreements. If this product is excluded, the large corporation percentage drops to 41 percent, with small businesses accounting for 59 percent of the total sales.

Large corporations accounted for nearly 58 percent of the **U.S. military sales** resulting from DoD license agreements. This is because large defense contractors are the primary license holders of munitions technologies developed in DoD laboratories. Small companies accounted for the remaining 42 percent of the sales to the U.S. military. Within the small business category, "medium-sized" companies accounted for less than 3 percent of the military sales, "small" companies for not quite 17 percent, and "very small" companies for the remaining 23 percent.

Table 3. Sales by company size resulting from DoD license agreements, 2000-2014

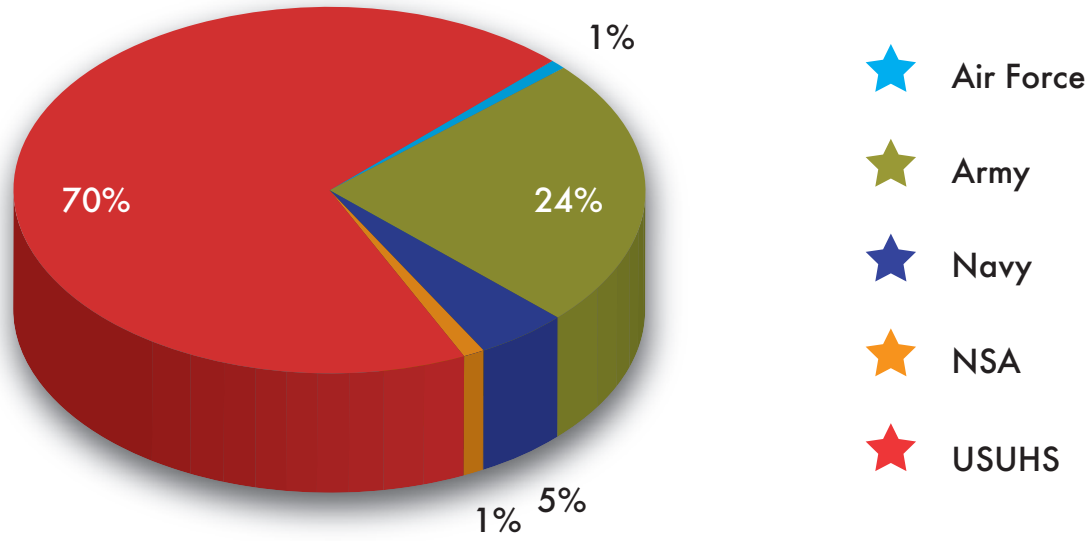
Company Size	Total Agreements with Sales	Percent of Total Agreements with Sales	Total Sales	U.S. Military Sales
Large (500 or more employees)	61	17	$16,722,169,461	$1,985,451,228
Small (<500 employees)	292	83	$3,720,057,750	$1,446,896,746
Medium-Size (100-499 employees)	30	9	$550,409,999	$86,048,000
Small (10-99 employees)	116	33	$992,463,276	$567,280,399
Very Small (1-9 employees)	146	41	$2,177,184,475	$793,568,347
Total	353	100	$20,442,227,211	$3,432,347,974

Source: Cumulative sales reported by companies to TechLink, Montana State University, during survey from January to September 2015.

Sales by Technology Source

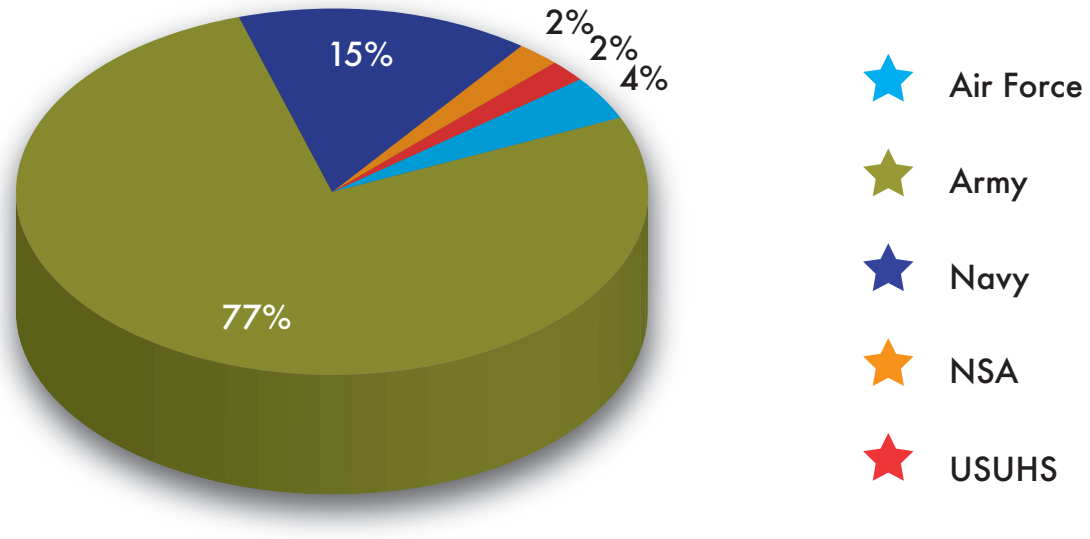
Figures 1 and 2 present the sales results by the DoD branch from which the licensed technology originated. The difference between the two charts is that Fig. 1 includes sales of Synagis related to the USUHS license agreement while Fig. 2 does not. Sales of technologies licensed from USUHS were approximately $14.221 billion, or nearly 70 percent of the total; from the Army, almost $4.9 billion, or 24 percent; from the Navy, $977 million, or 5 percent; from the Air Force, approximately $257 million, or slightly over 1 percent; and from the National Security Agency (NSA), $120 million, or less than 1 percent.

Figure 1. Sales Results by DoD Technology Source



When Synagis is excluded, the picture changes significantly (*see* Fig. 2). Sales of technologies licensed from the Army increase to 77 percent of the total; from the Navy, to 15 percent; from the Air Force, to 4 percent; and from the NSA to nearly 2 percent. The USUHS portion drops from 83 percent to just over 2 percent.

Figure 2. Revised Sales Results by DoD Technology Source *(Excluding Synagis)*



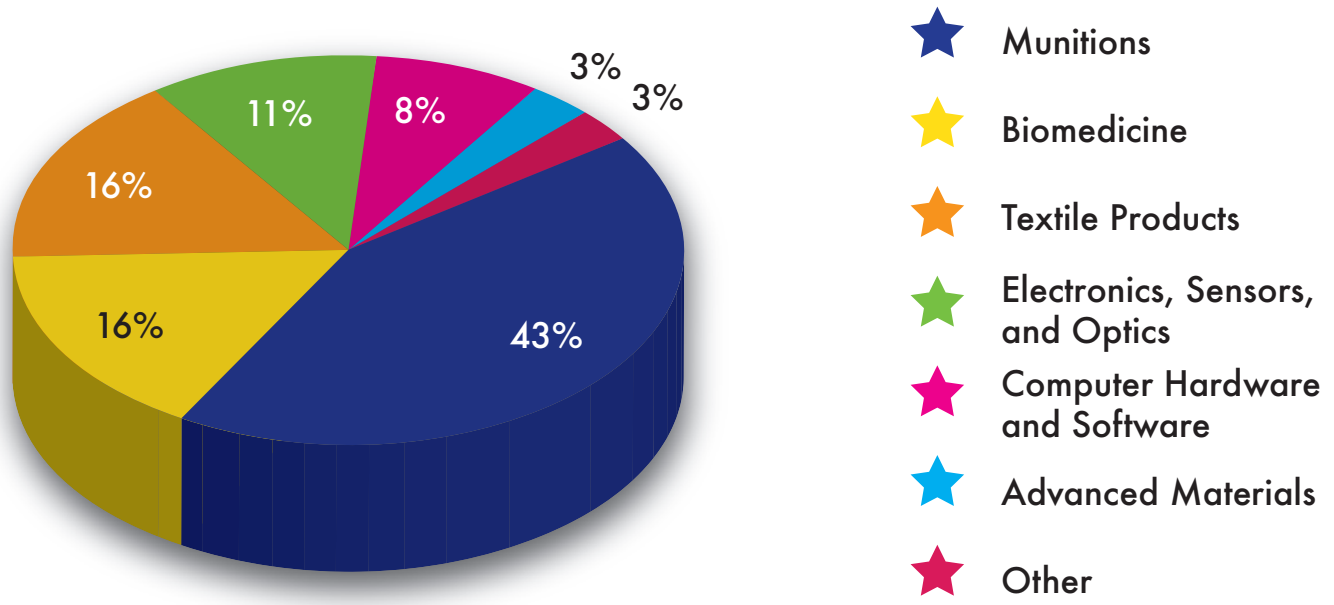
Sales by Technology Sector

Figure 3 presents the sales results by technology sector. It excludes the top-selling drug, Synagis, which otherwise would have caused the medical sector to dwarf all other sectors. **"Munitions"** comprised the largest sector, with 43 percent of the total sales (excluding Synagis). This sector consisted of various types of armaments and ammunition, including projectile tail cones for tank training rounds, a stabilizer for cannon projectiles, an improved grenade launcher, and weapon sighting devices. It was followed by the **"Textile Products"** and **"Biomedicine"** sectors, both comprising approximately 16 percent of the total sales. Textile products consisted primarily of backpacks and parachutes sold to the U.S. military. The Biomedicine sector encompassed a wide range of technologies that included preventative and therapeutic vaccines and drugs, diagnostic tests, medical devices, wound care products, antibodies used in research, and health-related software.

"Electronics, Sensors, and Optics" was the next largest sector at 11 percent. This also was a very broad sector and included technologies ranging from communications devices and antennas, to lasers and wearable transmission devices, to avionics diagnostics and sensors for environmental contaminants and biowarfare threats. The **"Computer Hardware and Software"** sector, with 8 percent of the total sales, included circuit designs, cybersecurity hardware and software, image processing algorithms and hardware, and all other software products outside of the medical field, including facilities and project management software programs.

"Advanced Materials" accounted for 3 percent of the total sales and ranged from metal coatings and specialized alloys to bullet-absorbing concrete and nanomaterials. The **"Other"** category, also accounting for 3 percent of the total sales, consisted of all technologies not included in the above sectors, primarily various types of mechanical devices.

Figure 3. Sales by DoD Technology Sector *(Excluding Synagis)*



Accuracy of Company Sales Information

Most companies in the study made a sincere effort to provide accurate responses to the questions posed about sales of new products and services related to their license agreements. Their responses ranged from highly detailed spreadsheets of sales figures, broken down by year, to verbal estimates of their cumulative sales, provided over the phone. The research team attempted to verify as much of the sales information as possible. However, this was possible for only a relatively small number of the license agreements. For most agreements, the companies themselves were the only source of information about their sales, including commercial and military sales of new products and services directly related to the licensed DoD technologies, R&D contracts to further develop these technologies, royalties from sublicensing the licensed DoD technologies, sublicensee sales of the licensed technologies, and sales of products or services embodying the licensed technologies by start-up or spin-out companies.

In an attempt to verify as many of the sales as possible, the research team employed Internet searches of the previously mentioned U.S. government contract and budget web sites and audited company annual reports. In addition, in the case of an Army lab that develops almost exclusively military technology and is closely tied to the procurement process, the research team was able to obtain highly accurate information on U.S. military and foreign military sales by the licensees (all major defense contractors), broken down by each year of the study period.

Using these methods, the research team was able to definitively verify the accuracy of approximately $17.6 billion of the $20.4 billion in total sales reported by companies. This represents 86 percent of the total sales. This means that even if the remaining 14 percent of unverified sale figures were off by a third, the reported $20.4 billion in total sales would be over 95 percent accurate. However, for the reasons summarized in the following section, the total sales figures reported are believed to significantly understate the reality.

