

Consumer Project on Technology

<http://www.cptech.org>
P.O. Box 19367, Washington, DC 20036
Voice +1.202.387.8030, Fax +1.202.234.5176

July 1, 2004

Department of Commerce
International Trade Administration
14th and Constitution Avenue
Room 4039
Washington, DC 20230.

Attn: Kristie Mikus via: drugpricing@ita.doc.gov.

Re: Study of international drug pricing as required by
section 1123 of the Medicare Prescription Drug,
Improvement and Modernization Act of 2003.

Table of Contents

1. Introduction.....	1
2. US Residents Pay The Most For Global Pharmaceutical R&D	1
3. Private Sector R&D is Not Very Productive or Innovative	2
4. US Residents Pay Higher Prices For Government Funded Inventions	3
5. Reasons Why US Residents Pay More	3
6. US Consumers Are Harmed by High Drug Prices.	4
7. Drug Manufacturers Abuse Patent Rights.....	5
8. US Residents Need Protections from Abuses	6
9. Most OECD Cost Control Approaches Rely upon Rationing	7
10. Trade Paradigm Should Not Rely Upon High Drug Prices	7
11. R&D+ Trade Paradigm -- Sharing of Global R&D Costs	8
12. Trading Partners Will Be More Receptive to R&D+	9

1. Introduction

The Consumer Project on Technology (CPTech) is a non-profit organization that represents consumer interests in policies designed to promote innovation in new medicines. CPTech has considerable experience and expertise in the international aspects of these issues, including trade related aspects of intellectual property rights, drug pricing and financing of R&D.

2. US Residents Pay The Most For Global Pharmaceutical R&D

US residents pay more as taxpayers and consumers for pharmaceutical R&D than do persons in other OECD countries.

The most important US contributions to global R&D are from the public sector. The \$28+ billion per year the US government spends on the National Institutes of Health and the significant amounts spent on health care R&D in other federal agencies (CDC, DOE, DOD, NSF, FDA, etc) are highly valued resources for the entire global scientific community. These public sector expenditures on R&D are more than 25 basis points of US GDP. No other country comes close.

The US tax expenditures are another important factor in supporting health care R&D. US incentives for private individuals to donate money to health care research supports important efforts such as those of the Ford, Rockefeller, and Gates Foundations and many important smaller efforts. The Orphan Drug Tax Credit subsidizes half of the cost of clinical trials for qualifying diseases.

US consumers also face relatively higher prices for patented medicines than do most other OECD countries. The prices US consumers pay depends greatly upon how purchases are financed. Uninsured persons who pay out-of-pocket generally pay more than those who have insurance. Because of the importance of negotiations between third party payers and manufacturers, the differences in prices are often substantial, particularly for drugs that have some competition within a therapeutic class. However, sellers of drugs for severe illnesses, particularly those that are not substitutable for medical reasons, often have more rigid pricing for persons with insurance, combined with some programs to provide discounts to uninsured patients. Government funded programs, like the VA, Medicaid or ADAP, have other discount provisions. On the whole, however, the US pays higher prices for patented medicines than do most other OECD countries.

Based upon data from the US IRS regarding the federal R&D Tax Credit and other sources, CPTech estimates that 13 percent of US pharmaceutical sales are reinvested in R&D. Given current outlays on medicines, this is more than 25 billion dollars in private sector R&D that is financed from purchases of drugs by US residents -- or about 25 basis points of GDP from consumers.

Taken together, US residents, taxpayers and consumers pay for R&D in amounts greater than 50 basis points of GDP. We estimate that other OECD countries pay considerably less, probably in the range of 5 to 20 basis points of GDP.

3. Private Sector R&D is Not Very Productive or Innovative

CPTech estimates that the patent system increased the cost of pharmaceutical products by \$400 billion globally in 2003. This higher cost is justified on the grounds that it finances R&D.

Despite staggering increases in consumer outlays for new medicines, the rate of innovation in new drugs is modest. Over the past eleven years, about 70 percent of New

Chemical Entities (NCEs) registered with the US FDA were judged not significantly better than existing treatments. Clinical trials for the “me too” products were almost twice as large as the trials on the innovative products, suggesting an even greater bias in investment toward “me too” drugs.

