

**Rx R&D Myths:  
The Case Against The Drug  
Industry's R&D "Scare Card"**



**Congress Watch  
July 2001**

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# **Rx R&D Myths: The Case Against The Drug Industry's R&D "Scare Card"**

## **Executive Summary**

This new Public Citizen report reveals how major U.S. drug companies and their Washington, D.C. lobby group, the Pharmaceutical Research and Manufacturers of America (PhRMA), have carried out a misleading campaign to scare policy makers and the public. PhRMA's central claim is that the industry needs extraordinary profits to fund expensive, risky and innovative research and development (R&D) for new drugs. If anything is done to moderate prices or profits, R&D will suffer, and, as PhRMA's president recently claimed, "it's going to harm millions of Americans who have life-threatening conditions." But this R&D scare card – or canard – is built on myths, falsehoods and misunderstandings, all of which are made possible by the drug industry's staunch refusal to open its R&D records to congressional investigators or other independent auditors.

Using government studies, company filings with the U.S. Securities and Exchange Commission and documents obtained via the Freedom of Information Act, Public Citizen's report exposes the industry's R&D claims:

- The drug industry's claim that R&D costs total \$500 million for each new drug (including failures) is highly misleading. Extrapolated from an often-misunderstood 1991 study by economist Joseph DiMasi, the \$500 million figure includes significant expenses that are tax deductible and unrealistic scenarios of risks.
- The actual after-tax cash outlay – or what drug companies really spend on R&D – for each new drug (including failures) according to the DiMasi study is approximately \$110 million. (That's in year 2000 dollars, based on data provided by drug companies.) (See Section I)
- A simpler measure – also derived from data provided by the industry – suggests that after-tax R&D costs ranged from \$57 million to \$71 million for the average new drug brought to market in the 1990s, including failures. (See Section II)
- Industry R&D risks and costs are often significantly reduced by taxpayer-funded research, which has helped launch the most medically important drugs in recent years and many of the best-selling drugs, including all of the top five sellers in one recent year surveyed (1995).
- An internal National Institutes of Health (NIH) document, obtained by Public Citizen through the Freedom of Information Act, shows how crucial taxpayer-funded research is to top-selling drugs. According to the NIH, taxpayer-funded scientists conducted 55 percent of the research projects that led to the discovery and development of the top five selling drugs in 1995. (See Section III)

- The industry fought, and won, a nine-year legal battle to keep congressional investigators from the General Accounting Office from seeing the industry's complete R&D records. (See Section IV) Congress can subpoena the records but has failed to do so. That might owe to the fact that in 1999-2000 the drug industry spent \$262 million on federal lobbying, campaign contributions and ads for candidates thinly disguised as "issue" ads. (See accompanying report, "The Other Drug War: Big Pharma's 625 Washington Lobbyists")
- Drug industry R&D does not appear to be as risky as companies claim. In every year since 1982, the drug industry has been the most profitable in the United States, according to *Fortune* magazine's rankings. During this time, the drug industry's returns on revenue (profit as a percent of sales) have averaged about three times the average for all other industries represented in the Fortune 500. It defies logic that R&D investments are highly risky if the industry is consistently so profitable and returns on investments are so high. (See Section V)
- Drug industry R&D is made less risky by the fact that only about 22 percent of the new drugs brought to market in the last two decades were innovative drugs that represented important therapeutic gains over existing drugs. Most were "me-too" drugs, which often replicate existing successful drugs. (See Section VI)
- In addition to receiving research subsidies, the drug industry is lightly taxed, thanks to tax credits. The drug industry's effective tax rate is about 40 percent less than the average for all other industries. (See Section VII)
- Drug companies also receive a huge financial incentive for testing the effects of drugs on children. This incentive called pediatric exclusivity, which Congress may reauthorize this year, amounts to \$600 million *in additional profits* per year for the drug industry – and that's just to get companies to test the safety of several hundred drugs for children. It is estimated that the cost of such tests is less than \$100 million a year. (See Section VIII)
- The drug industry's top priority increasingly is advertising and marketing, more than R&D. Increases in drug industry advertising budgets have averaged almost 40 percent a year since the government relaxed rules on direct-to-consumer advertising in 1997. Moreover, the Fortune 500 drug companies dedicated 30 percent of their revenues to marketing and administration in the year 2000, and just 12 percent to R&D. (See Section X)

# **Rx R&D Myths: The Case Against The Drug Industry's R&D "Scare Card"**

## **Introduction**

Major U.S. drug companies and their trade association, the Pharmaceutical Research and Manufacturers of America (PhRMA), have carried out a campaign to scare policy makers and the public. The central claim of PhRMA's campaign is ominous: if anything is done to restrain high U.S. prescription drug prices, then research and development (R&D) to find new drugs for life-threatening diseases will suffer.