Sales Figures Understate the Reality

For several reasons, total sales figures obtained by this survey understate the reality and are probably significantly smaller than the actual cumulative sales resulting from DoD license agreements during the 2000-2014 period. Reasons include the following:

- *Non-responding companies.* As previously noted, 82 companies with DoD license agreements active during the 2000-2014 period did not participate in the study—50 because they declined to participate and another 32 that could not be contacted because they had ceased to operate as corporate entities. Some companies in the first group are believed to be making sizeable commercial (non-military) sales of products based on the licensed technologies. While the research team was able to capture some of the U.S. military sales of these companies from Internet searches, it was unable to learn of any of their commercial sales.
- *Sub-licensee sales.* The total sales figures also underreport the reality because they do not include most of the sub-licensee sales. The TechLink team asked all companies if they had sublicensed the technologies that they had licensed from DoD. Many companies reported that they had. However, most of these companies declined to identify their sublicensees or to divulge what they knew of sublicensee sales. Some claimed that they were prevented from identifying sublicensees by the terms of their sublicensing agreements. Others simply declined to identify these sublicensees. Sublicensee sales of DoD-licensed technologies are probably substantial. For example, in 11 cases where licensees did report their sublicensee sales, the combined value was $443 million.[11]
- *Licensee underreporting of sales.* Another reason why the total reported sales are believed to be less than the actual sales is that underreporting is common in the licensing world. Historic royalty audit data from the Invotex Group, a well-established accounting and intellectual property management company, reveals that over 80 percent of licensees underreport and underpay royalties to their licensors.[12] There are various reasons why royalties are underreported. However, the Invotex Group found that at least half of the licenses it audited had underreported sales. Frequently, these involved next-generation products based on the licensed technology.
- *Inflation.* Finally, inflation contributes, in effect, to an underreporting of sales. All sales data are expressed in 2014 dollars, as previously discussed. However, some of the company sales date back to the early 2000s and most occurred prior to 2014. Use of 2014 as the reference year does not consider the higher value of the earlier sales figures. For example, a dollar in 2000 was worth 37 percent more than a dollar in 2014.

For all of the above reasons, the total sales figures reported in this survey are conservative and probably significantly understate the actual total sales resulting from DoD license agreements during the 2000-2014 period.

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[11] "Sublicensee sales" includes both direct product sales and R&D contracts related to the sublicensed technologies.

[12] D.R. Stewart and J.A. Byrd, "The Significance of Underreported Royalties-2007 Update: The Magnitude and Meaning of Royalty Misreporting," Invotex Group, Baltimore, MD, February 2007, online at: www.lawseminars.com/materials/07LICIL/licil%20m%20stewart2.pdf; D.R. Stewart and J.A. Byrd, "89% of Royalty Revenue is Underreported! Top Five Questions You Should Ask Your Licensee to Avoid Becoming a Statistic," Invotex Group, Baltimore, MD, April 2012, online at: http://nebula.wsimg.com/025008bfa2f13f473388c5848f4dd0c8?AccessKeyId=2ACC09671B2FE74DD41F&disposition=0&alloworigin=1

Other Economic Outcomes

In addition to sales, the companies in the study reported other significant economic outcomes. They reported approximately $609 million in total outside investment funding (including venture capital and angel funding) directly related to the licensed DoD technologies. In addition, 22 companies were acquired primarily because of their DoD license agreements, with a total acquisition value reported to be around $438 million. However, this figure certainly understates the actual value. A large majority of acquired companies stated that the terms of acquisition prevented them from disclosing the acquisition amount. Finally, companies in the study reported that they had sublicensed 48 technologies to other companies, and that they had created a total of 28 spin-out companies specifically to commercialize 29 of the licensed DoD technologies.

These other economic outcomes are summarized below:

- **Total outside investment funding:** **$609,285,000**
- **Number of companies that were acquired:** **22**
- **Total acquisition value of companies acquired:** **$438,000,000**
- **Number of DoD technologies sublicensed to other companies:** **48**
- **Number of spin-out companies created:** **28**
- **Number of technologies being commercialized by spin-outs:** **29**

ECONOMIC IMPACT ANALYSIS

Upon receiving the company sales and NAICS code data from TechLink, the Business Research Division at the University of Colorado Boulder employed IMPLAN to determine the economic contribution effects of the total sales figures. Results below are presented for output, value added, employment, labor income, and tax revenues. As previously noted, all dollar figures are reported in 2014 dollars.

Output

Output is the total value of purchases by intermediate and final consumers. According to the national IMPLAN model, the $20.4 billion (2014 $) in direct sales of new products and services reported by companies generated an additional $28.3 billion in sales economy-wide. Of this amount, approximately $15.2 billion was generated indirectly as the result of inter-industry purchases (firms purchasing from each other), and $13.1 billion was generated from the induced effect, the result of households spending payroll on goods and services economy-wide (*see* Table 4, p. 26). The total economy-wide output (the sum of direct, indirect, and induced sales) was $48.8 billion.

Dividing total economy-wide output ($48.8 billion) by the direct output of companies selling products and services related to their license agreements with DoD yielded an output multiplier of approximately 2.4. That is, for every dollar in sales directly attributable to the DoD license agreements, an additional $1.39 in sales was generated economy-wide.

Value Added

Value added is the difference between the value of an industry's or company's output and the cost of intermediate inputs. Expressed differently, it is the difference between a product's sale price and its production cost. This measure recognizes that companies buy goods and services from other companies in order to create products of greater value than the sum of the goods and services used to make these products. This increase in value resulting from the production process is the "value added." As estimated by IMPLAN, value added is equal to the total sales (plus or minus inventory adjustments) minus the cost of the goods and services purchased to produce the products sold.

The main difference between output and value added is that output includes the value of intermediate goods and services, while value added does not. Many economists prefer value added as an economic measure because, at the macroeconomic scale, output multiple-counts the value of inputs. For example, in the previously cited case of Company X, which sells an improved barcode scanner based on an Air Force laser invention: Company X purchases laser rods, electronic components, optical components, and various raw materials to make the barcode scanner. The value of Company X's sales incorporates the value of these laser rods and other inputs. Further, each of the companies from which Company X purchases its inputs incorporates the value of their respective inputs from other companies. By combining and aggregating the values of intermediate and final products, output overstates

the size of the U.S. economy by a factor of roughly 2. For this reason, Gross Domestic Product (GDP), a measure of value added, is used to track the size of the U.S. economy because it is a non-duplicative aggregation of production across all industries in the United States.

In the current study, value added measures the real contribution that each of the DoD technology transfer partners made to the national economy as a result of their license agreements with DoD. According to the national IMPLAN model, the $20.4 billion (2014 $) in sales reported by companies generated $23.9 billion in value added impact economy-wide. Of this total, $9.2 billion was generated directly, $7.6 billion was generated indirectly, and $7.1 billion was generated from the induced effect (*see* Table 4, p. 26).

Employment

According to the national IMPLAN model, an estimated 41,753 jobs were directly sustained economy-wide by the $20.4 billion in sales. Indirect effects were responsible for an additional 61,185 jobs, and induced effects for 80,047 jobs. The IMPLAN model estimates that, altogether, 182,985 jobs nationwide resulted from the direct, indirect, and induced effects of the DoD license agreements with U.S. industry during the 2000-2014 period. This means that, on average, the DoD license agreements generated approximately 12,199 jobs per year.

Using the procedure outlined above to derive the multiplier, an employment multiplier of 4.39 was calculated. That is, for every job directly attributable to the DoD license agreements, 3.39 additional job years were created or retained economy-wide. This substantial multiplier was mainly due to the relatively high-paying jobs associated with high-tech and technology-based industries, which accounted for the majority of the companies involved. That is, workers in these well-paying industries pumped more income back into the economy than lower-paid workers in other sectors, resulting in more job creation economy-wide.

Labor Income

Labor income consists of employee compensation (wage and salary payments, including benefits), paid to workers as well as proprietary income (income received by self-employed individuals). The national IMPLAN model estimated that labor income directly associated with the $20.4 billion in sales was $4.3 billion in 2014, or approximately $104,058 per job. This was more than double the average U.S. wage in 2014 of $46,482.[13]

The indirect labor income was estimated at $4.6 billion, or approximately $75,890 per job. The induced labor income was estimated to be $4.1 billion, or $50,789 per job. Average wages for the indirect and induced jobs were substantially lower than the average wage for the jobs directly created or retained because many of these additional jobs were in lower-paid manufacturing and service sectors. Together, the indirect and induced labor income amounted to $8.7 billion. The total economy-wide labor income resulting in 2014 from the DoD license agreements was $13.1 billion. The average wage of the approximately 182,985 jobs created or retained as a result of the DoD license agreements was $71,337, approximately 53 percent higher than the average U.S. wage of $46,482 in 2014.

The labor income multiplier was approximately 3.1, indicating that for every dollar in wage and salary income attributable to the DoD license agreements, an additional $2.10 was generated nationally in employee compensation and proprietary income.

[13] Per the Social Security Administration, https://www.ssa.gov/oact/cola/AWI.html

Tax Revenues

Tax revenues were estimated for the $20.4 billion in sales and their economy-wide indirect and induced effects. These tax revenues included social insurance taxes such as Social Security and Medicare (paid by employers, employees, and the self-employed), personal income taxes, motor vehicle licenses, property taxes, corporate profits taxes and dividends, and indirect business taxes (comprised mainly of excise and property taxes, fees, licenses, and sales taxes). Total taxes collected by federal, state, and local government entities were estimated at $1.6 billion. This included slightly over $1.2 billion in federal tax revenues and $400 million in state and local tax revenues. In sum, for every dollar of sales related to the DoD license agreements, an additional $0.08 was generated in federal, state, and local tax revenue.

SUMMARY

In summary, this study estimated the economic contribution to the U.S. economy of Department of Defense (DoD) license agreements in effect during the 2000-2014 period. Its purpose was to determine the extent to which these license agreements (1) contributed to new economic activity and job creation in the United States, and (2) resulted in the transition of new technology to U.S. military use.

The study surveyed 602 companies having license agreements with DoD during the 2000-2014 period. A total of 733 license agreements were involved because some companies had multiple agreements. Companies were asked to divulge the total sales of new products and services directly related to their DoD license agreements. They were also asked about their license-related sales to the U.S. military, either directly or through a defense contractor. Nearly half of the companies—353 out of 733—reported sales. Collectively, they reported slightly over $20.4 billion in total sales and $3.4 billion in military sales (in 2014 dollars).

IMPLAN economic impact assessment software was used to estimate the total economic impacts related to these sales. Impacts analyzed included economic output, value added, employment, labor income, and tax revenues. Total economy-wide sales, as measured by output, were estimated at $48.8 billion. Value added was estimated at $23.9 billion, representing new wealth creation in the economy. Employment impacts included 182,985 jobs with an average wage of $71,337. Labor income in 2014 was estimated at $13.1 billion. The $20.4 billion in sales and its economy-wide effects generated approximately $1.6 billion in federal, state, and local tax revenues. Table 4 summarizes the total economic contribution of the DoD license agreements with U.S. industry.

$20.4 B
Total sales
new products & services

$48.8 B
Total economic output

182,985
Full-time jobs created

$71,337
Average salary of
jobs created

Table 4. Nationwide Economic Impacts from DoD License Agreements, 2000-2014

Impact Type	Output *$ Billions*	Value Added *$ Billions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Billions*	Average Wage *(US = $46,482)*	Tax Revenue *$ Billions*
Direct Impact	$20.4	$9.2	41,753	$4.3	$104,058	
Indirect Impact	$15.2	$7.6	61,185	$4.6	$75,890	
Induced Impact	$13.1	$7.1	80,047	$4.1	$50,789	
Federal Tax Revenues						$1.2
State and Local Tax Revenues						$0.4
Total Economy-Wide Impact	$48.8	$23.9	182,985	$13.1	$71,337	$1.6

Source: BRD, University of Colorado Boulder; IMPLAN. Note: Totals may not tally due to rounding.