4. US Residents Pay Higher Prices For Government Funded Inventions

One particularly vexing issue concerns prices for drugs invented on US government funded grants and contracts. For drugs like ritonavir/Norvir (AIDS) or Lantanoprost/Xalatan (glaucoma), prices are far higher in the United States than in any other OECD country. For ritonavir/Norvir, an important drug for AIDS, US prices are about ten times the prices charged in Canada, Australia, New Zealand and some European countries. Lantanoprost/Xalatan is 2 to 5 times more expensive in the US than in several other OECD countries, despite the fact that US government funded the research that led to the drug’s discovery, and has rights to key patents under the Bayh-Dole Act. The Department of Health and Human Services could easily change this by announcing a policy that if products are priced higher in the US than in other high-income countries it would exercise its rights to issue licenses to federally funded patents under the March-In provisions of the Bayh-Dole Act. The fact that this does not happen illustrates how little the government has been willing to do in order to restrain prices for medicines in the US market. (See <http://www.essentialinventions.org> for additional background on the ritonavir and lantanoprost cases).

5. Reasons Why US Residents Pay More

There are many reasons why US drug prices are higher here than elsewhere. The primary reason is that the US government does not attempt to regulate drug prices or manage drug reimbursement policies on behalf of US consumers. If the US government would make even modest efforts to negotiate better drug prices, it would have a great impact. To appreciate this, consider the discounts on drug prices that are offered to countries with relatively small domestic markets (including individual provinces in Canada), and then consider the purchasing power associated with the US market. US consumers pay higher prices because the US government does almost nothing to obtain lower prices.

A different and related question is why this is so. Why have US voters tolerated high prices while also supporting large public expenditures on health care R&D? One possible explanation is that unlike virtually any other country, the US market is large enough to have a real impact on investor R&D decisions. Outside of the US or possibly Japan, even radical changes in national drug prices would have almost no impact on the global R&D market, taken by themselves. US public sector outlays on health care R&D are correctly perceived to have a large impact on innovation. US residents are largely optimistic about the benefits of pharmaceutical R&D, and they have been willing to pay a significant share of GDP on public sector expenditures for health R&D, even while other countries do not.

The US is also home to a large pharmaceutical and biotechnology industry, including domestic firms like Merck, Pfizer, Abbott, BMS and Amgen and foreign firms like Roche, GSK or Novartis that have substantial US operations. These firms provide employment opportunities for US workers, generating profits from foreign drug sales, and invest significantly in lobbying the US Congress and the Executive Branch, and in financing political campaigns. The domestic pharmaceutical industry uses its political power to advocate for higher US drug prices and also higher levels of public sector investments in health care R&D.

6. US Consumers Are Harmed by High Drug Prices.

Over the past two decades, outlays on medicines have increased sharply in absolute and relative terms. The rate of increase in drug prices appears to be rising. Steven Schondelmeyer from the Prime Institute notes that the average cost per day of therapy for new medicines had *increased* from \$1.09 per day before 1995, to \$3.44 per day by 2001. A recent AARP funded study found that the *increase* in the annual cost of therapy due to higher prices for widely used brand name drugs nearly doubled from 2000 to 2003, rising from \$33.76 to \$60.38.¹ For a typical older person who buys three prescriptions, the annual cost of buying medicines was *increased* by \$181 in 2003.

For medicines for severe illnesses, the costs can be far higher. In December 2003, Abbott increased the price of ritonavir by 400 percent. For AIDS patients who take 200 milligrams of ritonavir per day, the average wholesale price (AWP) increased from \$1,562 per year to \$7,811 per year. Ritonavir is typically taken in combination with at least three other ARV drugs. The new ARV products are far more expensive than the older drugs. The new AIDS drug T-20, which must also be taken in combination with other drugs, was introduced in the market at a cost of \$25 thousand per year, making this single drug more than twice as expensive as widely used three drug HAART combinations.

In a recent Washington Post guest editorial, cancer researcher and former BMS executive Dr. Robert Wittes described the impact of high drug prices on cancer patients.²

The average wholesale price (AWP, or the average price charged to hospitals and physician practices) of a month of treatment for a normal-size adult is roughly \$4,800 for Avastin and \$12,000 for Erbitux. Since most colorectal-cancer patients for whom these drugs are medically appropriate receive them not singly but in combination with other chemotherapeutics, the monthly AWP is more like \$11,000 for

¹ David J. Gross, AARP Public Policy Institute, Stephen W. Schondelmeyer, PRIME Institute, University of Minnesota, Susan O. Raetzman, AARP Public Policy Institute, *Trends In Manufacturer Prices Of Brand Name Prescription Drugs Used By Older Americans, 2000 Through 2003*. May 2004, Revised June 2004. Washington, DC AARP. http://research.aarp.org/health/2004_06_drugprices.pdf

² Robert E. Wittes "Cancer Weapons, Out of Reach," *Washington Post*, June 15, 2004. <http://www.washingtonpost.com/wp-dyn/articles/A42035-2004Jun14.html>

combinations including Avastin and \$16,000 for Erbitux. Providers pass these costs on to patients, along with charges that cover the costs of pharmacy and dispensing. Courses of treatment generally last several months, but they can be much longer for patients who respond favorably. In other words, the cumulative cost of treatment can be astronomical.