Alan Holmer, president of PhRMA, recently played this "R&D scare card" while on National Public Radio's "Talk of the Nation" program.

"Believe me," Holmer warned, "if we impose price controls on the pharmaceutical industry, and if you reduce the R&D that this industry is able to provide, it's going to harm my kids and it's going to harm those millions of other Americans who have life-threatening conditions."<sup>1</sup>

Later in the program, to reinforce his argument, Holmer made the claim that research costs "\$500 million just to get one medicine to market."

The drug industry's "R&D scare card" is built on the premise that drug companies need extraordinary profits – about three times those of the average Fortune 500 company – in order to conduct expensive and risky research on innovative new drugs. But evidence shows the research isn't as expensive, risky or innovative as the industry claims.

Instead, the evidence shows that such research may cost far less than \$500 million for every new drug – and may be less than \$100 million for every new drug (including failed drugs). The evidence also shows that the drug industry isn't all that innovative, as it produces far more "me-too" or copycat drugs of little medical importance than life-saving medicines.<sup>2</sup> And, the evidence suggests that drug industry research isn't all that risky because the industry is awash in profits while lightly taxed and heavily subsidized. In fact, an internal National Institutes of Health (NIH) study obtained by Public Citizen shows that taxpayer-funded scientists and foreign universities conducted 85 percent of the published research studies, tests and trials leading to the discovery and development of five blockbuster drugs.<sup>3</sup> It's no wonder the drug industry fought all the way to the Supreme Court to keep its R&D records hidden from congressional investigators.

In all, the evidence shows that the drug industry's R&D scare card is, in reality, an R&D "canard" – that is "an unfounded or false, deliberately misleading story."

## I. Deconstructing the \$500 Million Myth

The story of PhRMA's R&D canard starts with the drug industry's repeated – and unchallenged – claim that it costs \$500 million to develop a new drug, including money spent on failures. The \$500 million figure has become ubiquitous and widely accepted. Unfortunately, it is misleading at best and inaccurate at worst.

Public Citizen calculated more realistic R&D costs using methodology modeled after that employed by the congressional Office of Technology Assessment (OTA) in its 354-page report, "Pharmaceutical R&D: Costs, Risks and Rewards," published in 1993. (See Appendix A)

These are our findings:

- As the OTA noted, "the industry's collective response to charges that drug prices are too high or are increasing too fast has been to point to the high and increasing cost of pharmaceutical R&D." Specifically, "industry representatives have pointed to academic studies of the average cost of bringing a new pharmaceutical compound to the market."<sup>4</sup>
- This decade, industry representatives have pointed to one academic study above all for the \$500 million figure. That is a 1991 study by Joseph DiMasi of the Tufts Center for the Study of Drug Development. PhRMA representatives have acknowledged that the \$500 million figure is an extrapolation, adjusted for inflation and changes in research and development, based on the Tufts Center study.<sup>5</sup> DiMasi estimated the *pretax* cost of developing certain new drugs, including failures, at \$231 million in 1987.<sup>6</sup>
- OTA later revised DiMasi's \$231 million figure with significantly higher opportunity cost of capital. (Opportunity cost of capital is a calculation of what a R&D expenditure might be worth had the money been invested elsewhere. DiMasi used a 9 percent annual rate of return to calculate the cost of capital. OTA used a rate that went from 10 to 14 percent over time.) OTA put the "upper bound of the full capitalized cost" of R&D per new drug at \$359 million in 1990 dollars. Inflated to year 2000 dollars, this estimate becomes \$473 million, and it has been rounded up to \$500 million by the industry.<sup>7</sup>
- The Tufts Center for the Study of Drug Development is a self-described "independent research group affiliated with Tufts University." The center's sponsors include some of the world's largest drug companies such as Merck, Pfizer and Bayer.<sup>8</sup> According to the Tufts Center, corporate sponsors get to "help shape strategic objectives" and "influence key Center activities."<sup>9</sup>
- DiMasi's study relied on data provided by 12 drug companies.<sup>10</sup> This information has not been independently verified, nor checked for accuracy. The OTA issued this warning about DiMasi's data: "Any company that understood the study methods and the potential policy uses of the study's conclusions could overestimate costs without any potential for discovery. Thus, the motivation to overestimate costs cannot be discounted."<sup>11</sup>