APPENDIX 1

National Economic Impacts by DoD Components

The following appended tables provide a more focused look at the economic impacts from DoD license agreements during the 2000-2014 period. These tables break out the economic impacts by selected DoD components from which the licensed technologies originated. These include the three DoD services—Army, Navy, and Air Force—as well as the National Security Agency, the Uniformed Services University of the Health Sciences, and selected DoD commands and laboratories that had at least four license agreements achieving sales and total sales exceeding $10 million. Breakouts for other DoD labs are not included for two reasons. First, revealing the outcomes of the limited number of license agreements from these labs could enable fairly accurate guesses about the sales of specific companies, violating the need to keep company sales information confidential. Second, the total sales related to their license agreements were usually too small and geographically concentrated to be legitimately analyzed by the national IMPLAN model. For explanation of the economic terms used in the appendices, please refer to the main text of the report.

Tables

Tables (cont.)

License Agreements, 2000-2014

Table 1. Air Force

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$257	$115	1,033	$85	$81,886
Indirect Impact	$212	$104	1,033	$68	$65,814
Induced Impact	$222	$121	1,358	$69	$50,784
Total Economy-Wide Impact	$691	$340	3,425	$222	$64,702

Table 2. Air Force Research Laboratory (AFRL)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$225	$100	938	$75	$79,759
Indirect Impact	$185	$91	915	$60	$65,196
Induced Impact	$196	$107	1,196	$61	$50,786
Total Economy-Wide Impact	$606	$298	3,049	$195	$64,021

Table 3. AFRL Aerospace Systems Directorate

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$114	$55	631	$43	$68,257
Indirect Impact	$102	$49	540	$33	$61,468
Induced Impact	$111	$60	678	$34	$50,780
Total Economy-Wide Impact	$327	$165	1,849	$111	$59,868

Table 4. AFRL Information Directorate

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$18	$9	69	$7	$104,395
Indirect Impact	$11	$6	60	$4	$65,229
Induced Impact	$16	$9	99	$5	$50,769
Total Economy-Wide Impact	$45	$24	227	$16	$70,760

License Agreements, 2000-2014

Table 5. AFRL Materials & Manufacturing Directorate

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$12	$6	38	$4	$96,294
Indirect Impact	$10	$5	49	$3	$65,462
Induced Impact	$10	$5	62	$3	$50,821
Total Economy-Wide Impact	$32	$16	148	$10	$67,331

Table 6. AFRL Space Vehicles Directorate, Kirtland AFB

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$11	$6	48	$5	$98,761
Indirect Impact	$8	$5	50	$3	$62,649
Induced Impact	$11	$6	69	$4	$50,775
Total Economy-Wide Impact	$31	$17	167	$11	$68,002

Table 7. AFRL 711th Human Performance Wing

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$65	$23	141	$15	$105,825
Indirect Impact	$51	$24	201	$15	$75,439
Induced Impact	$44	$24	268	$14	$50,803
Total Economy-Wide Impact	$160	$71	610	$44	$71,623

Table 8. Army

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$4,866	$2,119	18,005	$1,266	$70,320
Indirect Impact	$4,457	$1,988	17,415	$1,231	$70,716
Induced Impact	$3,643	$1,985	22,268	$1,131	$50,790
Total Economy-Wide Impact	$12,966	$6,092	57,687	$3,629	$62,901

License Agreements, 2000-2014

Table 9. Army Research, Development and Engineering Command (RDECOM)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$3,966	$1,698	14,804	$976	$65,900
Indirect Impact	$3,747	$1,621	14,140	$1,002	$70,856
Induced Impact	$2,886	$1,572	17,637	$896	$50,790
Total Economy-Wide Impact	$10,598	$4,891	46,581	$2,873	$61,683

Table 10. Army Armament Research, Development and Engineering Center (ARDEC)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$2,487	$1,103	6,266	$483	$77,157
Indirect Impact	$2,281	$1,007	8,712	$620	$71,132
Induced Impact	$1,612	$878	9,851	$500	$50,792
Total Economy-Wide Impact	$6,379	$2,988	24,829	$1,604	$64,582

Table 11. Army Edgewood Chemical Biological Center

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$33	$17	115	$12	$104,821
Indirect Impact	$25	$13	121	$8	$64,365
Induced Impact	$29	$16	177	$9	$50,778
Total Economy-Wide Impact	$86	$45	414	$29	$69,832

Table 12. Army Natick Soldier Research, Development and Engineering Center

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$971	$377	6,632	$322	$48,538
Indirect Impact	$1,012	$403	3,621	$250	$69,005
Induced Impact	$832	$454	5,089	$258	$50,786
Total Economy-Wide Impact	$2,816	$1,234	15,342	$830	$54,114

License Agreements, 2000-2014

Table 13. Army Research Laboratory (ARL)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$323	$130	1,264	$108	$85,365
Indirect Impact	$291	$134	1,157	$84	$72,225
Induced Impact	$279	$152	1,708	$87	$50,794
Total Economy-Wide Impact	$894	$417	4,129	$278	$67,384

Table 14. Army Corps of Engineers

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$193	$81	949	$63	$66,722
Indirect Impact	$182	$87	834	$55	$65,610
Induced Impact	$172	$94	1,052	$53	$50,785
Total Economy-Wide Impact	$547	$262	2,836	$172	$60,482

Table 15. Army Corps of Engineers, Construction Engineering Research Laboratory

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$47	$28	230	$25	$107,110
Indirect Impact	$29	$17	178	$11	$61,826
Induced Impact	$52	$28	318	$16	$50,791
Total Economy-Wide Impact	$128	$74	726	$52	$71,358

Table 16. Army Corps of Engineers, Geotechnical and Structures Laboratory

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$129	$47	645	$34	$52,923
Indirect Impact	$133	$62	591	$39	$66,136
Induced Impact	$107	$58	653	$33	$50,787
Total Economy-Wide Impact	$369	$167	1,890	$106	$56,319

License Agreements, 2000-2014

Table 17. Army Medical and Materiel Command (USAMRMC)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$730	$346	2,102	$221	$104,992
Indirect Impact	$551	$293	2,514	$183	$72,995
Induced Impact	$589	$321	3,598	$183	$50,789
Total Economy-Wide Impact	$1,870	$960	8,213	$587	$71,458

Table 18. Army Medical Materiel Development Activity (USAMMDA)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$75	$33	335	$16	$47,714
Indirect Impact	$65	$34	279	$22	$78,132
Induced Impact	$55	$30	337	$17	$50,784
Total Economy-Wide Impact	$195	$96	951	$55	$57,732

Table 19. Army Medical Research Institute of Infectious Diseases (USAMRIID)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$500	$240	1,096	$149	$135,651
Indirect Impact	$361	$192	1,583	$119	$75,354
Induced Impact	$390	$213	2,386	$121	$50,789
Total Economy-Wide Impact	$1,252	$644	5,065	$389	$76,835

Table 20. Walter Reed Army Institute of Research (WRAIR)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$128	$61	575	$47	$81,157
Indirect Impact	$104	$55	534	$35	$64,977
Induced Impact	$118	$65	724	$37	$50,790
Total Economy-Wide Impact	$350	$180	1,833	$118	$64,450

License Agreements, 2000-2014

Table 21. National Security Agency

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$120	$46	231	$28	$120,754
Indirect Impact	$130	$61	514	$38	$73,683
Induced Impact	$96	$52	586	$30	$50,787
Total Economy-Wide Impact	$346	$160	1,330	$95	$71,769

Table 22. Navy

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$977.3	$431.2	3,425	$345.9	$101,004
Indirect Impact	$811.4	$421.3	4,113	$269.5	$65,511
Induced Impact	$896.4	$488.4	5,479	$278.3	$50,788
Total Economy-Wide Impact	$2,685.0	$1,340.9	13,018	$893.7	$68,653

Table 23. Naval Air Systems Command

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$171	$72	432	$52	$119,220
Indirect Impact	$155	$75	670	$47	$70,433
Induced Impact	$144	$78	879	$45	$50,787
Total Economy-Wide Impact	$470	$225	1,981	$143	$72,362

Table 24. Naval Air Warfare Center, Aircraft Division (NAWCAD)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$130	$50	278	$36	$127,858
Indirect Impact	$125	$57	486	$35	$73,100
Induced Impact	$104	$56	633	$32	$50,795
Total Economy-Wide Impact	$358	$163	1,397	$103	$73,902

License Agreements, 2000-2014

Table 25. Naval Facilities Engineering and Expeditionary Warfare Center

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$69	$37	420	$38	$89,304
Indirect Impact	$48	$27	310	$19	$60,877
Induced Impact	$82	$45	502	$25	$50,780
Total Economy-Wide Impact	$200	$109	1,232	$82	$66,463

Table 26. Naval Medical Research Center (NMRC)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$44	$23	160	$17	$103,840
Indirect Impact	$32	$19	194	$12	$63,243
Induced Impact	$42	$23	257	$13	$50,786
Total Economy-Wide Impact	$119	$65	611	$42	$68,630

Table 27. Naval Research Laboratory (NRL)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$479	$217	1,733	$175	$100,843
Indirect Impact	$381	$196	1,885	$126	$66,855
Induced Impact	$438	$239	2,678	$136	$50,789
Total Economy-Wide Impact	$1,297	$652	6,296	$437	$69,378

Table 28. Naval Sea Systems Command

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$175	$65	557	$53	$95,158
Indirect Impact	$162	$88	906	$55	$60,276
Induced Impact	$157	$85	958	$49	$50,787
Total Economy-Wide Impact	$493	$238	2,420	$156	$64,549

License Agreements, 2000-2014

Table 29. Naval Surface Warfare Center, Carderock Division

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$16	$7	60	$5	$76,712
Indirect Impact	$12	$6	57	$4	$64,678
Induced Impact	$12	$7	74	$4	$50,821
Total Economy-Wide Impact	$40	$19	191	$12	$63,115

Table 30. Naval Surface Warfare Center, Crane Division

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$13	$6	36	$3	$78,960
Indirect Impact	$12	$5	47	$3	$69,870
Induced Impact	$9	$5	55	$3	$50,797
Total Economy-Wide Impact	$34	$16	138	$9	$64,696

Table 31. Naval Undersea Warfare Center, Division Newport

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$137	$50	427	$43	$100,345
Indirect Impact	$129	$72	761	$45	$58,917
Induced Impact	$128	$70	780	$40	$50,790
Total Economy-Wide Impact	$393	$191	1,968	$127	$64,678

Table 32. Space and Naval Warfare Systems Center Pacific

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$33	$14	98	$10	$101,655
Indirect Impact	$28	$14	120	$9	$72,734
Induced Impact	$27	$15	166	$8	$50,801
Total Economy-Wide Impact	$88	$43	384	$27	$70,588

License Agreements, 2000-2014

Table 33. Uniformed Services University of the Health Sciences (USUHS)

Impact Type	Output *$ Millions*	Value Added *$ Millions*	Employment *(Number of jobs created or retained)*	Labor Income *$ Millions*	Average Wage *(US = $46,482)*
Direct Impact	$14,221	$6,485	19,065	$2,621	$137,465
Indirect Impact	$9,608	$5,036	38,114	$3,037	$79,672
Induced Impact	$8,240	$4,489	50,363	$2,558	$50,789
Total Economy-Wide Impact	$32,069	$16,011	107,542	$8,215	$76,392

Source of the information in the tables is: TechLink survey of licensees, January to September 2015; BRD, University of Colorado Boulder; IMPLAN.
Note: "Employment" is measured in job-years. Totals may not tally due to rounding.