Although the uninsured and medically indigent may feel the effects of these pricing decisions most keenly, those with insurance will also face a nasty dilemma. The increasing co-pay percentages of most plans and the capping of benefits in others will compel a major financial outlay for those determined to have the treatments. And those who do not want their families to assume the financial burden will be left with bitter resentment.

Third-party payers will not react passively to pricing that increasingly threatens their balance sheets, especially as more drugs like these are commercialized over the next few years. They will carefully scrutinize all proposed uses of expensive new drugs. Historically, an FDA judgment of "safe and effective" -- the statutory criterion for drug approval -- has almost automatically triggered an agreement by payers to reimburse, which is the real gateway to widespread use and market success. We may now see payers deciding, for the first time, that certain novel "safe and effective" medicines are simply not worth paying for. In addition, payers will surely try to limit "off-label" uses of these drugs -- that is, uses other than the FDA-approved ones. Unlike other areas of medicine, physicians have commonly prescribed cancer drugs for a broader array of indications than specifically approved by the FDA, as clinical research routinely reveals additional uses after market introduction. A very high bar to new uses by payers is a virtual certainty.

7. Drug Manufacturers Abuse Patent Rights

We will not provide extensive discussions of this point, but will quote from a recent testimony by the Chairman of the United States Federal Trade Commission (FTC) concerning abuses by BMS in the marketing of two government funded cancer drugs (Taxol and Platinol) and BuSpar.³

Just last month, the FTC reached a major settlement with Bristol-Myers Squibb ("BMS") to resolve charges that BMS engaged in a series of anticompetitive acts over the past decade to obstruct entry of low-price generic competition for three of BMS's widely-used pharmaceutical products: two anti-cancer drugs, Taxol and Platinol, and the anti-anxiety agent BuSpar.⁽⁴⁶⁾ Among other things, the Commission's complaint alleged that BMS abused Food and Drug Administration ("FDA") regulations to obstruct generic competitors; misled the FDA about the scope, validity, and enforceability of patents to secure listing in

³ Prepared Statement of Timothy J. Muris, Chairman of the Federal Trade Commission, before the Subcommittee on Commerce, Justice, State, the Judiciary and Related Agencies of the Committee on Appropriations, United States House of Representatives Washington, D.C. April 9, 2003.

the FDA's "Orange Book" list of approved drugs and their related patents; breached its duty of good faith and candor with the U.S. Patent and Trademark Office ("PTO"), while pursuing new patents claiming these drugs; filed baseless patent infringement suits against generic drug firms that sought FDA approval to market lower-priced drugs; and paid a would-be generic rival \$72.5 million to abandon its legal challenge to the validity of a BMS patent and to stay out of the market until the patent expired. (*Footnotes omitted*)

The US FTC's discussion of the BMS cases is relevant, because in bilateral trade negotiations, the USTR is proposing mandatory linkages between patents and drug registration. These linkages are proposed as mechanisms to enhance the enforcement of the patent rights. But as evidenced in the BMS and similar cases, an unintended consequence is the abuse of the linkage for anticompetitive purposes.

We note also the increasing tendency of the incumbent drug manufacturers to game the patent system to block competitors, and also the negative impact on follow-on innovation:⁴

The increasing number of patents on minute and obscure aspects of pharmaceutical products is fast becoming the principle obstacle facing the industry. In the year 2000, for example, while the US Patent Office granted 6,730 pharmaceutical patents, the US Food and Drug Administration only registered 27 new chemical entities (NCE). This growing global trend is resulting in a tangled web of patents that creates a complex legal minefield protecting pharmaceutical inventions well-beyond a product's basic patent.

Designed to delay the entry of market competition from lower-priced generic products, the practice also allows the originator industry to reap continued benefits from older products. This not only keeps the cost of medicines unnecessarily high, but more worryingly, it eliminates the stimulus needed by research companies to discover new cures for life-threatening illnesses.

