REQUEST FOR MARCH-IN ON ABBOTT PATENTS FOR RITONAVIR ON GROUNDS THAT ABBOTT PRIVATE SECTOR PRICES FOR RITONAVIR ARE HIGHER IN USA THAN IN OTHER HIGH INCOME COUNTRIES, AND ABBOTT'S REFUSAL TO LICENSE PATENTS FOR NON-ABBOTT FIXED DOSE COMBINATIONS OF HIV DRUGS

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1. Executive Summary

The American Medical Students Association (AMSA), Knowledge Ecology International (KEI), U.S. Public Interest Research Group (PIRG) and the Universities Allied for Essential Medicines (UAEM) request the Secretary to issue 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.

The two policy rules we propose are as follows:

Rule 1: Ceiling on prices to U.S. residents
The Secretary shall normally grant open licenses to third parties to use patented inventions that have benefited from federal funding, subject to the payment of a reasonable royalty and an appropriate field of use, if a product or products based upon those inventions are sold in the United States at prices higher than in other high income countries. In implementing this rule, we suggest the following standard for a ceiling on prices to U.S. residents.

Proposed standard for ceiling on prices to U.S. residents

The Government should consider the high, mean and median prices charged in the ten largest foreign economies, as measured by GNP, among the countries determined by the World Bank to be high income. U.S. prices will presumptively not be considered reasonable, and contracts will be given or licenses granted to competitors to supply the products to U.S. consumers, if any of the following are true for either public or private sector prices:

(1) U.S. prices are higher than seven of the comparison countries, or

(2) U.S. prices are 10 percent higher than the median price of the reference countries.

A licensee may rebut the presumption of unreasonable pricing by providing evidence that its actual risk adjusted R&D costs would not be recovered, but for the charging of higher prices in the U.S. market, or other evidence specific to the risk adjusted costs for the licensed invention.

Rule 2: Use of invention for a dependent technology
The Secretary shall grant licenses to third parties to use patented inventions that have benefited from federal funding, subject to the payment of a reasonable royalty and an 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.

The two proposed rules are without prejudice to the exercise of march-in to remedy other anticompetitive, abusive or unfair practices by a patent holder or licensee. We note that examples of other abuses may include, but are not limited to, tying arrangements, sudden and arbitrary price increases, or price setting disproportionate to drugs in the same class.

We ask that the two rules be applied to six patents held by Abbott on the drug ritonavir. The patents in question are U.S. Patent No. 5541206, No. 5635523, No. 5648597, No. 5674882, No. 5846987, and No. 588604, all owned by Abbott Laboratories. As disclosed in the patents, all inventions benefited from federal funding from the National Institute for Allergies and Infectious Diseases (NIAID).

The facts presented in this petition will show that Abbott's private sector prices for Norvir are far higher than the Abbott price for Norvir in other high income countries.

The facts presented in the petition will also show that Abbott's failure to license its patents on ritonavir have harmed patients by reducing the number of medicines co-formulated with ritonavir.

The petition calls upon the Secretary to grant open licenses to said patents for the manufacture and sale of ritonavir either as a standalone product or as a co-formulated product for the treatment of HIV/AIDS and for any other FDA approved use.

2. Background and Context

A previous request for march-in on the patents for ritonavir[1] was submitted by Essential Inventions, Inc. to the Secretary of the Department of Health and Human Services on January 29, 2004 and rejected on August 4, 2004. Petitioners revisit issues raised in the earlier dispute, and examine them in the current context, including the medical needs facing patients, consequences of the financial crisis, and the challenges of high healthcare costs for U.S. private sector employers.

This petition focuses on two areas where Abbott has abused the exclusive rights of the patents.

1. The U.S. private sector price Abbott charges for the standalone version of ritonavir is far higher than the price Abbott charges in other high income countries. This pricing causes financial hardships and barriers to access for patients, and also increases the operating costs of U.S. businesses that pay for health care, thereby undermining the international competitiveness of employers who pay for drugs in the private sector, contributing to unemployment and downward pressure on wages in the U.S.

[1] See attachment.

2. Abbott has refused to license the patents on ritonavir to other drug makers for use in co-formulated fixed dose combination drugs used for the treatment of HIV/AIDS or other illnesses. Because of this refusal to license, patients living with HIV/AIDS are denied the most effective methods of administering antiretroviral drugs, which among other things, leads to poorer compliance by patients and growing levels of drug resistance.

2.1. Private sector prices for ritonavir are higher in the U.S. than in foreign countries

Like many pharmaceutical products, ritonavir prices vary considerably for different purchasers of the product. Within the U.S., Abbott charges a high price for the private sector, and a much lower price for government run programs, such as Medicaid or state ADAP programs. The lower prices for federally subsidized purchases of ritonavir were offered as a concession during the 2004 dispute over the 400-percent price increase in ritonavir that led to the 2004 march-in case by Essential Inventions. In response, Abbott sought to mitigate the chances of the march-in request being granted by offering concessions on the pricing for the government run programs in return for the government tolerating the 400-percent price increase for the private sector.