APPENDIX 2

Comparison of Results: 2015 vs. 2012 DoD Licensing Economic Impact Studies

The current study is an update of a similar study undertaken in 2012. That study focused on the economic impacts from DoD license agreements during the 2000-2011 period. This study extends the timeframe by three years, covering the period through 2014. The methodology used in these two studies was essentially the same. Differences in the total and U.S. military sales are primarily a function of the longer time period for the latest study. An additional 131 license agreements were established during the intervening three years—a 22 percent increase in the number of active agreements. More important, previously established agreements had three additional years in which to come to fruition or further accumulate sales. The differences in the value added, total economic output, and employment reflect these changes in sales and also are a function of the differences in the IMPLAN models used (2011 vs. 2014).

$13.4B → $20.4B = 52%

in sales 2012 → in sales 2015 = increase

Table 1. Comparison of 2012 and 2015 DoD Licensing Economic Impact Study Results

	2012 Economic Impact Study	2015 Economic Impact Study	Percentage Increase
Total Sales, New products and services	$13.4 Billion	$20.4 Billion	52
Sales to U.S. Military	$1.3 Billion	$3.4 Billion	162
Value Added	$17.4 Billion	$23.9 Billion	37
Total Economic Output nationwide	$36.3 Billion	$48.8 Billion	34
Full-Time Jobs created or retained	163,067	182,985	12

INFORMATION PAPER—SUPPLEMENT & DISCUSSION
March-in Rights Request by KEI to NIH and DoD Pertaining to Xtandi®

APPENDIX G
GAO Report 09-742, Federal Research: Information on the Government's Right to Assert Ownership Control over Federally Funded Inventions

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United States Government Accountability Office

GAO

Report to Congressional Committees

July 2009

FEDERAL RESEARCH

Information on the Government's Right to Assert Ownership Control over Federally Funded Inventions

GAO-09-742

July 2009

FEDERAL RESEARCH

Information on the Government's Right to Assert Ownership Control over Federally Funded Inventions

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Highlights

Highlights of GAO-09-742, a report to congressional committees

Why GAO Did This Study

The Bayh-Dole Act, passed in 1980, allows recipients of federal research funds the option to retain patents on any inventions they create using those funds. At the same time, the act provides the government with rights intended to ensure that the public benefits from these federal research investments. One of these rights is known as the "march-in" authority, which allows federal agencies to take control of a patent when they have credible information that certain conditions described in the act have been met.

Until March 2009, the Bayh-Dole Act required GAO to report periodically on its implementation. To meet that requirement, for select federal agencies, GAO reviewed (1) the policies and procedures used to determine whether march-in authority should be exercised; (2) how the march-in authority has been used; and (3) what barriers and disincentives have been encountered in exercising the march-in authority.

GAO selected four agencies for this review that accounted for 89 percent of the federal research funding for fiscal year 2006. These were the Departments of Defense and Energy (DOD and DOE), the National Aeronautics and Space Administration (NASA), and the National Institutes of Health (NIH).

GAO is not making any recommendations in this report. DOE, NASA, and NIH provided technical comments on this report that GAO incorporated, as appropriate.

View GAO-09-742 or key components.
For more information, contact Ms. Anu K. Mittal at (202) 512-3841 or mittala@gao.gov.

What GAO Found

Officials at DOD, DOE, NASA, and NIH rely on Commerce regulations for the Bayh-Dole Act and on their agencies' interpretations of the act to determine whether to exercise their march-in authority. Agency officials said that the administrative processes developed by Commerce are detailed and time-consuming, and may make it difficult to initiate and exercise a march-in proceeding. However, some officials said the detailed regulations ensure that appropriate and fair processes are followed during march-in proceedings. The agencies have chosen not to develop agency-specific guidance for a variety of reasons. For example, none of the officials believe that the regulations are onerous enough to warrant the development of agency-specific guidance and agency-specific guidance would reduce the flexibility agencies have to examine the specific circumstances of each case. In addition, an array of agency-specific regulations could hinder the transfer of research results to the market by increasing the regulatory burden on recipients of federal research funds.

None of the four agencies has chosen to exercise march-in authority. DOD, DOE, and NASA have neither discovered nor received information that would lead them to initiate a march-in proceeding or exercise their march-in authority during the last 20 years. In contrast, NIH has been petitioned formally three times, but in each case determined that the statutory requirements for march-in proceedings had not been met. Nevertheless, officials at DOD, NASA, and NIH said they value the authority because it provides leverage to promote commercialization of federally funded inventions. DOE officials disagree, in part, because no agency has ever exercised the authority. Agency officials said they do not have ongoing efforts to identify potential candidates for a march-in proceeding and primarily rely on the public, including potential competitors, to provide information that could lead to a march-in proceeding. According to these officials, their agencies would have to expend significant additional resources to track federally funded inventions because of the large number of inventions and because commercialization can take many years. Officials at DOD, NASA, and NIH said they value the march-in authority because it helps ensure that federally sponsored research results are commercialized. Also march-in authority is not the only tool to achieve the goals of the Bayh-Dole Act. For example, the government can take a patent without a license subject to reasonable compensation being paid to the patent owner or licensee that may allow for more timely interventions than would occur under the Bayh-Dole march-in process.

Federal and technology transfer officials identified four disincentives to the use of march-in authority. One of these is that the use of the march-in authority could have a "chilling effect" on federal research. These officials said that if a march-in occurred, investors would be less likely to provide the funds to commercialize federal inventions for fear of losing their investments. Also, because the march-in process can be long, these officials believe that it would have limited utility in an emergency situation. For example, the time to complete the fact-finding process in the three cases NIH reviewed ranged from 5 to 8 months.

Contents

Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
DOD	Department of Defense
DOE	Department of Energy
GAO	Government Accountability Office
HIV	Human Immunodeficiency Virus
NASA	National Aeronautics and Space Administration
NSF	National Science Foundation
NIH	National Institutes of Health
NIST	National Institute of Standards and Technology

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United States Government Accountability Office
Washington, DC 20548

July 27, 2009

The Honorable Patrick J. Leahy
Chairman
The Honorable Jeff Sessions
Ranking Member
Committee on the Judiciary
United States Senate

The Honorable John Conyers, Jr.
Chairman
The Honorable Lamar Smith
Ranking Member
Committee on the Judiciary
House of Representatives

Technological innovation is widely seen as responsible for much of the economic growth and increased standard of living in modern societies. Patent rights give inventors, or other patent owners, exclusive control over the use of their inventions for about 20 years, which promotes commercialization of new ideas and allows inventors to profit from their ideas. Patent rights ownership encourages the additional, and often substantial, investment of time and money needed to transform the technological innovations developed in the laboratory into goods, services, and processes available in the marketplace. Patent owners—including individuals, companies, and universities—may grant licenses to one or more businesses to complete this transformation and, in return, receive payments in the form of license fees or royalties.

The federal government supports technological innovation through a wide range of research activities that focus on the mission needs of various departments and agencies. In addition, it supports work in areas where a specific need has been identified that the private sector has not addressed. Although the largest share of research funding comes from the private sector, the federal government funds a majority of the nation's basic research, which produces the innovations that drive technological progress. Moreover, federal support accounts for over half of the research conducted at colleges and universities in the United States. Because the public benefits when technological advances are transformed into new goods and services in the marketplace, the federal government has an interest in facilitating the commercialization of new inventions that arise from the research that it funds.

Since its enactment in 1980, the Bayh-Dole Act has provided recipients of federal research and development funding—often referred to as contractors—the option to retain patents on the inventions they create, provided they adhere to certain requirements.[1] A main goal of the act is to promote the utilization of inventions arising from federally supported research or development, and observers have judged the act a success in this regard. Prior to 1980, when the government routinely retained the patents on federally sponsored inventions, only 5 percent of these patents were ever used in the private sector. In contrast, some stakeholders, including federal and technology transfer officials, today believe inventions that arise from federally funded research are routinely commercialized, although comprehensive data are not available on how often this happens. Each federal agency that enters into funding agreements subject to the Bayh-Dole Act is responsible for administering the act's requirements and the implementing regulations developed by the Department of Commerce.

The Bayh-Dole Act also provides the federal government with certain rights to protect the public against nonuse or unreasonable use of federally funded inventions. One of these rights, known as the "march-in" authority, authorizes federal agencies, at their discretion, to require the contractor or licensee to grant a license to any responsible entity or entities when credible information exists that certain statutory conditions in the act have been met. For example, an agency may march in if it determines that an inventor is not taking the necessary steps toward commercialization of the technology, or that such action is needed to meet public health or safety needs. [2]

Until recently, the Bayh-Dole Act also contained a requirement that GAO issue a report on how agencies have implemented the act's provisions at least once every 5 years. In consultation with your offices we began work

[1]The term "contractor" means any person, small business firm, or nonprofit organization that is a party to a federal funding agreement, which includes contracts, grants, or cooperative agreements for the performance of experimental, developmental, or research work.

[2]The two additional statutory conditions under which agencies may exercise march-in authority are (1) the use of an invention is required by the federal government and the contractor cannot meet the government's requirements; and (2) the patent owner or exclusive licensee has failed to take certain steps to ensure that any products embodying the invention or produced through the use of the invention will be manufactured substantially in the United States.

on this review to meet that reporting requirement. However, subsequent to our initiating this review, the Omnibus Appropriations Act for fiscal year 2009, eliminated the recurring study requirement on March 11, 2009.[3] As agreed with your offices, we have completed this review and addressed the following objectives: (1) what policies and procedures have federal agencies with significant research budgets established to determine whether march-in authority under the Bayh-Dole Act should be exercised; (2) to what extent have these selected federal research agencies used Bayh-Dole march-in authority and what do they believe are its benefits; and (3) what barriers and disincentives, if any, have these agencies encountered to the exercise of their march-in authority under the Bayh-Dole Act.

To determine which agencies to focus our review on, we analyzed federal research and development budgets for all federal research agencies. We selected the Department of Defense (DOD), the Department of Energy (DOE), the National Aeronautics and Space Administration (NASA), and the National Institutes of Health (NIH) within the Department of Health and Human Services because together they accounted for 89 percent of the total federal research funding for fiscal year 2006—the most recent year for which complete data were available. For each of the objectives, we reviewed key agency documents and interviewed officials from the technology transfer offices of each agency. In addition, for each of the objectives we spoke with officials in stakeholder groups such as the Association of University Technology Managers, the Biotechnology Industry Organization, and the American Intellectual Property Law Association, as well as academics who have evaluated the Bayh-Dole Act.

We conducted our work from November 2008 to July 2009 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

[3]Pub. L. No. 111-8, Div. G, Title I, section 1301(h), 123 Stat. 829 (2009).