8. US Residents Need Protections from Abuses

The current US intellectual property right and regulatory regimes are imploding. Total US expenditures on medicines, through all channels including government programs, retail pharmacy sales and hospitals are now approaching 3 percent of US GDP, and increasing. Anticompetitive practices and abusive drug prices are also increasingly common. Unless the US government is willing to confront these problems realistically, we will face an increasing gap between our means and the prices of new medicines. The

⁴ "Tangled Patent Linkages Reduce Stimulation for Pharmaceutical Innovation: 6,730 patents for only 27 pharmaceutical inventions," European Generic Medicines Association Press Release, July 1 2004

uncontrolled use of patents to block competition and monopolize fields of medicine will also harm the public.

The US is asking for rules in bilateral trade agreements that will prevent both foreign trading partners and the US from effectively addressing abuses of patent rights or excessive pricing of pharmaceutical products.

Among the most important tools the US will need in the future is the ability to issue compulsory licenses on patents, in the event the patent owner refuses to sell products at reasonable prices, or if the patent owner uses patents to prevent follow-on research, and monopolize a field of medicine. A clear example of such abuse is in the Abbott ritonavir case, where Abbott increased prices for ritonavir by 400 percent, but the price increase only applied in the US, and only when ritonavir was used in combination with non-Abbott protease inhibitors. Abbott is seeking to monopolize the protease inhibitor market and to discourage competitive R&D in this market. The US Singapore/FTA would prevent the US government from adopting a general compulsory licensing statute similar to those common in European countries, leaving only the costly, time consuming and awkward US antitrust laws to address such abuses.

9. Most OECD Cost Control Approaches Rely upon Rationing

In most OECD countries, governments allow freedom to set drug prices, but use government reimbursement policies as incentives to reduce drug prices. Governments in Canada, Australia, New Zealand, the UK and elsewhere can creditably threaten to withhold reimbursement, or to increase the consumer co-payments, because they have a record of not paying for medicines that are considered too expensive. Taxol, an important cancer drug, was off-formulary for years in some OECD member countries, and then slowly introduced for limited applications. Singulair, a good drug for Asthma, is off-formulary in many OECD member countries.

Countries can avoid the problems of rationing if they are willing to issue compulsory licenses to patents when prices are unreasonable. However, US trade policy has sought to limit the use of compulsory licenses, particularly in OECD countries.

10. Trade Paradigm Should Not Rely Upon High Drug Prices

In November 2001, the members of the World Trade Organization (WTO) adopted the Doha Declaration on TRIPS and Public Health, which said the TRIPS Agreement “can and should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all.” This was a symbolic step toward fairness. But within months the US government launched a plethora of bilateral

trade negotiations seeking tough new “TRIPS Plus” intellectual property measures⁵ that plainly undermine the declaration.

The European Commission, the United States and Japan have also raised issues concerning drug pricing in various bilateral trade discussions. In 1999, the European Commission⁶ and the US⁷ asked Korea to accept hefty prices for patented medicines. The European Commission brought a similar case against Turkey in 2003.⁸ The United States has a long history of attacking price control mechanisms in poor countries, and has launched a campaign to undermine price negotiations by higher income countries.⁹

The TRIPS agreement and the growing number of new “TRIPS Plus” trade agreements are flawed. They seek to increase investment in R&D, but only by increasing prices.

Very little private R&D is invested in basic research, public goods such as the Human Genome Project (HGP), the development of vaccines, or higher priority medicines, such as new treatments for malaria. Higher IPR protection for products is also associated with a number of other problems, including excessive secrecy and anti-competitive barriers to follow-on innovation.¹⁰

11. R&D+ Trade Paradigm -- Sharing of Global R&D Costs

We propose a new trade framework -- focused directly on R&D rather than patent rights or drug prices, which are mechanisms to finance R&D.¹¹ The idea is to change the context. Rather than frame the agreement as one about commerce, it becomes an agreement about health care.

Money is important, and the development of new medicines is expensive. The global framework for R&D would not be about patent rights or high prices, which are indirect and sometimes inappropriate instruments to promote R&D, but rather the core issue of sharing the burden of paying for R&D. The trade framework has to prevent “free riding,” but it does not have to promote high drug prices.

Agreements on IPR or drug prices are partial steps to address free riding, but only consider one financing mechanism -- high drug prices. There are other options. Countries can impose

⁵ For patents: limitations on compulsory licensing, extension of terms, broader patent scope and lower novelty standards, and linkage to drug registration. Also, exclusive rights in health registration data.