The 2003/2004 re-pricing of ritonavir by 400 percent-was implemented only in the U.S. As a consequence, price sector prices for ritonavir in the U.S. are several multiples of the prices that Abbott charges in foreign countries, including other high income countries.

While the federal government has benefited from the pricing restraint for government subsidized purchases of ritonavir, private employers and consumers who pay out-of-pocket have not. The harm to persons buying ritonavir in the private sector are two-fold. First, the high cost of the drug depletes their financial resources and in some cases causes financial hardship or barriers to obtaining access to the drug. Second, the inequality between the U.S. and foreign prices has placed U.S. employers at a distinct disadvantage, as it contributes to the higher cost of employing workers in the U.S.

The price differences between the U.S. and the rest of the world are huge.

In an August 12, 2010 survey of prices for ritonavir as a standalone product, the average retail price in the U.S. for a 100 mg tablet or soft-gel capsule, was $10.70. For twelve other high-income countries, the price range was a high of $2.63, and a low of $1.04. In other words, for a drug invented under an NIH grant for the treatment of AIDS, private sector purchasers in the U.S. pay 4 to 10 times more than the price in all other high-income countries. (*See* Anne Mira Guha, “Prices for Abbott's Norvir (generic name Ritonavir) as a Standalone Product in 2010,” *KEI Research Note* 2010:4, keionline.org/prices/ritonavir).

An August 2012 survey of the prices for 100 mg tablets or capsules of Abbott's Norvir reveals continued disparities between the private sector prices for ritonavir in the U.S. and foreign prices charged by Abbott for the same drug. In the eight high income countries in the survey, the August 2012 Abbott price for a single 100 mg tablet or capsule of ritonavir ranged from $1.02 to $2.16, compared to $10.29 in the U.S. for the average wholesale price and $12.63 as the cash price at CVS in the Washington, D.C. area.

Table 1: August 2012 Survey of Norvir prices (100mg tab)

Country	Date	Price in USD per pill
USA, CVS (Cash price)	08/23/2012	$12.63
USA, AWP	March 2012	$10.29
Norway, AUP (retail)	8/20/2012	$2.16
Italy	08/20/2012	$1.54
France: prix public toutes taxes comprises (PPTTC)	08/20/2012	$1.54
Canada, Ontario formulary	08/20/2012	$1.48
Australia	08/20/2012	$1.48
The Netherlands	08/20/2012	$1.21
New Zealand (PhRMAC)	08/20/2012	$1.17
UK (British National Formulary)	08/22/2012	$1.02

These high private sector prices are not only unfair to U.S. consumers, but also impact the private sector employers in the U.S. that pay for ritonavir through third-party or self-funded insurance.

As noted above, when drug companies charge higher prices for drugs sold in the U.S. than they charge in other high-income countries, U.S. employers are put at an economic disadvantage. If forced to pay more for health care costs, private sector employers are less competitive in global markets, leading to reduced employment and lower wages for U.S. residents.

While at one point in time the U.S. economy was so healthy and dominant it could ignore such concerns, this is no longer the case. The U.S. economy as a whole is now smaller than the combined economy of the members of the European Union. Between 1970 and 2011, the U.S. share of the global GDP declined from 35 percent to 22 percent, and the U.S. share of high income country GDP has declined from 45 percent to less than 34 percent.

With the current financial crisis, U.S. unemployment is at high levels, our share of global GDP has shrunk sharply since 2000, and we no longer can afford the luxury of paying more for drugs invented on NIH grants than do our trading partners in other high income countries.

Table 2: U.S. Share of World and High-Income GDP

Year	Share of world GDP	Share of High Income Country GDP
1960	39%	51%
1970	35%	45%
1980	25%	33%
1990	26%	33%
2000	31%	39%
2010	23%	35%
2011	22%	34%

2.2. In the U.S., ritonavir should be available as co-formulated non-Abbott products

2.2.1 Use of ritonavir

Since 1987, the FDA has approved roughly one new molecular entity per year in seven classes of antiretroviral drugs. These drugs are normally taken in 3 or 4 drug combinations, in a course of treatment known as Highly Active Antiretroviral Therapy (HAART).

On March 1, 1996, ritonavir was the first protease inhibitor approved for the treatment of HIV/AIDS. While originally used as a third drug in a three drug combination treatment with a dose of 1200 mg per day, researchers discovered that ritonavir was most useful when used in low doses (100 to 200 mg per day) in combination with other protease inhibitors. Ritonavir inhibits a liver enzyme and has the beneficial effect of increasing the efficacy of other protease inhibitors, allowing them to be taken in lower doses with fewer adverse side effects. It is in this role that ritonavir has become an important drug, particularly for patients who can no longer tolerate a regime based upon non-nucleoside reverse transcriptase inhibitors (NNRTIs).