- It's important to note that DiMasi's study only focuses on the cost of developing "new chemical entities" (NCEs), which he defines as drugs that have never been tested before in humans.<sup>12</sup> (His definition of NCE differs only slightly from the Food and Drug Administration definition of a new molecular entity, or NME.<sup>13</sup>) Furthermore, DiMasi focuses only on "self-originating" NCEs, which are new entities developed by companies as opposed to those they acquire from other research organizations. Many new drugs approved for market are not NCEs, but are new dosage forms or new combinations of existing drugs.<sup>14</sup> Thus, DiMasi focuses only on the most expensive new drugs, not *all* new drugs, resulting in a *higher* cost estimate.
- DiMasi's original \$231 million figure does not represent what companies *actually spend* to discover and develop new molecular entities. Rather, it includes the cost of all failed drugs and the expense of using money for drug research rather than other investments. It also *does not* account for huge tax deductions that companies get for R&D. Therefore, it substantially *overestimates* net expenditures on R&D.
- According to the OTA, "The net cost of every dollar spent on R&D must be reduced by the amount of tax avoided by that expenditure. Like all business expenses, R&D is deductible from a firm's taxable income."
- The OTA revised DiMasi's calculation, subtracting the expenses that are tax deductible under Section 174 of the federal tax code and the opportunity cost of capital.
- The tax deduction reduces the cost of R&D by the amount of the corporate marginal tax rate (currently 34 percent). This means, in effect, that every dollar spent on R&D costs \$0.66.<sup>15</sup> The OTA concluded that DiMasi's original \$231 million figure (in 1987 dollars) was \$171 million (in 1990 dollars) after accounting for the R&D tax deduction.
- The opportunity cost of capital accounts for slightly more than half (51 percent) of DiMasi's total figure. After subtracting tax deductions and the opportunity cost of capital, OTA found that DiMasi's after-tax R&D cash outlay for a new NME was \$65.5 million (in 1990 dollars). That is the estimate of how much the drug companies in DiMasi's study actually spent on new chemical entities, including failures.
- It should be noted that five of the seven previous R&D cost studies that DiMasi references *did not* include opportunity cost of capital in their calculations.<sup>16</sup>
- Public Citizen inflated this figure to year 2000 dollars and found that actual after-tax cash outlay for NCEs (including failures) was \$110 million – based on DiMasi's data. (See Table 1)
- It's important to stress that this is the R&D cost for new chemical entities – which require the most expensive type of research – not all new drugs brought to market. The R&D

costs for all new drugs brought to market, based on PhRMA’s own data, is detailed in Section II.

- Several additional points about DiMasi’s estimate: First, it does not account for R&D tax credits available to the drug industry (these are different from the R&D deductions). DiMasi estimated that R&D tax credits amounted to a 6.8 percent subsidy for R&D expenditures from 1978 to 1986.
- Second, DiMasi assumes an FDA review time of 30 months in his calculations. FDA review time has dropped dramatically since 1991 and now averages 11 to 17 months. DiMasi said a one-year decrease in review time would cut his R&D estimate by \$19 million (in 1987 dollars, or \$29 million in year 2000 dollars).
- Third, evidence suggests that the time required to conduct clinical trials on new drugs is also decreasing – particularly for the most efficient companies. A January 2000 report by the Tufts Center for the Study of Drug Development stated that clinical testing time declined by 19 percent for drugs approved in 1996-1998 when compared with drugs approved in 1993-1995.<sup>17</sup> In addition, the five quickest pharmaceutical companies shaved, on average, more than one-year off the industry-wide median time (5.7 years) for clinical research.<sup>18</sup>
- Fourth, the advent of new technologies such as genomics and combinatorial chemistry, has led, according to investment analysts at Lehman Brothers, “to a growing school of thought that the cost of discovering new biological targets and the cost of creating drug leads is falling.”<sup>19</sup>
- Finally, it should be stressed that DiMasi’s estimate of R&D costs was far higher than in previous studies, including one published by the pharmaceutical industry in 1987. That study by S.N. Wiggins put the pre-tax cash outlay per NCE at \$65 million (in 1986 dollars).<sup>20</sup> After-taxes, the figure becomes \$67 million in year 2000 dollars.