Background

The Bayh-Dole Act was enacted in 1980, in part, to address the low utilization rate of federal patents. At the time the bill was considered, 26 different federal agency policies existed regarding the use of results from federally funded research. Prior to Bayh-Dole's enactment, agencies frequently retained title to inventions made with federal support whether the research was performed in federal laboratories, in universities, or by individual companies. Licenses to use and further commercialize the patents on federally funded inventions were then negotiated with firms typically on a non-exclusive basis or, more rarely, for the exclusive use by one manufacturer. The Bayh-Dole Act established a governmentwide policy that gave contractors the opportunity to retain ownership of federally funded inventions. In addition, it was designed to use the patent system to promote the utilization of inventions arising from federally supported research or development and to encourage maximum participation of small business firms in federally supported research and development efforts, among other things. Many experts continue to believe that certainty in the ownership of patents and exclusivity in the right to develop the related technology are important for both large and small firms.[4]

In exchange for the right to retain ownership of federally sponsored inventions under the Bayh-Dole Act, contractors must agree to certain reporting requirements. More specifically, contractors agree to notify the funding agency within 2 months after the contractor learns that an invention has been created and to notify the funding agency within 2 years after this notification of the contractor's decision to retain title to the invention. In addition, contractors agree to apply for a patent on the invention typically within 1 year of the election of title, attempt to commercialize the invention, and to provide additional reports. These additional reports, if requested by the agency, can provide such information as utilization of the invention and patent-related information such as the filing date, patent application number and title, and patent number and issue date for the invention in any country in which the contractor has applied for a patent. Failure by the contractor to disclose the invention, elect title to it, or file a patent application within the times

[4]The Bayh-Dole Act by its terms applies to universities, non-profit organizations, and small businesses that receive federal research funding. A presidential memorandum in 1983, followed by an Executive Order in 1987, directed federal agencies, to the extent permitted by law, to establish policies for all businesses that are substantially the same as those contained in the Bayh-Dole Act.

specified, or failure to follow through with the patent application process, allows the relevant federal agency to obtain ownership of the invention.

The Bayh-Dole Act also reserved certain rights for the government to protect the public's interests. Specifically, the government retains "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," also known as a nonexclusive royalty-free license. In addition, the act provides the government march-in authority. Under this authority, the federal agency that funded the development of an invention has the right to require the contractor or exclusive licensee to grant a license in any field of use to a responsible applicant upon terms that are reasonable under the circumstances, if the agency determines that:

- the contractor has not made, and is not expected to make, efforts to commercialize the invention within an agreed upon time frame;
- public health or safety needs are not reasonably satisfied by the contractor or licensee;
- the use of the invention is required by the federal government and the contractor or licensee cannot meet the government's requirements; or
- the owner of an exclusive license is not ensuring that the invention is "manufactured substantially" in the United States and has not obtained the necessary waivers to do so.

Implementation of the Bayh-Dole Act is decentralized across the federal government. Each federal agency that enters into funding agreements subject to the Bayh-Dole Act is responsible for administering the act's requirements. However, the act directs the Department of Commerce to develop regulations to implement the provisions contained in the act, including procedures for agencies to follow regarding the exercise of the march-in authority.[5] The regulations Commerce issued in 1987 also allow agencies to develop supplemental procedures regarding their march-in authority. Although Commerce does not maintain any overall Bayh-Dole

[5]As originally enacted, the act required the Office of Federal Procurement Policy to develop these regulations. In 1984 Congress transferred this regulatory authority to the Department of Commerce. Pub. L. No. 98-620, § 501(10), 1984.

databases, other agencies rely on Commerce as a coordinator and consultant for Bayh-Dole related issues.

The regulations established by Commerce detail the procedures an agency must follow when it receives information that it believes might warrant the exercise of march-in rights. Specifically, the agency must notify the contractor, in writing, that it has information it believes might warrant the exercise of its march-in authority. As part of this notification, the agency is to provide the contractor 30 days to respond informally, either verbally or in writing, with relevant information. Once the agency has received the contractor's response, it may initiate the march-in procedures within 60 days through written notice to the contractor and its assignee or exclusive licensee, as appropriate and if known to the agency. The notice must include the reasons for the proposed march-in and the specific uses of the invention for which the agency may require licensing. Within 30 days after receiving written notice of the proposed march-in proceeding, the contractor may submit information opposing the proposed march-in to the agency in person, in writing, or through a representative. If the agency determines that the contractor's information raises a dispute over the facts of the case, it must undertake a fact-finding process that gives the contractor the opportunity to appear with counsel, submit documents, present witnesses, and question individuals presented by the agency. The results of the fact-finding process and a recommendation are presented to the head of the agency (or his or her designee) as well as to the contractor. Both the agency and the contractor have 30 days to submit written arguments to the head of the agency or designee. In addition, the contractor may request to present oral arguments. Within 90 days after the completion of the fact-finding or oral arguments, whichever is later, the agency must provide a written decision regarding whether march-in rights will be exercised. Any decision unfavorable to the contractor will be held in abeyance pending the exhaustion of the contractor's administrative and judicial appeals. At any point, the agency may terminate the fact-finding process if it decides not to exercise its march-in authority.

The time from when an agency announces a funding opportunity to the time a viable commercial product reaches the marketplace may take many years and substantial financial investment. During the period of agency funding, which may last 8 to 10 years for drugs and biologics, the agency's program, procurement, and/or grants office monitors the progress of the research and maintains contact with the contractor. In fiscal year 2007 federal agencies devoted $116 billion to conduct research on various topics related to their respective missions. Pharmaceutical-related inventions, which may arise from research sponsored by NIH, may require

an additional 10 to 15 years after the invention is made to obtain the federal approvals necessary to reach the market. According to industry officials, pharmaceutical-related inventions may require an investment of between $800 million and $1.3 billion to conduct the safety and other studies required for approval.

Additional time may be required to obtain a patent on the invention and to develop a market ready process or product. [6] More specifically, the U.S. Patent and Trademark Office issues a patent in 32 months, on average, but the time ranges from 28 months for inventions in the fields of semiconductors and electrical items to almost 44 months for computer software and communications inventions. Once a patent is granted, the patent owner has, in most instances, a period of 20 years from the date the application was filed during which time the patent owner has the right to exclude others from making, using, or selling the patented invention.

Federal Agencies Use Department of Commerce Regulations to Implement the March-in Authority under the Bayh-Dole Act

Officials at DOD, DOE, NASA, and NIH rely on Commerce regulations for the Bayh-Dole Act and on their agencies' interpretations of the act to determine whether to exercise their march-in authority. These officials told us that the administrative processes developed by Commerce for agencies to use when considering whether marching-in may be warranted are detailed and time-consuming, and may make it difficult to initiate a march-in proceeding. However, some officials also acknowledged that because the regulations are detailed, they ensure that appropriate and fair processes are followed during march-in proceedings. One official noted that there is no way to pre-empt the process and retain the necessary legal protections for all of the participants in the process. According to this official, the regulations, while detailed and time-consuming, allow everyone to be heard during the process. For example, during the fact-finding procedure the contractor has the opportunity to appear with counsel, submit documentary evidence, present witnesses, and cross-examine witnesses who the agency presents. Moreover, both the contractor and agency staff have an opportunity to rebut an agency's decision and contractors may appeal adverse decisions to the federal courts, which delays action on the agency's decision until the appeals process is concluded.

[6]The time required to obtain a patent may overlap with the period of federal funding for the research.

However, according to agency officials we spoke with, the agencies have chosen not to develop agency-specific guidance for a variety of reasons. First, none of the agency officials we spoke with believe that the regulations developed by Commerce are onerous enough to warrant the development of agency-specific guidance. Second, both agency and technology transfer officials told us that agency-specific guidance would, in essence, pre-define how the federal government would exercise its march-in authority and reduce the flexibility agencies have to examine the specific circumstances of each individual case. Third, federal officials—as well as officials from organizations that represent technology transfer offices in colleges and universities—told us that creating an array of agency-specific regulations could hinder the transfer of research results to the market by increasing the regulatory burden on contractors.[7] For example, one technology transfer official said that many universities receive funding concurrently from more than one federal agency. In such cases, these contractors could be required to follow a different set of regulations from each of their agency partners. As a result, these officials believe that Commerce should remain in charge of developing march-in regulations, rather than have individual agencies issue their own policies and procedures. Finally, technology transfer officials we spoke to also said that march-in regulations should be centralized at a high enough level to ensure consistency among federal research agencies in their march-in decisions.

Until August 2007, if federal agencies or contractors had any questions concerning Bayh-Dole Act implementation issues, including march–in procedures, they generally coordinated with officials in Commerce's Technology Administration. However, since August 2007, as a result of changes mandated by the America COMPETES Act, the Technology Administration has been disbanded and Commerce has shifted responsibility for the Bayh-Dole Act to the National Institute of Standards and Technology (NIST). Officials from two technology transfer organizations told us that, as a result of this change, the department currently has little expertise on the march-in process. Specifically, technology transfer officials told us they were concerned that NIST did not have the knowledge and experience of the Technology Administration with regard to oversight of march-in procedures and officials at one

[7]Throughout this report we refer to officials from organizations that represent technology transfer offices in colleges and universities as technology transfer officials.

organization believed that this might cause some ambiguity in facilitating agencies' implementation of the act.

NIST officials acknowledged that no one currently in their office has any experience with the march-in authority and said the process appears to be very time-consuming and complex. However, these officials told us that when the Technology Administration was disbanded, the same lawyers who worked on Bayh-Dole issues continued to provide their services, which allowed continuity in the overall legal aspects of oversight for the act. They also noted that most of the questions they have addressed for agencies concern aspects of the act other than the march-in authority. They also believe that because agencies are not required to contact NIST with questions related to the Bayh-Dole Act, that NIST's role in any future march-in proceedings will likely be very limited.

None of the Agencies We Reviewed Has Used March-in Authority, but Three Value It as a Way to Promote Commercialization of Inventions

None of the four agencies we reviewed has chosen to exercise march-in authority under the Bayh-Dole Act. DOD, DOE, and NASA have neither discovered nor received information that would lead them to initiate a march-in proceeding or exercise their march-in authority during the last 20 years. In contrast, NIH has been petitioned formally to exercise its march-in authority three times, but in each case determined that the statutory requirements for march-in proceedings had not been met. Nevertheless, officials at three of the four agencies told us they value the authority because, together with other tools, it provides them leverage to promote commercialization of federally funded inventions. In contrast, DOE officials do not believe march-in authority has significant value as leverage, in part, because no agency has ever exercised the authority.

Officials at all four agencies included in our review acknowledged that their agencies have not conducted any march-in proceedings. They further acknowledged that while they monitor contractors' compliance with reporting requirements, their agencies do not have ongoing efforts to identify potential candidates for march-in proceedings from the wide-array of federally funded inventions. These officials told us that they primarily rely on public and private sources of information, including news reports, interest groups, and potential competitors, to provide them with information that could lead to a march-in proceeding. For example, according to one official, participants in the science and technology market are very aware of emerging technologies and information on patents is publicly available, which allows interested entities to know what inventions and technologies are being developed. In addition, companies employ technology scouts to report on the technologies being produced by

other companies. Officials told us that one source of information regarding a potential march-in proceeding could be a person or business that wants to enter into a licensing agreement but is unable to negotiate agreeable terms. However, they also acknowledged that such instances are generally uncommon because most contractors are very interested in licensing their inventions.

According to the agency officials we spoke with, relying on the public for information is a more efficient and effective mechanism for tracking federally funded inventions, which would otherwise require federal agencies to expend significant additional resources to monitor a large volume of federally funded inventions for possible situations that might lead to march-in proceedings. In fiscal year 2008, NIH provided 50,980 awards, worth about $21 billion, to 2,606 institutions. The agency's awards for the previous 5 fiscal years were steady at about this same level. Monitoring such a large number of awards and institutions would be very resource intense. Moreover, because many inventions require substantial investments of time to produce a market-ready product or process, agencies would need to monitor awards and their subsequent inventions over a number of years. For example, NIH officials said that pharmaceutical inventions may take as many as 14 years to reach the marketplace. In addition, although contractors report information on inventions that result from federally funded projects, they are not required to report information on progress toward commercialization of those inventions or other details of the licensing agreements they enter into, which are considered proprietary information. Consequently, agencies do not always receive information on the extent to which licensees are making progress toward commercialization of the inventions the agencies have funded. Officials also told us that proactive efforts to track federally funded inventions are further complicated by the fact that a single invention may result in multiple licensing agreements for different uses. For example, a contractor who owns a cancer treatment could license the technology to one entity to treat eye cancer and to another to treat liver cancer.