On September 15, 2000, Abbott registered Kaletra, a co-formulated combination of ritonavir and the protease inhibitor lopinavir. (Lopinavir is only sold in combination with ritonavir, and is not sold separately). Manufacturers of other protease inhibitors, as well as some of the newer classes of antiretroviral drugs, have been rebuffed in efforts to license the patents on ritonavir for use in other co-formulated products.

On November 18, 2011, Matrix Labs received FDA approval for a co-formulated fixed dose combination of ritonavir with atazanavir, under a special program in the FDA to register products for sale in developing countries, as part of the United States President's Emergency Plan for AIDS Relief (PEPFAR). The U.S. government can buy the Matrix combination product for use outside of the U.S., but the combination is not available in the U.S. because of Abbott's refusal to license the ritonavir patents.

Many treatment experts consider the atazanavir/ritonavir combination superior to the lopinavir/ritonavir product, and it is unconscionable that the superior drug combination is not available in the U.S., given the federal government's role in funding the invention of both ritonavir and lopinavir.

2.2.2 The FDA approval of cobicistat does not eliminate the need for open licenses to use ritonavir in fixed dose combinations

The August 27, 2012 approval of the Gilead drug, cobicistat (COBI), a protease inhibitor similar to ritonavir, does not diminish the necessity for march-in rights on ritonavir.

Cobicistat has only been approved as part of a four drug fixed dose combination, and it must still be evaluated for effectiveness and appropriateness across larger populations than those who participated in clinical trials. Some studies on cobicistat have raised concerns regarding toxicity on the kidney; thus, patients who have had kidney problems in the past may not be well-

served using co-formulated products with cobicistat as a booster.[2] Some have cautioned the use of co-formulating cobicistat with tenofovir because of implications on kidney function.[3] Greater evaluation of the drug's effect on a wider population will be necessary before conclusions can be properly drawn regarding the appropriateness of its use as a replacement for ritonavir in all cases.

Furthermore, even though a competing "boosting" drug now exists in cobicistat, there is no guarantee that Gilead will permit the drug to be developed for co-formulation with other drugs outside of the recently FDA approved use for the "Quad." As a result, patients suffering from HIV/AIDS still will not be able to access the full range of possible co-formulations.

Additionally, we note that the creation and development of cobicistat was necessary precisely because of Abbott's monopoly over ritonavir and refusal to license its product for use in co-formulation of other HIV/AIDS medicines. To the extent that cobicistat is a similar product to ritonavir in some respects, this development may be seen as wasteful or unnecessary.

2.3. Government funding of ritonavir research into patented inventions

In 1988, Abbott Laboratories received a grant from the NIH's National Institute for Allergies and Infectious Diseases (NIAID), 5U01AI027220-050002 (referred to as AI027220) to study the biochemistry of HIV protease enzymes. The grant was also intended to determine whether medicines could be invented to block the enzyme and inhibit the spread of HIV/AIDS to new cells. NIAID grant AI027220 continued to fund Abbott's pre-clinical work in this area through 1993.

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[2] *See, e.g.*, Liz Highleyman, "Cobicistat matches ritonavir as atzanavir booster" AIDSmap (July 30, 2012), *available at* http://www.aidsmap.com/Cobicistat-matches-ritonavir-as-atazanavir-booster/page/2459036/ ("People with poor kidney function were not included in this trial, as earlier studies suggested cobicistat might cause kidney toxicity."); Positively Aware, *available at* http://www.positivelyaware.com/2012/12_02/drugs/cobicistat.shtml ("Seen in clinical studies . . . increased serum creatinine, and decreased estimated glomerular filtration rate (e-GFR). . . signs of possible kidney malfunction."); *But see* Liz Highleyman, "ICAAC: Cobicistat Matches Ritonavir as Booster, Studies Clarify Effects on Kidney Function," (Sept. 2011), *available at* http://www.hivandhepatitis.com/hiv-aids/hiv-aids-topics/hiv-treatment/3252-cobicistat-matches-ritonavir-as-booster-studies-clarify-effects-on-kidney-function (Study found that "Mean estimated GFR (eGFR; Cockcroft-Gault, mL/min)—a marker of kidney function—decreased by -9 in the cobicistat arm and by -4 in the ritonavir arm." However, a Gilead study disputed these findings as not significant because "while cobicistat can cause mild increases in serum creatinine, leading to a small decrease in estimated GFR, it does not affect actual GFR as measured by iohexol.")

[3] Liz Highleyman, "Gilead's Quad Pill Matches Atripla, New Booster Cobicistat (GS 9350) Looks Good with Atazanavir (Reyataz), (Feb. 19, 2010) *available at* http://www.hivandhepatitis.com/2010_conference/croi/docs/0219_2010_c.html (In comparing ritonavir with cobicistat, "The main concern . . . was the signal of kidney toxicity suggested by elevated serum creatinine and reduced eGFR in people taking cobicistat. . . Prior studies of health HIV negative volunteers suggested cobicistat may inhibit kidney tubular secretion—leading to elevated creatinine—but does not seem to cause the type of nephrotoxicity seen with other drugs. Nevertheless, caution may be warranted with a pill that combines cobicistat and tenofovir, which has been linked to kidney impairment.")