**Table 1**

**Comparative Analysis of Pharmaceutical R&D Costs (\$ millions per New Chemical Entity)**

Study (Year)	Expressed in Dollars for Which Year	Pre-tax Including Cost of Capital (9%)	Pre-tax Excluding Cost of Capital	After-tax Actual Cash Outlay*
DiMasi Original (1991)	1987	\$231	\$114	\$61.6**
Office of Technology Assessment (1993)	1990	\$259	\$127	\$65.5
Public Citizen (2001)	2000	\$341	\$167	\$110.2***

\* Excludes the opportunity cost of capital. \*\*DiMasi did not calculate after-tax costs; the \$61.6 million figure was calculated by Public Citizen based on the 46 percent corporate tax rate in effect at the time of the expenditures

DiMasi studied. \*\*\* The \$110 million figure is calculated using the current corporate tax rate of 34 percent; this is the rate used to deduct R&D expenses from taxable income.

## **II. PhRMA's Own Data Contradicts the \$500 Million Claim**

Not all R&D is created equal. DiMasi studied the most expensive of all new drugs. Only 36 percent of drugs the FDA approved for market in the 1990s were NMEs (similar to DiMasi's NCEs). The others were mostly new combinations of drugs or new formulations of existing drugs. (For example, from pill to syrup form.)

The drug industry's own data about this larger universe of new drugs reveal that the actual cash outlay for a new drug is far less than \$500 million – and perhaps as low as \$57 million per drug in recent years (including failures).

Here's how Public Citizen arrived at this conclusion:

PhRMA's annual survey lists aggregate R&D spending by year in two categories: domestic (spending in the U.S. by both foreign and domestic companies) and abroad (spending overseas by U.S.-based companies.)

Public Citizen uses PhRMA's domestic spending for its analysis, in part, because that's what DiMasi did when he ran a check on his study using aggregate data. His reasoning: "We include only domestic expenditures in our analysis under the assumption that the foreign expenditures of U.S.-owned firms will be directed primarily to non-U.S. introductions."<sup>21</sup> (Public Citizen has calculated R&D costs with combined domestic-overseas spending in Appendix B. Spending in the last decade ranges between \$69 million and \$87 million per drug.)

According to PhRMA, U.S. and foreign drug companies spent \$139.8 billion on domestic R&D in the 1990s.<sup>22</sup> During that same period, the U.S. Food and Drug Administration approved 857 new drugs for market.<sup>23</sup> Simple division suggests that drug companies spent \$163 million on R&D for every new drug approved for market in the U.S. in the 1990s (expressed in year 2000 *pre-tax* dollars).

This measure is very generous to the industry. It counts total R&D expenditures – which include salaries, equipment, overhead, lab tests (pre-clinical) and clinical trials.<sup>24</sup> And it counts all failed drugs as well as successful drugs. In addition, it uses PhRMA's own R&D figures, which have not been independently verified and may be inflated with marketing research costs.<sup>25</sup> Finally, it uses pre-tax figures; in fact, R&D expenses are tax deductible and every dollar spent on R&D has a net cost of only \$0.66.

A more accurate measure – according to pharmaceutical experts such as Stephen Schondelmeyer, director of the PRIME Institute at the University of Minnesota – would account for R&D tax deductions and the approximate seven-year lag between R&D spending and drug approval. (DiMasi said "approvals in one year should be associated with R&D expenditures lagged 2 to 12 years."<sup>26</sup>) Therefore, a more accurate measure would compare R&D spending for 1994 to new drug approvals for the year 2000.

To be even more accurate, the measure should account for years in which R&D spending on new drugs was extraordinarily high or low. In other words, it should smooth out the peaks and valleys. Thus, this measure would compare R&D spending over seven-year periods with new drug applications (NDAs) approved over corresponding seven-year periods. An annual average should be calculated for each period, which has the effect of smoothing out peaks and valleys. (See Appendix B for more detailed methodology)

The results? From 1984-1990, PhRMA reported that R&D spending totaled \$32.8 billion. (That's domestic R&D spending by U.S. companies and foreign-based companies.)<sup>27</sup> Adjusted for inflation, that total is \$48.2 billion in year 2000 dollars. Divide that amount by the number of new drugs (563) approved from 1990-1996 and it appears that \$85.6 million was the average R&D cost for every new drug approved in that period (in pre-tax dollars). After subtracting tax deductions, worth 34 cents on the dollar, the actual cost plummets to \$56.5 million.