Since Congress enacted the Bayh-Dole Act in 1980, only NIH, of the four agencies we reviewed, has received formal march-in petitions—one in 1997 and two in 2004. In each of these cases, the agency determined after a 5- to 8-month fact-finding process that the circumstances did not meet any of the statutory conditions under which march in could occur. Specifically, in 1997, NIH received a petition in which the petitioner alleged that the invention's owner and exclusive licensee had failed to take reasonable measures to bring a stem cell separation device to market and that doing

so would alleviate patient health and safety needs. NIH found no basis to initiate a march-in proceeding because it determined that the invention's owner and exclusive licensee had taken effective steps to develop the device and that it was already being marketed. In 2004, NIH received two more petitions, in which the petitioner expressed concern that the price of two drugs—one to treat HIV/AIDS and the other to treat glaucoma—made them unaffordable for many people living with these diseases, posing a threat to their health and safety. However, NIH determined that the drugs were already on the market and widely prescribed, and therefore marching in would not alleviate health and safety needs that were not already being satisfied by the producer. NIH also stated in its decisions that drug pricing is an issue more appropriately left to the Congress.[8] Furthermore, as NIH noted in its decision on the 1997 petition, the agency is "wary of forced attempts to influence the marketplace for the benefit of a single company."

Although DOE has not been petitioned to exercise its march-in authority nor has it used the authority on its own, the department used the Bayh-Dole march-in framework to review a dispute brought by a company against a contractor and its exclusive licensee over the use of two inventions that could identify gene sequences. According to the company, the contractor and its licensee had not taken effective steps to achieve substantial utilization of the inventions, and had not given the requisite preference to small businesses. While this dispute did not arise under the Bayh-Dole Act, DOE suggested, and all parties agreed, to settle the dispute using the march-in procedures detailed in the Commerce regulations. During a 30-month fact-finding process, both parties to the dispute submitted evidence and counter evidence and reviewed the draft decision prior to its release. DOE decided not to march in based on its determination, among other things, that the terms of the exclusive license were fair and that the company making the allegations had failed to offer sufficient evidence to support its contentions.

Although none of the agencies we reviewed has actually used its authority to march in, officials in three of the four agencies we contacted said they value the authority and they do not want it eliminated because it helps to ensure that federally sponsored research results are commercialized. These officials told us that the march-in authority is particularly valuable

[8]In its decision on the drug for treating HIV/AIDS, NIH also stated that the Federal Trade Commission was the appropriate agency to address allegations that the drug manufacturer had engaged in anti-competitive practices.

as leverage in informal discussions between contractors and sponsoring agencies and in license negotiations between contractors and potential licensees to encourage commercialization of technologies developed with federal funding. However, neither the agencies we reviewed nor the technology transfer organizations we contacted maintain data on the extent to which the potential for a march-in proceeding is discussed informally during negotiations.

According to some agency and technology transfer officials, the parties to licensing negotiations are usually sufficiently aware of the potential for march-in that it may not be necessary to explicitly discuss this possibility during meetings. However, neither could provide us with any metrics by which they could measure this effect, and no data exist on the extent to which contractors or licensees are aware of the potential for an agency to march in and to what extent this influences their decisions. Executives from two bio-technology firms told us that they are well aware of the Bayh-Dole Act and its march-in provision. They consider the potential for a march-in as one of several business risks, but said it is not a subject they typically discuss during licensing negotiations. Nevertheless, according to one technology transfer official, an explicit discussion of march-in authority can provide effective leverage to push a company struggling to meet its obligation to pursue commercialization of a federally funded invention. DOE officials, on the other hand, said an awareness of the march-in authority did not appear to have much influence on its contractors and their licensees. DOE officials said their contractors generally produce inventions, processes, and technologies that are intended for the market and are already strongly motivated by potential profits to move forward quickly. Consequently, these officials said it is difficult to see how the potential for a march-in proceeding under the Bayh-Dole Act would provide an additional incentive to these contractors.

Although most of the officials we spoke with value the leverage that the march-in authority provides, they said they prefer to work with contractors informally to resolve commercialization issues. For example, NIH officials noted that contractors often resolve such issues—without agency involvement—by reviewing the milestones in the licensing agreement to determine whether the licensee has met its obligations, and if it has not, the contractor may adjust the terms of the agreement based on speed and results of the licensee's efforts or revoke the license and seek a new licensee. According to one NIH official, if NIH enters such discussions its mere involvement often serves as enough leverage to encourage resolution of the problem without resorting to an explicit mention of march-in. Similarly, DOD officials said that in the early 1990s,

during a patent-related dispute between two defense contractors, one of the companies raised the possibility of petitioning DOD for a march-in proceeding to settle the disagreement. DOD entered into informal discussions with both companies, then withdrew, and the companies subsequently resolved their dispute without petitioning for a march-in.

Some officials also told us that the march-in authority is not the only available tool to achieve commercialization goals for federal research efforts or to meet the government's needs. For example, NIH officials told us that one useful tool is the agency's guidance for contractors to use when negotiating license agreements. Contractors can enter into such agreements with parties who wish to commercialize an invention. The NIH guidance recommends including specific commercialization milestones and a termination clause to ensure that inventions are commercialized by licensees. For example, if an invention has a potential therapeutic use, the agreement may include requirements to reach federal approval for various clinical trials by certain dates, as well as the anticipated date of first sale. Technology transfer officials we spoke with said that the widespread use of commercialization milestones and termination clauses reduces the likelihood that an agency would need to march in because contractors are already assuring that commercialization is achieved.

The government can also use patented technology without a license subject to reasonable compensation being paid to the patent owner or licensee, regardless of whether the invention had been developed with federal funding. This allows the federal government to use an invention without a license, if the use is "by or for the United States." Further, under federal law if the federal government uses a patent, the patent owner or licensee may sue the government to recover reasonable compensation but may not stop the government from using the invention.[9] This option might be of greater value than the Bayh-Dole march-in authority in the case of a public health emergency because it allows for rapid action and it allows the government to use inventions that incorporate federally funded technologies as well as technologies that were not federally funded. In addition, officials told us that the Bayh-Dole Act itself contains another tool—the royalty-free license—that allows federal agencies to use federally funded inventions without risk of infringing the ownership rights of the contractor or licensee. For example, federal agencies may contract with a third party to manufacture products containing such inventions for,

[9] 28 U.S.C. § 1498(a).

or on behalf of, the government. However, if the product or process contained inventions that were not developed with federal funds, the government would need to negotiate a license to use them. Finally, some agencies, including DOD, DOE, and NASA, have been granted other statutory tools that provide additional flexibility to negotiate ownership terms with contractors. For example, all three have similar statutory authorities—called "other transaction authority"—that apply to certain research efforts conducted under contracts. DOD and DOE have used this authority to obtain cutting-edge research and prototypes for their use and NASA has used its authority to negotiate ownership rights that will foster the commercialization of inventive work produced under collaborative research projects that are not being conducted specifically for the agency.

Four Key Concerns May Create Disincentives to the Use of Bayh-Dole March-in Authority by Federal Agencies

Four key disincentives inhibit federal agencies use of Bayh-Dole march-in authority. First, the potential "chilling effect" that such an action might have could deter investors from investing in the commercialization of the research results and some researchers from participating in federal research efforts. Second, the lengthy march-in process could be unworkable in an emergency or other time-critical situation. Third, commercial products or processes based on federal inventions sometimes employ multiple patents, some of which are not federally funded. Such circumstances often pose difficult, if not intractable, issues that could make marching in unattractive for federal officials seeking to commercialize an invention. Finally, agencies might be disinclined to march in if current licensees have specialized knowledge that makes them particularly well positioned to bring a product to market, and if the loss of such knowledge through a march-in proceeding might jeopardize the commercialization of an invention. This section further describes these four disincentives.

Some agency, university, and industry officials we contacted said the march-in authority could have a "chilling effect" on the willingness of venture capital firms and other investors to provide funding for the further commercial development of federally funded inventions. For example, three of the technology transfer officials we contacted said the chilling effect on investors would be increased if agencies used the march-in authority under circumstances that were not well supported by the facts. According to these officials, investors are looking for profitable technologies and inventions that either have, or are close to obtaining, a patent, which allows them to capture profits in relative safety. They said that for some investors the mere existence of an agency's march-in authority makes such investments more risky because, should an agency

actually exercise its authority, investors may believe the value of their investment could evaporate or decline significantly and these perceived risks could increase significantly.

However, executives from two bio-technology firms—both of which hold licenses to commercialize technologies developed in part with federal funds and which must raise money from investors to pursue commercialization—told us the perceived risk that an agency might march in is far less important to investors than other risks they face. For example, they cited the product's likely efficacy as perhaps the key factor for investors to consider in making such decisions. The executives added that one of the greatest concerns of their potential investors is how soon the product or process can be marketed and, as a result, return a profit on their investment. These executives expressed confidence that if licensees take care to follow the requirements of the Bayh-Dole Act, then march-ins would be rare and should not negatively affect the flow of federally funded inventions to the market. In addition, technology transfer officials noted that at the time the act was passed companies were often unwilling to enter into licensing agreements due to concerns about how agencies would use the authority. They said such concerns have diminished, in part because the small number of fact-finding proceedings has not led agencies to march in.

The march-in authority would also have a chilling effect if researchers, particularly private-sector researchers, were unwilling to apply for federally funded projects because the potential for an agency to march in creates uncertainty with regard to ownership of an invention. However, none of the officials we contacted was aware of specific instances when a researcher had declined to apply for federal funding and they said it is impossible to know the extent to which researchers decide against applying for federal funds due to such concerns. In contrast, officials at DOE said they do not believe the potential for a march in is a concern for their contractors. For example, DOE officials noted that following the release of a recent solicitation, 60 small businesses called with questions about the march-in authority. However, even after DOE officials explained the march-in authority to these callers, overwhelmingly they submitted applications.

Because the march-in process itself can be long and the outcome unknown pending a possible appeal of the agency's decision to the federal courts, the NIH officials we contacted believe march-in authority could have limited utility in an emergency situation, such as an important public health issue, that required prompt federal action. More specifically, the

Commerce regulations that govern march-in procedures provide for a quasi-judicial process that may require more time to complete than the other legislative options mentioned above. The march-in procedures allow for contractors to be represented by counsel, the opportunity to call and confront witnesses, and the chance to introduce documentary evidence and review the evidence others have presented. In the four fact-finding instances we reviewed, the time to reach a decision not to initiate march-in proceedings ranged from 5 to 30 months. According to NIH officials, the specifics of each Bayh-Dole fact-finding effort are likely to vary, but the process to determine whether a march-in proceeding is warranted will usually require at least several months to accomplish. Moreover, in the event an agency decides to march in, action on the decision may be delayed pending review by the federal courts if the contractor or licensee appeals the decision. In emergency situations, NIH officials said the government could use other legal authorities, discussed above, to obtain the necessary rights.

Officials at NASA and NIH also reported that a march-in proceeding would be complicated by the fact that most products and processes include multiple technologies covered by multiple patents, and that in many cases only some of them have been developed with federal funding. As a result, federal agencies may only have the authority to march in on one aspect of a product or process, yet marching in may negatively affect the value of all the other patented inventions associated with the product or process. For example, NIH officials described the development of a single genome test that used 17 patents from 13 organizations (3 from outside the U.S.), some of which used government funding and some did not. These officials said it would be impossible for NIH to determine that 1 of those 17 patents is not being commercialized fast enough, or not meeting a health need, in the face of its dependence on 16 other patents. Any such effort would require the cooperation of 12 other organizations, and an unknown number of licensees. The officials concluded that it would be an impossible task for NIH, or any agency, to decide to march in under those circumstances.