2.4. Clinical trials of ritonavir

With regard to clinical trials, ritonavir was approved extraordinarily quickly and therefore required less investment from Abbott than is typically the case for a clinical development program. The initial FDA approval of ritonavir was based upon just three clinical trials with a total of 1,583 patients.[4] Marketing approval was given less than one year after Abbott filed its key patents for ritonavir. Furthermore, none of the clinical trials used for FDA approval lasted more than 48 weeks and the FDA review of ritonavir was completed in the astonishingly short time period of just over two months.[5]

If Abbott spent $10,000 per patient for the three clinical trials cited by the FDA in approving the drug, the cost of the trials would have been approximately $15 million.[6]

By the end of 2001, just a few years after Abbott received marketing approval, ritonavir had generated total sales of over $1 billion, far exceeding Abbott's initial investment in the drug, even after liberal adjustments for risk or capital costs.

3. Analysis

3.1. Ritonavir is a subject invention subject to the federal government's rights under the Bayh-Dole Act

The rights of the Government to use its nonexclusive, irrevocable paid up license or its march-in rights, applies to "subject inventions" which are any patented inventions "conceived or first actually reduced to practice in the performance of work under a funding agreement." 35 USC 201(e), 202(a). Ritonavir is a "subject invention" for the purposes of the Act because it was conceived of and reduced to practice through NIAID grant A1027220.[7] Each of the six patents-at-issue in this petition included a statement of identification, stating that "This invention was made with Government support under contract number AI27220 awarded by the National Institute of Allergy and Infectious Diseases (NIAID). The Government has certain rights in this invention."[8]

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[4] *See* Attachment: 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 at Section 4.1.2 and n. 1 and accompanying text. A review of 17 of 30 New Molecular Entities approved by the FDA in 1998 found that the average number of patients in trials was 5,697, and the median number was 4,325. Source: Parexcel's Pharmaceutical R&D Statistical Sourcebook 1999.

[5] Id. at Section 4.1.2 and n. 2-3 and accompanying text.

[6] DataEdge estimated the out-of-pocket investigator and central laboratory costs per patient for Phase I-III clinicial trials were $6,454 in 1996. Parexcel's Pharmaceutical R&D Statistical Sourcebook 2002/2003, page 148.

[7] In the 2004 proceeding the fact that the patents were subject to federal rights was not in dispute.

[8] This statement complies with the requirement that patent applicants for inventions conceived of by federal funding identify the federal grant used.

3.2. Abbott is charging U.S. consumers higher prices than consumers in other high-income countries

Abbott's policy of charging U.S. residents five to nine times higher than consumers in other high income countries harms patients, makes U.S. private sector employers less competitive in international markets, limits access to ritonavir, has a negative impact on the public's health and welfare, and does not meet the requirement of making the benefits of the invention "available to the public on reasonable terms."

There is no question about the nature of Abbott's global pricing strategy -- it is to gouge U.S. private sector consumers for a drug that was invented on a government grant. Consider the following:

- In the U.S., the average wholesale price of per 100 mg tablet of Norvir $10.29 in March 2012. In August, the price of Norvir at a Washington, DC CVS pharmacy was $12.63 per tablet.

- The price for a 100 mg tablet of Norvir is $2.16 in Norway, $1.54 in France and Italy, $1.48 in Ontario Canada, $1.43 in Australia, $1.21 in the Netherlands, $1.17 in New Zealand, and $1.02 in the UK.

- Abbott's U.S. private sector AWP prices for Novir were 4.8 to 10.1 times higher than the prices in the eight foreign countries included in the price survey, all of which are members of OECD and considered high income by the World Bank. For a U.S. resident without insurance, the price can be 12 times the UK price.

3.3. Background of the Bayh-Dole Act

When Congress enacted the Bayh-Dole Act in 1980, making it easier for recipients of federal funding to retain title to the inventions developed from these funds, the statement of Policy and Objective said "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 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 USC 200

In creating safeguards to "protect the public against nonuse or unreasonable use of inventions," Congress provided the funding federal agency with a royalty free license to practice or have practiced any subject invention anywhere in the world. 35 USC 202(c)(4). Additionally, Congress provided for "march-in rights," which give the Government the power to require the contractor to issue a license "upon terms that are reasonable under the circumstances" or for the Government itself to grant licenses to third parties. 35 USC 203(a)

3.4. The Federal Government has broad authority to remedy cases where U.S. residents pay more for government inventions than do foreign consumers.

On the issue of charging US consumers more than foreign consumers, there are two issues before the NIH. First, does the statute permit the NIH to exercise its march in rights in such cases, and second, if such authority exists, will the NIH take a stand on behalf of the U.S. public?