For new drugs approved in the more recent seven-year NDA period 1994-2000, the average pre-tax cost of R&D was \$107.6 million. Adjusting for R&D tax deductions makes the figure \$71.0 million. (See Table 2)

**Table 2**  
**Average R&D Cost per New Drug Approved During the 1990s**  
**(Rolling 7-Year Average with 7-Year Lag, \$ in millions, all in year 2000)**

**Domestic R&D Spending Only**

7-Year R&D Period	Average Annual R&D Spending	7-Year NDA Period	Average Annual NDA's Approved	Pre-Tax R&D Spending per New Drug	After-Tax R&D Spending per New Drug
1988-1994	\$10,255.3	1994-2000	95.3	\$107.6	\$71.0
1987-1993	\$9,387.8	1993-1999	91.3	\$102.8	\$67.9
1986-1992	\$8,473.3	1992-1998	92.4	\$91.7	\$60.5
1985-1991	\$7,613.0	1991-1997	88.6	\$86.0	\$56.7
1984-1990	\$6,887.1	1990-1996	80.4	\$85.6	\$56.5

Source: Spending data comes from Pharmaceutical Research and Manufacturers of America, PhRMA Annual Survey, 2000; NDA data comes from U.S. Food and Drug Administration, Center for Drug Evaluation and Research, December 31, 2000. (All spending figures have been inflated to year 2000 dollars.)

Note: Domestic R&D includes expenditures within the United States by research-based pharmaceutical companies.

Two additional notes:

Some might quarrel with the seven-year lag, arguing that in accounting terms, today's R&D expenses are paid by today's revenue. Thus, R&D spending in any year ought to be compared with drugs brought to market that same year. This study rejects that argument. It doesn't reflect the reality that R&D spending invariably precedes the marketing of a drug and our purpose is to

understand what it costs to bring a drug to market, not how that R&D is paid for in accounting terms. In addition, as noted earlier, DiMasi agrees that spending should be lagged two to 12 years. Nevertheless, Public Citizen calculated R&D spending for current drug approvals and current research expenditures in Appendix B and found that spending remained close to \$100 million per drug, with costs in the 1990s ranging from \$99 million to \$118 million per drug.

Finally, it has also been suggested that our analysis should focus only on NCEs or NMEs because that's what DiMasi studied, and that's where the bulk of industry R&D is spent, and those new compounds are the drugs that make the industry risky. That analysis is below (see Table 3) although our intent was not to mirror DiMasi in this section. Rather, this section aims to point out that there are many kinds of drugs approved each year – not just the elite group in DiMasi's study. More important, PhRMA's R&D spending figures – the figures that it constantly touts – are for all drugs, not just NMEs or NCEs. So it's only fitting to compare PhRMA's spending for all drugs to all drugs approved for market. (That said, an all-NME analysis shows R&D spending of \$114 million to \$150 million per drug.)

**Table 3**  
**Average R&D Cost per New Molecular Entity During the 1990s**  
**(Rolling 7-Year Average with 7-Year Lag, \$ in millions)**

**Domestic R&D Spending Only**

7-Year R&D Period	Average Annual R&D Spending	7-Year NME Period	Average Annual NME's Approved	Pre-Tax R&D Spending per NME	After-Tax R&D Spending per NME
1988-1994	\$7,588.9	1994-2000	33.4	\$227.02	\$149.8
1987-1993	\$6,947.0	1993-1999	33.1	\$209.61	\$138.3
1986-1992	\$6,270.2	1992-1998	31.9	\$196.82	\$129.9
1985-1991	\$5,633.6	1991-1997	31.9	\$176.84	\$116.7
1984-1990	\$5,096.4	1990-1996	29.6	\$172.34	\$113.7

Source: Spending data comes from Pharmaceutical Research and Manufacturers of America, PhRMA Annual Survey, 2000; NDA data comes from U.S. Food and Drug Administration, Center for Drug Evaluation and Research, December 31, 2000. (All spending figures have been inflated to year 2000 dollars.)

Note: Domestic R&D includes expenditures within the United States by research-based pharmaceutical companies.