Officials at NIH also said that agencies might be disinclined to march in if current licensees have specialized knowledge about how to bring a particular product to market. If the loss of such knowledge would jeopardize the commercialization of an invention, agencies might be reluctant to pursue a march-in. For example, licensees may possess information such as trade secrets, other patented technologies related to product development, experience with the federal approval process, or marketing experience. If NIH were to force a contractor or licensee to grant a license to another entity, it would have to consider whether the

other patented technologies would be available to the new licensee and whether the new licensee would have the knowledge, resources, and commitment needed to commercialize the product.

Agency Comments and Our Evaluation

We provided a copy of a draft of this report to DOD, DOE, NIH, and NASA for their review and comment. In commenting on the draft, NASA stated that the report provides a balanced view of the issues related to the regulations associated with the Bayh-Dole Act. NASA also provided technical comments that we incorporated, as appropriate. NASA's overall comments are included in appendix II. DOD, DOE, and NIH did not provide overall comments, but NIH provided technical comments that we incorporated, as appropriate.

We are sending copies of this report to the appropriate House and Senate committees, interested Members of Congress, the Secretaries of the Departments of Defense and Energy, the Administrator of NASA, and the Director of NIH. The report will also be available at no charge on the GAO Web site at http://www.gao.gov.

If you or your staffs have questions about this report, please contact me at (202) 512-3841 or mittala@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made key contributions to this report are listed in appendix III.

Anu K. Mittal
Director, Natural Resources and Environment

Appendix I: Objectives, Scope, and Methodology

The objectives of this report were to determine (1) what policies and procedures federal agencies with significant research budgets have established to determine whether march-in authority under the Bayh-Dole Act should be exercised; (2) the extent to which these selected federal research agencies have used Bayh-Dole march-in authority and what they believe are its benefits; and (3) what barriers and disincentives, if any, these agencies have encountered to the exercise of their march-in authority under the Bayh-Dole Act.

We sought to focus our review on those federal agencies whose combined research and development spending represent a significant portion of total federal research and development spending. To identify the federal research agencies that meet this criterion, we obtained and analyzed research and development funding data from the National Science Foundation (NSF) on preliminary federal obligations for research and development for all federal research agencies. The top four agencies receiving research and development funding were the Department of Defense (DOD), the Department of Energy (DOE), the National Aeronautics and Space Administration (NASA), and the National Institutes of Health (NIH) within the Department of Health and Human Services. We judgmentally selected these four agencies as the focus of our review. We compared the combined percent of funding from the total research and development allotment for these four agencies to the total allotment for the federal government and found that these four agencies accounted for approximately 89 percent of the total federal research funding for fiscal year 2006—the most recent year for which NSF had complete data. In assessing the reliability of the NSF data, we noted that it reports a 100 percent response rate, with responses to all items; thus, we determined it was sufficient for the purposes of this analysis.

To gain insights into the history of the Bayh-Dole Act, including its provision for march-in authority, as well as to understand the context in which the law was enacted and its current environment, we reviewed the act's legislative history, including congressional hearing statements made by the act's sponsors and other stakeholders. We also reviewed the available literature on the Bayh-Dole Act's implementation and the effects it has had on federal research. To understand the law's requirements, we reviewed all provisions of the act, giving special emphasis to those sections that establish march-in authority. To understand how agencies are to implement their responsibilities under the act, we reviewed the Department of Commerce's Bayh-Dole regulations.

For each of our three objectives, we interviewed officials from the technology transfer offices and offices of general counsel at DOD, DOE, NASA, and NIH, as well as officials from the National Institute of Standards and Technology. In addition, we contacted officials in stakeholder groups such as the Association of University Technology Managers, the Biotechnology Industry Organization, the American Intellectual Property Law Association, the Association of Public and Land-grant Universities, and Essential Inventions, as well as academics who have evaluated the Bayh-Dole Act. We also contacted representatives from the biotechnology industry who invest in and/or develop federally funded technologies. We reviewed the three march-in petitions that NIH received, and NIH's determinations in these cases, to understand how NIH applies the Commerce regulations. Finally, we studied NIH's research tool guidelines to determine their impact on agency decisions on whether to conduct march-in proceedings.

We conducted our work from November 2008 to July 2009 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Appendix II: Comments from the National Aeronautics and Space Administration

National Aeronautics and Space Administration
Headquarters
Washington, DC 20546-0001

July 16, 2009

Reply to Attn of: Office of the General Counsel

Ms. Anu K. Mittal
Director, Natural Resources & Environment
United States Government Accountability Office
Washington, DC 20548

Dear Ms. Mittal:

Thank you for the opportunity to review draft report, "FEDERAL RESEARCH: Information on the Government's Right to Assert Ownership Control Over Federally Funded Inventions," (GAO-09-742).

We found the report to be complete, concise, and accurate. In our opinion, it provides a balanced view of the issues related to the regulations associated with the Bayh-Dole Act. Technical comments to the draft report have been provided separately.

Again, thank you for the opportunity to provide comments on the draft report and for your continued interest in technological innovation and march-in authority.

Sincerely,

Michael C. Wholley

Michael C. Wholley
General Counsel

Appendix III: GAO Contact and Staff Acknowledgments

GAO Contact

Anu Mittal (202) 512-3841 or mittala@gao.gov

Staff Acknowledgments

In addition to the contact named above, Cheryl Williams, Assistant Director; Richard Johnson; Amanda Leissoo; Benjamin Shouse; Elizabeth Wood; and Eugene Wisnoski made significant contributions to this report.

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INFORMATION PAPER—SUPPLEMENT & DISCUSSION
March-in Rights Request by KEI to NIH and DoD Pertaining to Xtandi®

APPENDIX H

Written Statement of Senator Birch Bayh to the National Institutesof Health, May 25, 2004.

"Our Law Helps Patients Get New Drugs Sooner, The Washington Post, April 11, 2002.

NIH Public Meeting on Norvir/Ritonavir March-in Request
May 25, 2004

Agenda

Introductory Remarks by Dr. Mark Rohrbaugh

Written Comments Received:

- Senator Birch Bayh
- Robert Huff, Editor, GMHC Treatment Issues
- Norman J. Latker, former Patent Counsel, HEW
- John Erickson, President & CSO, Sequoia Pharmaceuticals
- Dan Ravicher, Executive Director, Public Patent Foundation
- C. Peter Magrath et al., National Association of State Universities and Land Grant Colleges, Association of American Universities, and American Council on Education
- Carl E. Gulbrandsen, Managing Director, Wisconsin Alumni Research Foundation
- Katharina Phillips, Council on Governmental Relations
- Patricia Harsche Weeks, Immediate Past President, Association of University Technology Managers
- Joseph P. Allen, President, National Technology Transfer Center
- Heather L. Mason, Vice President, Pharmaceutical Specialty Operations, Abbott Labs
- Benjamin Young, OHHP, Organization of Healthcare Providers
- Lynda Dee, Co-Chair, AIDS Treatment Activists Coalition, Drug Development Committee
- Julie Britton Haden, West Virginia Coalition for People with HIV/AIDS
- Rhonda Connard and Amanda Lowther, Co-Coordinators, Covenant House AIDS Program
- Michael Weinstein, President, AIDS Healthcare Foundation
- Stephan E. Lawton, Vice President & General Counsel, BIO
- David D. Ho, Director & CEO, The Aaron Diamond AIDS Research Center
- David Gollaher, President & CEO, California Health Care Institute
- David Miller, President, iBio™
- David Halperin, Attorney Counselor
- James Love, President, Essential Inventions, Inc.
- Jerome Reichman, Bunyan S. Womble Professor of Law, Duke University School of Law

PUBLIC MEETING

National Institutes of Health - Building 50
May 25, 2004

9:00	**INTRODUCTION**
9:05	The Honorable Birch Bayh
9:20	Ted Poehler, Ph.D., Vice Provost for Research, Johns Hopkins University, American Association of Universities
9:35	Daniel Ravicher, Executive Director, Public Patent Foundation
9:50	John Erickson, President & Chief Scientific Officer, Sequoia Pharmaceuticals
10:05	Robert Huff, Editor, *Treatment Issues*, Gay Men's Health Crisis, NYC
10:20	**BREAK**
10:30	Norman J. Latker, former Patent Counsel, Department of Health, Education and Welfare
10:45	James Love, President, Essential Inventions, Inc.
11:00	Andrew Neighbour, Board Member and Chair, Intellectual Property Committee, Council on Governmental Relations
11:15	Jerome Reichman, Bunyan S. Womble Professor of Law, Duke University School of Law
11:30	Benjamin Young, M.D., Ph.D., Organization of Healthcare Providers
11:45	Jeff Leiden, M.D., Ph.D., President and Chief Operating Officer, Pharmaceutical Products Group and Chief Scientific Officer, Abbott Laboratories
12:00	**ADJOURN**

INTRODUCTORY REMARKS

Welcome . . .

My name is Dr. Mark Rohrbaugh and I am the Director of the Office of Technology Transfer at the NIH.

Seated next to me is my Deputy Director, Dr. Bonny Harbinger.

Doris Campos-Infantino, the Deputy Ombudsperson for the National Institutes of Health, will be serving as the moderator for this public meeting.

This public meeting is being held pursuant to requests from various constituencies that the Government exercise its march-in rights under the Bayh Dole Act in connection with patents owned by Abbott Laboratories. The constituencies expressed concern over the price of ritonavir (sold under the tradename Norvir), which is covered by these patents and marketed by Abbott for the treatment of patients with HIV/AIDS.

The purpose of this public meeting is to give us an opportunity to listen to comments from representatives of constituencies and to hear various points of view. These comments and viewpoints then will be considered by the NIH in making the decision of whether we have received information that might warrant the exercise of march-in rights. The NIH will make that initial determination and, if necessary, will initiate any formal march-in proceeding as required under the regulations. We will make every effort to come to a decision as quickly as possible.

I will now turn this meeting over to Ms Campos-Infantino.

STATEMENT OF SENATOR BIRCH BAYH TO THE NATIONAL INSTITUTES OF HEALTH

MAY 25, 2004

I appreciate NIH's invitation to comment on the intent of Congress when it enacted the Bayh-Dole law. I am accompanied by Joe Allen, currently President of the National Technology Transfer Center, and formerly my primary staff member who worked on this legislation. The focus of my comments will be the contention that Bayh-Dole gives NIH the ability to control the price of a product developed under the law by exercising the march-in rights provided in Section 203 of its provisions.

Before proceeding, I should emphasize that I am not being compensated to appear here today. Also, I should note that I am not familiar with the specifics of the drug which is the basis of the petition before NIH, so I will not comment on the merits of this particular case. However, I do know the intent of this legislation which I was privileged to sponsor with my friend, Senator Bob Dole.

As NIH proceeds with this examination of the petition, it should prove informative to the responsible officials here at NIH and the petitioners as well, to be reminded of the history behind the introduction and passage of Bayh-Dole. Particular attention should be given to the economic environment which existed prior to the introduction of Bayh-Dole.

By the late 70s, America had lost its technological advantage:

- We had lost our number one competitive position in steel and auto production. In a number of industries we weren't even No. 2.
- The number of patents issued each year had declined steadily since 1971.
- Investment in research and development over the previous 10 years was static.
- American productivity was growing at a much slower rate than that of our free world competitors.
- Small businesses, which had compiled a very impressive record in technological innovation, were receiving a smaller percentage of Federal research and development money.
- The number of patentable inventions made under federally supported research had been in a steady decline.

What had happened to American innovation, which had sparked generation after generation of international economic success?

Our investigation at the Patent and Trademark Office disclosed that the U.S. government owned 28,000 patents, only 4 percent of which had been developed as a product for use by the consumer.