When these issues were raised in 2004, the NIH refused to take any action on the drug pricing issue, and justified its position as follows:

> July 2, 2004 Decision of Elias A. Zerhouni, Director of NIH, In the Case of NORVIR® Manufactured by ABBOTT LABORATORIES, INC.
>
> 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 prices. The issue of drug pricing has global implications and, thus, is appropriately left for Congress to address legislatively.
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> /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.

The 2004 NIH decision does not dispute that the statute permits the NIH to address cases of excessive or discriminatory pricing, but, rather, the NIH chose not exercise this authority in the context of the 2004 ritonavir case.

It is our view that the NIH, as is the case with other federal agencies, has broad discretion when considering march-in requests under 35 USC 203. This includes broad discretion to act or not act. In deciding to reject the 2004 march-In request, some say the NIH acted within the law, arguing the law permits the NIH to make decisions that are indifferent to the impact of the policy on the public as consumers of drugs, purchasers of insurance, or as employers paying for drugs.

The decision before the Government is of course partly about the law, but also about the policies the NIH chooses to enforce. The Petitioners ask the NIH to reach a different conclusion than the one in the 2004 decision by Elias A. Zerhouni. It should not take an act of Congress to address an abuse of patent rights that is actionable under an existing act of Congress.

The NIH has four possible legal mechanism for addressing the outrageously high prices of Norvir to U.S. residents.

3.4.1. Royalty free contract

The government's "nonexclusive, nontransferable, irrevocable, paid-up license" can be used "to practice or have practiced for or on behalf of the United States any subject invention throughout the world." In the case of ritonavir, a treatment for a contagious and deadly disease, the U.S. government can break the Abbott monopoly without any finding of a patent abuse, simply by entering into agreements with generic suppliers to manufacture and distribute generic versions of the drug, including cases where the drug is co-formulated with other products.

While this approach is relatively simple from the point of exercising the governments rights, which are absolute, immediate, and not dependent upon the actions of Abbott, it does require a level of engagement in the manufacturing and sale of products that presents its own challenges, but those challenges are manageable and the efforts are worthwhile relative to the benefits to the public.

The NIH can exercise its royalty free license to the subject patents, and enter into contracts with third parties to provide services to the US government, including to provide generic versions of ritonavir, in both standalone products and in coformulated combination products. Such contracts could specify maximum prices, informed by the fact that Abbott is now providing ritonavir for $.11 per pill in some developing country markets, and five generic companies are selling FDA approved versions of ritonavir outside the U.S. under the PEPFAR program.

3.4.2 The March-In approach

In addition to the royalty free license to practice or have practiced the inventions by or for the government, there is the option of granting licenses to third parties under the march-in provisions of 35 USC 203. The march-in statute provides four separate causes of action (35 USC 203(a)(1-4), including two (1-2) that are relevant and actionable solely on the basis of Abbott's actions, and another (3) that would require a finding that the action relates to "requirements for public use specified by Federal regulations."

> 35 USC 203(a) (1) Action to remedy a failure to achieve "practical application" of the subject invention in a particular field of use, where "practical application" is defined in 35 USC 201(f) as making the benefits of the invention "available to the public on reasonable terms."
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> 35 USC 203(a) (2) "Action necessary to alleviate health or safety needs which are not reasonably satisfied" by the patent holder.
>
> 35 USC 203(a) (3) Action is necessary "to meet requirements for public use specified by Federal regulations" which are "not reasonably satisfied" by the patent holder.

In the march-in approach, the agency may require the contractor to issue a license "upon terms that are reasonable under the circumstances" or may grant a license itself. *Id*.

3.4.1.1. March-In for failing to achieve "practical application" of the invention.

The NIH can make a finding that under 35 USC 203(a)(1), the patent holder has not taken "effective steps to achieve practical application of the subject invention" in the field of use of treatments for HIV/AIDS or other FDA approved applications. This approach was a focus of a 2001 article by Professors Peter Arno and Michael Davis in the Tulane Law Review. Arno and Davis argued the Government ignored its authority and responsibility to protect the public from unreasonable prices on government funded medical inventions.[9]

The statute authorizes a march-in when:

> **35 USC 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;

The importance of this provision in the present case is enhanced by the definition of the term "practical application," which references "benefits. . . available to the public on reasonable terms."

> **35 USC 201 Definitions.**
> (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.

In the 2004 case, Abbott and a number of persons from the university and professional technology transfer community argued that "benefits . . . available to the public on reasonable terms" did not extend to the price of the product -- an argument we reject. The plain meaning of the statutory language is "available to the public on reasonable terms," and is also read in the context of the "Policy and Objective" of the Act, which expresses the intent of Congress:

> 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 USC 200, *emphasis added*]

The place within the Act where one can most directly address the need to "protect the public" against any "unreasonable use" of inventions is 35 USC 203(a)(1).