### III. U.S. Taxpayers Play A Crucial Role in Pharmaceutical R&D

Drug companies stress how difficult it is to discover new drugs – particularly innovative life-saving drugs. But the evidence suggests it's not all that risky because the federal government is doing much of the crucial research. The National Institutes of Health (NIH) budget reached \$20.3 billion in fiscal year 2001 (a 14 percent increase over FY 2000) with much of that money going to research that ultimately helps with the discovery and development of pharmaceuticals - how much exactly is hard to say. The NIH admits it doesn't track its spending on drug development. NIH officials claim it's a tough task because so much NIH work is basic research

into diseases that is converted years later – often through several other related discoveries that build on one another – into a marketed drug.<sup>28</sup>

What we do know is that several studies have shown that many important and popular drugs were developed with taxpayer support. That’s why publicly-funded researchers have 90 Nobel Prizes compared to just four by industry scientists, although the industry spends more on R&D.<sup>29</sup> For instance:

- A study by a Massachusetts Institute of Technology (MIT) scholar of the 21 most important drugs introduced between 1965 and 1992 found that publicly funded research played a part in discovering and developing 14 of the 21 drugs (67 percent).<sup>30</sup>
- 45 of the 50 top-selling drugs from 1992-1997 received government funding for some phase of development, according to an investigation by *The Boston Globe*. In all, taxpayers spent at least \$175 million helping to develop these 50 drugs.<sup>31</sup>

### **Publicly-funded Researchers Conducted Most Studies Behind Blockbuster Drugs**

An NIH internal document obtained by Public Citizen through the Freedom of Information Act (“NIH Contributions to Pharmaceutical Development,” February 2000, see Appendix C) reveals much more detail about the importance of taxpayer-funded research to drug companies.

The NIH report looked closely at the role of public research in developing the most popular drugs in the U.S. To avoid well-known NIH success stories, such as the agency’s work in developing treatments for cancer and AIDS, the NIH decided to examine the top five selling drugs in 1995, each of which had over \$1 billion in sales. Before scrutinizing the research behind these drugs, NIH did not know what, if any, role taxpayer-funded scientists played in bringing these drugs to market.

- NIH found that “NIH-funded research played a critical role in drug discovery in each of these cases.”<sup>32</sup> In all, U.S. taxpayer-funded researchers conducted 55 percent of the published research projects leading to the discovery and development of these drugs (and foreign academic institutions 30 percent). “Researchers at U.S. universities and at NIH contributed by discovering basic phenomena and concepts, developing new techniques and assays, and participating in clinical applications of the drugs.”
- In the case of the hypertension drugs captopril and enalapril, the NIH concluded that the drugs were developed thanks to 14 public U.S. research projects and five foreign academic studies. Only three significant studies were conducted by the drugs’ patent holders, Squibb and Merck.
- Furthermore, four of the taxpayer-funded studies were deemed “key” and six of the studies were referenced in the industry’s work. The studies sponsored by the patent holders for these two drugs were of less consequence – none were considered “key” by

the NIH. In fact, for the five drugs it studied, the NIH deemed only one industry study “key.” (Public Citizen acknowledges the fact that academics generally have greater incentive to publish research than industry scientists.)

Table 4 shows the NIH findings on the top five selling drugs: ranitidine (better known as Zantac), which treats ulcers; acyclovir (Zovirax), which treats herpes simplex; captopril (Capoten) and enalapril (Vasotec – a slight alteration of captopril/Capoten) for hypertension; and fluoxetine (Prozac), an anti-depressant. The table reflects the NIH methodology, which was to count all the published research projects behind a drug’s discovery and development and classify them as U.S. taxpayer-funded studies, foreign academic studies, or industry studies (which are then divided into those done by the patent-holding company and those done by other companies).

The NIH study also attempted to weight the importance of the studies by identifying those that were “key” and those that were later referenced in industry studies.

**Table 4**  
**Who Contributed Most to Development of Top Five Selling Drugs (1995)**

Importance of Research	Affiliation of Scientist	Ranitidine (Zantac)	Acyclovir (Zovirax)	Captopril (Capoten) and Enalapril (Vasotec)	Fluoxetine (Prozac)	Total
<b>Key Contributions to Discovery and Development of Drug*</b>	U.S. taxpayer studies	2	4	4	1	11
	Foreign academic studies	1	1	1	2	5
	Industry sponsored studies (excluding patent holder)	0	0	0	0	0
	Patent-holder sponsored studies	0	0	0	1	1
<b>Referenced in Patent Holders' papers*</b>	U.S. taxpayer studies	0	7	1	1	9
	Foreign academic studies	0	1	0	1	2
	Industry sponsored studies (excluding patent holder)	0	0	0	0	0
	Patent-holder sponsored studies	0	0	0	0	0
<b>Other Contributions to Discovery and Development of Drug</b>	U.S. taxpayer studies	6	21	9	16	52
	Foreign academic studies	15	8	4	6	33
	Industry sponsored studies (excluding patent holder)	4	0	0	3	7
	Patent-holder sponsored studies	2	2	3	4	11
<b>Total</b>		<b>30</b>	<b>44</b>	<b>22</b>	<b>35</b>	<b>131</b>
<b>Percent of total research projects sponsored by U.S. taxpayer or foreign academic institutions</b>		<b>80%</b>	<b>95%</b>	<b>86%</b>	<b>77%</b>	<b>85%</b>