⁶ 1999/C 218/03.

⁷ Korea agreed to price innovative drugs at the average price in the United States, United Kingdom, Germany, France, Italy, Switzerland, and Japan. *2002 National Trade Estimate Report on Foreign Trade Barriers*, USTR.

⁸ 2003/C 311/04.

⁹ The Australia Pharmaceutical Benefits Scheme (PBS) is regulated by the US/Australia FTA. Also International Trade Administration, Drug Pricing Study *Federal Register*: June 1, 2004, Volume 69, Number 105, Page 30882-30883.

¹⁰ *Keeping science open: the effects of intellectual property policy on the conduct of science*. Royal Society. April 2003.

¹¹ TJ Hubbard and J Love. “A New Trade Framework for Global Healthcare R&D” *PLoS Biology*, 2004. 2(2): p147-150.

R&D mandates on private firms, such as requirements that a percentage of drug sales or insurance premiums be invested in R&D. Mechanisms like the US Orphan Drug tax credit provide decentralized funding for clinical trials, as do tax incentives to donate money to charitable trusts, such as the Gates, Ford or Rockefeller Foundations. There is also the option of direct funding of R&D via the public sector, such as the \$100 per capita US taxpayers spend for the National Institutes of Health (NIH). Some economists and political leaders are advocating greater use of public or private sector funded “prizes” as a reward for successful innovation.

While other countries spend less (per capita) on public sector R&D than the US does, they all do something, and there is growing interest in alternative mechanisms to finance R&D, such as public private partnerships (PPPs), tax breaks, research mandates, competitive intermediaries, or prize funds. These also cost money.

A trade framework that only recognizes IPR skews global investments, and forces us to choose high drug prices to finance new medicines. It does nothing to address free riding in public goods, and it leads to more rationing and less access for medicines.

The R&D+ approach would address both public and private support for R&D, since both are important. It would also allow countries the freedom to choose the optimal mix of public and private sector spending, and it would allow more flexibility in terms of finance mechanisms. Most importantly, it would allow countries to choose mechanisms that are consistent with desired levels of access, and which are more efficient in promoting useful innovation. Competition among financing mechanisms would be encouraged.

12. Trading Partners Will Be More Receptive to R&D+

There is considerable resistance and resentment in foreign countries toward US pressures to impose TRIPS+ IPR obligations or to dismantle or weaken cost control tools. For this reason, the “high price” strategy is unlikely to be very successful within the OECD. Most importantly, the members of the European Union are unlikely to agree to US efforts to weaken European cost control measures.

In an ambitious multilateral setting, the R&D+ approach would involve setting targets for R&D that are reasonably related to incomes and stages of development -- such as 10 to 15 basis points of GDP. In meeting such targets, countries would have several options, including the purchase of patented medicines, and getting credit for the share of sales manufacturers actually reinvest in R&D. But countries could choose other options, such as investing money in their own universities or businesses, using resources domestically to build capacity and provide skills and jobs.

For bilateral, regional or more limited multilateral negotiations, the R&D+ approach can supplement or co-exist with traditional IPR agreements. R&D+ is an important alternative that addresses legitimate concerns about sharing of R&D costs. In negotiations with the US for Free Trade Agreements (FTAs), the US or its trading partners could propose that the foreign partner increase domestic spending on R&D, particularly for priority projects, such as

the new proposal announced at the G8 for a global effort to financing R&D on a new AID vaccine.

While R&D+ will require some trading partners to do more than they do now to pay for global R&D, they can choose approaches that both permit the protection of consumer interests, and provide for domestic jobs in the R&D field.

By framing the issue in terms of public health, and by providing a flexible path for implementing national obligations, R&D+ agreements will be seen in a more positive light -- rather than as concessions to rent seeking demands by the US. There will also likely be support from European finance and health ministers, who are increasingly facing the same types of fiscal pressures, as are US corporate insurers, and the US taxpayers.

Ultimately, we need a more rational international trade framework, that addresses the fair sharing of the costs of new drug development, but which also do not eliminate or hamstring the tools needed to address abuses of patent rights or drug prices. R&D+ is the best approach, and the perhaps the only approach that will receive global support.

Sincerely,

James Love
Director, CPTech
P.O. Box 19367, Washington, DC 20036
Voice +1.202.387.8030
Fax +1.202.234.5176
<mailto:james.love@cptech.org>