Senator Birch Bayh was among those testifying during a 2004 NIH meeting on the ritonavir request, asserting that the Bayh-Dole safeguards had nothing to do with the price of the product. Not only did Senator Bayh not disclose that his law firm represented Abbott, but he failed to explain why he had taken a contrary position in 1997 when he and Lloyd Cutler wrote to Secretary Shalala and invited DHHS to consider taking action under the Act to address the

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[9] Peter Arno & Michael Davis, "Why Don't We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed upon Patents Deriving in Whole or in Part from Federally Funded Research," 75 *Tulane Law Review* 631 (2001).

impact of high royalties on the prices on medical care. For example, in a March 3, 1997 letter, Bayh and Cutler wrote:[10]

> "Moreover, investigation may be needed to determine whether the royalty layering that plainly exists in the present case . . . is a common problem that leads to unreasonably high royalties (and prices of medical care) that should be dealt with by regulation."

In this case, there should be no hesitation in describing Abbott's private sector prices as unreasonable, and likewise, no hesitation in recognizing the taxpaying public expects its government officials to fashion and implement a remedy to this injustice.

3.4.1.2. March-In for failing to reasonably satisfy health and safety needs.

Under 35 USC 203(a)(2), a march-in request may be granted when

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

The high U.S. private sector prices for Norvir are not reasonable, and it is absurd to suggest that prices are irrelevant as regards health needs. The Bayh-Dole Act should not be read as though there is no limit on the prices that one can charge on a government funded invention, as if any price is reasonable or that prices have no impact on the ability of the public to access the inventions.

Because of its high price, Norvir has been listed as a "Tier 4" drug for some insurance plans, and as a consequence, some patients have a co-pay of 25 percent of the cost of the drug to the plan. For a person who takes two 100 mg tablets of ritonavir per day, the co-payment will run more than $150 per month, and this is for only one of four drugs in an antiretroviral treatment regime. The co-payment is more than four times the total cost of the drugs in many high income countries. For someone without insurance, including the many people who are no longer eligible for the increasingly restrictive ADAP programs, the cost of the drug can be $7.7 to $9 thousand per year, which is taken together with at least three other drugs, all of which can be expensive.

When drugs become expensive, there are several negative impacts on health, including poor compliance and deferred or interrupted treatment. HIV/AIDS is a deadly, contagious disease, and new research demonstrates that access to medicine not only improves health outcomes, but also reduces significantly the chances for new infection.

3.4.1.3. March-In when necessary to meet requirements for public use specified by Federal Regulations.

High drug prices make it more difficult for employers and insurance companies to comply with the requirements set forth by federal regulations implementing acts such as the Americans with Disabilities Act (ADA) or the Patient Protection and Affordable Care Act (PPACA).

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[10] See: Birch Bayh's competing interests and evolving views," August 23, 2012. http://www.keionline.org/node/1537.

Under the Bayh-Dole Act, "march-in" rights may be granted where "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." 35 USC 203(a)(3).

The Equal Employment Opportunity Commission (EEOC) regulations implementing the ADA prohibit companies subject to the ADA from discriminating against those with disabilities, including those persons who are HIV-positive. These regulations protect against discrimination from, *inter alia,* recruitment, hiring, promotion, award of tenure, leaves of absence, and sick leave. Employers are not permitted to deny a qualified individual under the Act equal access to insurance.[11] The Appendix to these regulations provide interpretive guidance and the portion relevant to the definition of "qualified individual" explicitly states that determining whether an individual with a disability is qualified for employment purposes, "should not be based on speculation that the employee may become unable in the future or may cause increased health insurance premiums or workers compensation costs."[12] Federal regulations prohibit employment discrimination on the basis of increased health insurance premiums or costs; high drug prices for HIV/AIDS medicines can make it more difficult for employers, particularly smaller employers that have just 15 or more employees, to comply with these regulations.

The interim regulations implementing the PPACA prohibit the current practice of implementing annual or lifetime caps, or exclusions based on pre-existing conditions. The summary to these PPACA interim regulations state that "These limits particularly affect people with high-cost conditions, which are typically very serious"[13] and specifically note concerns regarding high costs of treatment for cancer patients and HIV/AIDS patients. These regulations provide a general rule that "a group health plan, or a health insurance issuer offering group health insurance coverage, may not establish any annual limit on the dollar amount of benefits for any individual" and also "may not establish any lifetime limit on the dollar amount."[14] Similarly group plans and health insurance companies "may not impose any preexisting condition exclusion."[15] In the past, insurance companies have instituted caps or exclusions due to the high costs of treatment for those suffering from specific diseases, but will no longer be permitted to do so. While the regulations aim to protect those who would normally be impacted by such caps or exclusions, we note that unnecessarily high costs of treatment could create difficulty for insurers to comply with these regulations. As a result, insurers will be forced to find ways to cover the amounts that generally exceed lifetime or annual cap expenditures. The NIH should therefore exercise its march-in rights under the Bayh-Dole Act to ensure that employers and insurers can comply with federal regulations.