Close examination disclosed that most patents procured as a result of government research grants, particularly those developed in university laboratories, resulted from basic research. The ideas patented were in the embryonic stages of development. Often millions of dollars were required to produce the sophisticated products necessary for marketability. Since the government refused to permit ownership of the patents, private industry and business refused to invest the resources necessary to bring the products to consumers. As Thomas Edison said: "Invention is 1% inspiration and 99% perspiration." With regard to publicly funded research, government typically funds the inspiration and industry the perspiration.

The well-intentioned voices, such as Senator Russell Long and Admiral Hyman Rickover, opposed Bayh-Dole on the basis "If the taxpayer funds the research, the taxpayer should own the ideas produced." However, the result of this policy was billions of taxpayer dollars spent on thousands of ideas and patents which were collecting dust at the PTO. The taxpayers were getting no benefit whatsoever.

Changes to Bayh-Dole should be made only after giving careful consideration to what has been accomplished by those who have utilized the provisions of the law. The London "Technology Economist Quarterly" called Bayh-Dole "Possibly the most inspired piece of legislation to be enacted in America over the past half century." (I have attached the full text of the article for your information.)

The Economist estimated that Bayh-Dole created 2,000 new companies, 260,000 new jobs, and now contributes $40 billion annually to the U.S. economy. This assessment was made almost six years ago and more progress has been made since then.

One is entitled to second guess us and say that we should have allowed the government to have a say in the prices of products arising from federal R&D. However, if changes are believed warranted, we have a process for doing so. That is to amend the law. You simply cannot invent new interpretations a quarter of a century later. This is what is being proposed.

When Congress was debating our approach fear was expressed that some companies might want to license university technologies to suppress them because they could threaten existing products. Largely to address this fear, we included the march-in provisions that are the subject of today's meeting.

The clear intent of these provisions is to insure that every effort is made to bring a product to market. If there is evidence that this is not being done, the funding agency can "march-in" and require that other companies be licensed. If the developer cannot satisfy health and safety requirements of the American taxpayer, agencies may march-in.

It was first brought to my attention that attempts were underway to rewrite history when I saw an article in the **Washington Post** on March 27, 2002, entitled *Paying Twice for the Same Drugs.*. The crux of the article was that:

> Bayh-Dole ... states that practically any new drug invented wholly or in part with federal funds will be made available to the public at a reasonable price. If it is not, then the government can insist that the drug be licensed to more reasonable manufacturers, and if refused, license it to third parties that will make the drug available at a reasonable cost.[1]

This view mistakes how our law works. Bob Dole and I responded in a letter to the editor of the **Washington Post** on April 11, 2002 setting the record straight.[2]

You can imagine my surprise when I see the same arguments were being formally presented in a petition to NIH in an attempt to control drug prices. The quotations in the petition flagrantly misrepresent the legislative history supporting Bayh-Dole. The petition shows complete lack of understanding of how the legislative process works. The current petition says: "The clear language of the Bayh-Dole act requires reasonable pricing of government supported inventions."[3] It later adds: "The legislative history evidences an intent to require that government supported inventions be priced reasonably."[4]

All but one of the citations in the petition used to conclude that march-in rights were intended to control prices actually refer to hearings on bills other than Bayh-Dole. While perhaps interesting, these are not pertinent legislative history. I could find only one citation from the real legislative history. Here is the petition language:

> This consensus was recorded in the Senate's Committee Report on the bill, which explained that march-in rights were intended to insure that no 'windfall profits,' or other "adverse effects result from retention of patent rights by these contractors."[5]

The petition footnote on this section adds "statement of Senator Bayh that the march-in provisions were meant to control the ability of 'the large, wealthy, corporation to take advantage of Government research and thus profit at taxpayers' expense."[6]

Rather than being a statement of fact, my quotation is actually taken from a question I asked the Comptroller General on another topic altogether.

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[1] Peter Arno and Michael Davis, "Paying Twice for the Same Drugs," Washington Post 27 Mar. 2002: A21.

[2] Birch Bayh and Robert Dole, "Our Law Helps Patients Get New Drugs Sooner," Washington Post 11 Apr. 2002: A28.

[3] Petition to use Authority Under Bayh-Dole Act to Promote Access to Ritonavir. Supported by National Institute of Allergy and Infectious Diseases Contract No. AI27220 (Essential Inventions, Inc., 2004) 9.

[4] Ibid., 10

[5] Petition to use Authority Under Bayh-Dole Act to Promote Access to Ritonavir. Supported by National Institute of Allergy and Infectious Diseases Contract No. AI27220 (Washington: Essential Inventions, Inc., 2004) 10.

[6] Ibid.

The petition language taken from the Committee report mixes up references to two different sections of the law so that the original meaning is unrecognizable.

Let's see what happens when the petition quotes are placed in their proper context. I highlighted the following language referred to in the petition as it actually appears in the legislative history.

With regard to the petition's footnote, during his testimony I asked Elmer Staats, then the Comptroller General of the United States, a question regarding concerns expressed about the Bayh-Dole bill. Here it is:

Mr. Bayh: "The other criticism comes from those that feel that this bill is a front to allow ***the large, wealthy corporation to take advantage of Government research dollars and thus to profit at the taxpayers' expense.*** We thought we had drafted this bill in such a way that this was not possible. Would you care to comment on this scenario as a valid criticism?"

Mr. Staats: "Of course, this is the key question. There is no doubt about that. In my opinion, the bill does have adequate safeguards..."

The petition also mixes up Senate Judiciary Committee report language describing two unrelated parts of Bayh-Dole. Here's how the report actually reads with the petition extract highlighted:

> The agencies will have the power to exercise march-in rights to insure that no **adverse effects result from the retention of patent rights by these contractors.**[7]

That was the language on section 203, the march-in rights provision. The report continues:

> The existence of section 204 of the bill, the Government pay back provision, will guarantee that the inventions which are successful in the marketplace reimburse the Federal agencies for the help which led to their discovery. Although there is no evidence of ***"windfallprofits"*** having been made from any inventions that arose from federally-sponsored programs, the existence of the pay back provision reassures the public that their support in developing new products and technologies is taken into consideration when these patentable discoveries are successfully commercialized."[8]

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[7] United States. Congress. Senate. Committee on the Judiciary, University and Small Business Patent Procedures Act: Report of the Committee on the Judiciary. United States Senate, on S.414 (Washington: U.S. Government Printing Office, 1979) 30.

[8] Ibid.

Thus, it is only by inappropriately combining language describing an entirely different section of the law that the words **"windfall profits"** can be made to refer to march-in rights. They clearly do not. Such a representation is highly misleading.

When read in context, the real meaning could not be clearer. Rather than controlling product prices, the language actually provided that the Government should be able to recoup a percentage of its investment when an invention from its extramural funding hits a home run in the market.

In fact, this payback provision of Section 204 was later dropped from the bill altogether because the agencies said that the administrative costs of tracking university royalties would far outweigh any monetary benefits from the one-in-a-million breakthrough invention.

NIH itself has found that price controls are not contemplated by Bayh-Dole. Under pressure in 1989, NIH placed a provision in its intramural collaborations with industry that resulting inventions must demonstrate "a reasonable relationship between the pricing of a licensed product, the public investment in that product, and the health and safety needs of the public."[9]

When industry collaborations began evaporating, and NIH explored the reasons and found:

> Both NIH and its industry counterparts came to the realization that this policy had the effect of posing a barrier to expanded research relationships and, therefore, was contrary to the Bayh-Dole Act.[10]

If NIH found that price controls on its intramural research are "contrary to the Bayh-Dole Act," how can the same provisions be applied to extramural research?

If Congress does decide to amend Bayh-Dole someone must clearly define what is a "reasonable price." Congress must keep in mind that the vast majority of technologies developed under the law are commercialized by small companies that "bet the farm" on one or two patents. Copycat companies are always waiting until an entrepreneur has shown the path ahead. They can always make things cheaper since they have no significant development costs to recover.

What will happen to the start-up companies arising from Bayh-Dole that are driving our economy forward with this sword hanging over their heads? What evidence is there that large drug companies will not simply walk away from collaborations with our public sector? That is what happened to NIH.

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[9] National Institute of Health, NIH Response to the Conference Report Request for a Plan to Ensure Taxpayers' Interests are Protected (Washington: U.S. Government Printing Office, 2001) 9.

[16] Ibid., 8.

NIH wisely realized that the greater good is to allow American taxpayers to have access to important new products and processes, along with the new jobs and taxes they create than to try and regulate prices.

Bob Dole and I made the same choice in 1980. I still believe that we were correct.

I empathize with the countless individuals in the U.S. and around the world who are suffering from AIDS. If it can be shown that the health and safety of our citizens is threatened by practices of a government contractor, then Bayh-Dole permits march-in rights, not to set prices, but to ensure competition and to meet the needs of our citizens. However, such a procedure must be supported by hard evidence that the need exists. Speculative claims and misrepresentation of the legislative history supporting Bayh-Dole will not suffice.

Let me urge the wisdom of approaching such a decision which great caution. The success of Bayh-Dole goes far beyond the efforts of Bob Dole and Birch Bayh. This legislation combined the ingenuity and innovation from our university laboratories with the entrepreneurial skills of America's small businesses. Most importantly, this combination created the incentive necessary for private investment to invest in bringing new ideas to the marketplace. The delicate balance of ingenuity, entrepreneurship, and incentive upon which the success of Bayh-Dole has depended must not be disrupted.

A few of the products which have been produced in the last six years are:

- Taxol, the most important cancer drug in 15 years, according to the National Cancer Institution.
- DNA sequencer, the basis of the entire Human Genome Project.
- StormVision™, which airport traffic and safety managers use to predict the motion of storms.
- Prostate-specific antigen test, now a routine component of cancer screening.
- V-Chip, which allows families to control access to television programming.

It would be the ultimate folly to march in and alleviate the problem addressed by the petition, availability of a drug to treat AIDS today, and in so doing dampen the ingenuity, entrepreneurial skills and incentive necessary to develop a permanent cure for AIDS, or for that matter the cure for other diseases that plague all too many American mothers, fathers, children and seniors today.

As you search for a solution to the problem before us today, be aware of unintended consequences tomorrow. Insuring the health of our citizens requires the wisdom and determination for a long journey. The procedures of Bayh-Dole have saved countless lives and pain and suffering. It provides an incentive for further progress in the future.

Thank you

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The Washington Post

Our Law Helps Patients Get New Drugs Sooner

April 11, 2002

As co-authors of the Bayh-Dole Act of 1980, we must comment on the March 27 op-ed article by Peter Arno and Michael Davis about this law.

Government alone has never developed the new advances in medicines and technology that become commercial products. For that, our country relies on the private sector. The purpose of our act was to spur the interaction between public and private research so that patients would receive the benefits of innovative science sooner.

For every $1 spent in government research on a project, at least $10 of industry development will be needed to bring a product to market. Moreover, the rare government-funded inventions that become products are typically five to seven years away from being commercial products when private industry gets involved. This is because almost all universities and government labs are conducting early-stage research.

Bayh-Dole did not intend that government set prices on resulting products. The law makes no reference to a reasonable price that should be dictated by the government. This omission was intentional; the primary purpose of the act was to entice the private sector to seek public-private research collaboration rather than focusing on its own proprietary research.

The article also mischaracterized the rights retained by the government under Bayh-Dole. The ability of the government to revoke a license granted under the act is not contingent on the pricing of a resulting product or tied to the profitability of a company that has commercialized a product that results in part from government-funded research. The law instructs the government to revoke such licenses only when the private industry collaborator has not successfully commercialized the invention as a product.

The law we passed is about encouraging a partnership that spurs advances to help Americans. We are proud to say it's working.

BIRCH BAYH

BOB DOLE

Washington

The writers are, respectively, a former Democratic senator from Indiana and a former Republican senator from Kansas.