Source: National Institutes of Health, “NIH Contributions to Pharmaceutical Development,” Administrative Document, February 2000. \*As defined by the National Institutes of Health.

The NIH report also found:

- Public researchers often tackle the riskiest and most costly research, which is basic research, making it easier for industry to profit. The NIH report discovered that only 14 percent of the drug industry’s total R&D spending went to basic research, while 38 percent went to applied research and 48 percent was spent on product development.<sup>33</sup>
- This finding suggests that public researchers are doing the yeomen’s work of identifying possible new medicines, while most drug industry R&D spending occurs after companies believe they have a marketable drug. The NIH report concluded: “To the extent that basic research into the underlying mechanisms of disease drive new medical advances, *the R&D in industry is not performing the role played by public research funding.*”<sup>34</sup>
- Taxpayer-funded scientists do more than basic research. They also conduct clinical trials. NIH found that publicly-funded researchers either conducted or had their work cited in 61 percent of the clinical trials important to the development of the five blockbuster drugs it studied.
- NIH research enables drug companies to secure more lucrative monopoly patents. According to the study: “[P]harmaceutical companies that organize in ways that tap the results of publicly-funded science are those that are most successful. For example, they...obtained more patents per research dollar, on average, than firms whose scientists work less closely with the public sector.”<sup>35</sup>

#### **IV. R&D Data Kept Secret – What Are They Hiding?**

It’s impossible to know what the drug industry really spends on research and what it counts as research spending. The industry has fiercely fought attempts to open its books on R&D. In fact, the industry waged a nine-year legal battle against the General Accounting Office (GAO) – the investigative arm of Congress – to keep GAO from obtaining information about R&D.<sup>36</sup>

The battle eventually went all the way to the U.S. Supreme Court, where it hinged on two words (“directly pertinent”). In short, the GAO argued that it was entitled to examine all drug company financial records, because the companies had contracts with the U.S. Veteran’s Administration, and the GAO wanted to know if the companies’ high prices and profits were warranted by the costs of producing and selling the medicines. The drug companies countered that the law only allowed GAO access to records that were “directly pertinent” to those government contracts. Thus, interpreting these two words became the subject of litigation from 1974 to 1983.

Federal district courts were split on GAO’s right of access to “indirect” product costs such as R&D and marketing. The companies argued that indirect costs were not *directly pertinent* because only a small portion of indirect costs could be allocated to the federal government’s contracts. GAO reasoned that “direct” product costs were so small – only about 9 percent for a particular drug – that they were not meaningful.<sup>37</sup>

In the end, the U.S. Supreme Court, in *Bowsher v. Merck & Co. Inc.*, did draw the line between direct and indirect costs. In addition, the court held that since Congress had drafted the limiting language (“directly pertinent”), arguments for change should be directed to Congress.

Of course, the long legal battle would not have been necessary had Congress been willing to exercise its subpoena power to obtain the data. In fact, Congress can get all the information it wants. But, as a congressional study noted, this route is “perhaps not politically feasible.”<sup>38</sup>

Why not? It’s possible Congress has not acted because the industry has spent huge sums on political persuasion according to a new Public Citizen report (“The Other Drug War: Big Pharma’s 625 Washington Lobbyists”) including \$262 million in 1999-2000 on campaign contributions, lobbying and ads that benefited its congressional allies.<sup>39</sup> (The spending breaks down as \$177 million on lobbying, \$20 million on contributions to federal candidates and party committees, and \$65 million on issue ads.)

Opening the industry’s R&D books would be particularly useful because it’s not clear what the industry considers “R&D.” Claims have been made – by a U.S. Senate committee investigation<sup>40</sup> and the editor-in-chief of the *New England Journal of Medicine*<sup>41</sup> – that the industry inflates its R&D records with the costs of administration and marketing. Making industry information more transparent could help to resolve questions and charges that now hang over the industry.