3.5. The higher U.S. pricing of ritonavir restricts the ability of U.S. corporations to compete in a global world.

As noted several times above, the high pricing of ritonavir domestically restricts the ability of U.S. corporations to compete in a global world. President Barack Obama and his administration cited the high costs of health care insurance which include, in part, the pricing of prescription

[11] Appendix to 29 CFR Part 1630—Interpretive Guidance on Title I of the ADA, §1630.16, available at http://www.gpo.gov/fdsys/pkg/CFR-2011-title29-vol4/xml/CFR-2011-title29-vol4-part1630.xml
[12] Id. at §1630.2(m).
[13] U.S. Department of Labor, Employee Benefits Security Administration final rules, available at http://webapps.dol.gov/FederalRegister/HtmlDisplay.aspx?DocId=23983&AgencyId=8&DocumentType=2
[14] 25 CFR §54.9815-2711T.
[15] 25 CFR §54.9801-3(a)(1).

drug treatments, as harmful to employers, leading to layoffs, reduced benefits and a lack of competitiveness of U.S. corporations in the global market. For example, in a 2009 speech by President Obama to the American Medical Association, the President said “the cost our health care is a threat to our economy. It is an escalating burden on our families and businesses. It is a ticking time-bomb for the federal budget. And it is unsustainable for the United States of America.”

http://blogs.wsj.com/health/2009/06/15/text-of-obamas-speech-before-the-ama/

June 15, 2009, Text of Obama’s Speech to the AMA

....

Make no mistake: the cost of our health care is a threat to our economy. It is an escalating burden on our families and businesses. It is a ticking time-bomb for the federal budget. And it is unsustainable for the United States of America. . .

Our largest companies are suffering as well. A big part of what led General Motors and Chrysler into trouble in recent decades were the huge costs they racked up providing health care for their workers; costs that made them less profitable, and less competitive with automakers around the world. If we do not fix our health care system, America may go the way of GM; paying more, getting less, and going broke.

When it comes to the cost of our health care, then, the status quo is unsustainable. Reform is not a luxury, but a necessity. I know there has been much discussion about what reform would cost, and rightly so. This is a test of whether we – Democrats and Republicans alike – are serious about holding the line on new spending and restoring fiscal discipline.

But let there be no doubt – the cost of inaction is greater. If we fail to act, premiums will climb higher, benefits will erode further, and the rolls of uninsured will swell to include millions more Americans.

If we fail to act, one out of every five dollars we earn will be spent on health care within a decade. In thirty years, it will be about one out of every three – a trend that will mean lost jobs, lower take-home pay, shuttered businesses, and a lower standard of living for all Americans.
....

These comments are supported by reports by RAND and the Council of Economic Advisors[16] and several officials in the Obama Administration, speaking about the Affordable Care Act, echoed the views that lower health care costs will aid recovery of the domestic economy and make the U.S. more competitive in the global market.[17]

When drug prices are higher in the U.S. than elsewhere, U.S. companies must either reduce the number of U.S. based employees on its payroll or lower their salaries in order to compete in the global economy.

4. Remedy

It is the policy and objective of the Bayh-Dole Act:

> . . . 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 USC 200]

We do not ask that the NIH address all possible concerns about drug pricing in this petition, but we do ask that the NIH deal with a particular issue as regards drug pricing -- the cases when the prices for products based upon government funded inventions are higher in the U.S. than in other high-income countries.

We also ask the NIH to adopt a policy as regards the importance of licensing patents when necessary to develop a dependent technology, such as a coformulated fixed dose combination.

Additionally, we ask the NIH to adopt a policy to address other anticompetitive, abusive or unfair practices

In order to make the costs of administering a policy in this area less costly, and to provide clear guidance to other patent holders, we propose the NIH adopt two policy rules.

4.1. Rule 1: Ceiling on prices to U.S. residents

The Secretary shall normally grant open licenses to third parties to use patented inventions that have benefited from federal funding, subject to the payment of a reasonable royalty and an

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[16] See: "Rapid Growth in Health Care Costs Hurts U.S. Industries," *Rand Review* Vol. 33, No. 3 at 5 (2009-2010) *("*The rapid growth in health care costs in the United States is linked to job losses and lower gross economic output among industries that commonly provide workers with health insurance.")*; Executive Office of the President, Council of Economic Advisers, The Case of Health Care Reform* (June 2, 2009) (finding that lowering cost-growth of health care would lower the unemployment rate).

[17] White House, Office of the Press Secretary, "Obama Administration Officials: What They're Saying About the Affordable Care Act" (January 19, 2011), available at http://www.whitehouse.gov/the-press-office/2011/01/19/obama-administration-officials-what-they-re-saying-about-affordable-care. For example, Secretary of Commerce Gary Locke, in speaking generally about high U.S. health care costs, " These costs were forcing companies to ship jobs overseas and making it tougher for them to compete with foreign competitors who almost universally had lighter health care costs"

appropriate field of use, if a product or products based upon those inventions are sold in the United States at prices higher than in other high income countries. In implementing this rule, we suggest the following standard for a ceiling on prices to U.S. residents.

Proposed standard for ceiling on prices to U.S. residents

The Government should consider the high, mean and median prices charged in the ten largest foreign economies, as measured by GNP, among the countries determined by the World Bank to be high income. U.S. prices will presumptively not be considered reasonable, and contracts will be given or licenses granted to competitors to supply the products to U.S. consumers, if any of the following are true for either public or private sector prices:

(1) U.S. prices are higher than seven of the comparison countries, or

(2) U.S. prices are 10 percent higher than the median price of the reference countries.

A licensee may rebut the presumption of unreasonable pricing by providing evidence that its actual risk adjusted R&D costs would not be recovered, but for the charging of higher prices in the U.S. market, or other evidence specific to the risk adjusted costs for the licensed invention.

Discussion of Rule 1

This language is one of many possible formulations that would provide meaningful protections to the U.S. public, and would have the practical effect of ensuring that U.S. residents do not face higher prices than do foreigners for drugs invented with federal funding.

The NIH could consider other approaches, but under almost any formulation the U.S. private sector prices for Norvir would be found to be excessive or unreasonable when compared to foreign prices.

In considering this rule, the NIH should take note of other cases where government funded inventions are made available to U.S. residents at much higher prices than patent holders charge foreign consumers. In a November 11, 2011 survey of U.S. and foreign prices for 14 drugs with U.S. government rights in patents listed in the FDA Orange Book,[18] Tedmund Wan found that: "For 13 of 14 products, prices from drugstore.com are higher than any on the nine foreign countries, and at times significantly so." The sole exception was for the combination product Kaletra, which was lower than three country prices, and higher than six country prices. For Kaletra, the average retail U.S. price was 30 percent higher than the median foreign price. Among the 13 products where U.S. prices were higher than all foreign comparisons are these two examples:

[18] Tedmund Wan. Survey of drug prices for 14 drugs with US government rights in patents listed in the FDA Orange Book, KEI Research Note 2011:2. November 11, 2011

- "Also having a disproportionally high retail drug price in the United States is sitagliptin phosphate (Januvia), a diabetes medication. The price of this medication is available in all but one country in the survey (New Zealand). In no foreign market is Januvia being sold for more than $3.37USD per 100mg dose. In the United States however, the same dosage is being sold for $7.20USD, more than twice the price any consumer has to pay in any of the seven countries where pricing data for this drug is available."

- "Tobrex is another drug that cost American consumers significantly more than consumers in other countries. Tobrex is sold for $72.53USD per 5ml bottle on drugstore.com, while none of the other 5 countries with available data is selling the same medication for more than $19.92USD per 5ml bottle, slightly more than a quarter of what consumers in the U.S. pay for the exact same drug. In fact, aside from Australia, none of the other 4 countries sell Tobrex for more than $14.30USD per 5ml bottle, which means that U.S. consumers are paying 5 times as much as consumers in Denmark, the Netherlands, New Zealand, and Norway."

4.2. Rule 2: Use of invention for a dependent technology:

The Secretary shall grant licenses to third parties to use patented inventions that have benefited from federal funding, subject to the payment of a reasonable royalty and an 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.

Discussion of Rule 2

There are a growing number of cases where NIH funded inventions are being withheld from firms seeking to develop new products or services that are potentially important medically. The rationale for exclusive licensing is strongest when the invention has a single use and the temporary monopoly is justified as an inducement to invest in product development. When an invention can be used in a new product there is a strong public interest is mandating licensing under reasonable terms.

4.3 Taking Action now

Since the passage of the Bayh-Dole Act in 1980, the NIH has sought to avoid openly implementing safeguards to protect the public from unreasonable use of patented inventions. The failure to grant a single march-in request in more than 30 years has sent a signal to the patent holder that the NIH will permit almost anything, no matter how abusive that action is to

the public that paid for the research. For this to change the NIH has to accept that federal funding financed by taxpayers comes with obligations to treat the public fairly when it comes to the pricing or management of the invention.

In the present case the NIH could act immediately, by exercising its royalty free license to authorize multiple entities to manufacture and sell generic version of ritonavir in order to treat persons with HIV/AIDS.

The march-in case could be addressed, including any appeals, in order to establish a precedent for the march-in grounds, but by exercising the royalty free right now, as a parallel remedy, the NIH would send a loud and effective signal that U.S. residents should not face higher prices than people living in other high income countries.

Finally, the NIH can begin the process of long overdue rulemaking to address issues such as the reasonable royalties for licensing (and relicensing) of NIH patents (the proposal by Birch Bayh and Lloyd Cutler in 1997), the licensing of patents for use in dependent technologies, and other public interest concerns.

5. Attachments

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 (2004).

Tedmund Wan. Survey of drug prices for 14 drugs with US government rights in patents listed in the FDA Orange Book, KEI Research Note 2011:2. November 11, 2011