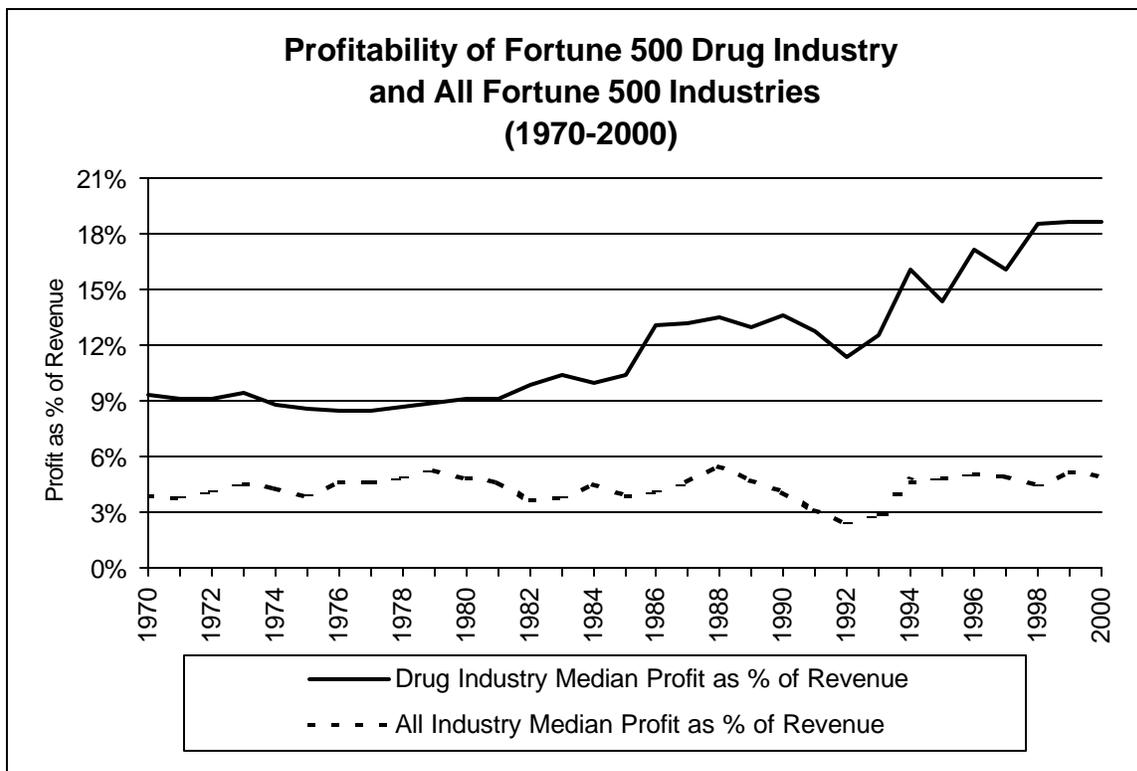
## V. What Risk? The Druggernaut Consistently Ranks Tops in Profits

PhRMA and major drug companies attempt to justify high U.S. prescription drug prices by characterizing their business as a high-risk enterprise, which must therefore be rewarded with high returns. But where’s the risk in an industry that has consistently been rated the most profitable in America? Company reports to the federal Securities and Exchange Commission and *Fortune* magazine’s annual surveys of comparative industry profits show that:

- The drug industry was again ranked “more profitable than any other” by the Fortune 500 analysis of America’s largest companies in the year 2000. And the “druggernaut” walloped its competitors. The 11 drug companies that made the Fortune 500 enjoyed 19 percent return on revenues (in other words, 19 percent of revenues went to profits). The median for all other Fortune 500 companies was 5 percent return on revenues.<sup>42</sup> (For a complete analysis of each company’s profitability, go to <http://www.citizen.org/congress/drugs/factsheets/mostprofitable.htm>.)
- The drug industry’s success in the Fortune 500 profitability rankings has become a rite of spring. Since 1982, the industry has topped *Fortune*’s rankings for return on revenue, and has been at or near the top for return on equity.<sup>43</sup>

- The drug industry's profitability has grown in recent decades. On average, in the 1970s the profitability of Fortune 500 drug companies (measured by return on revenue) was two times greater than the median for all companies in the Fortune 500. In the 1980s it was three times. And in the 1990s, the drug companies' profitability was almost four times greater than the median for all companies in the Fortune 500.<sup>44</sup> (See Figure 1)
- The drug industry often thrives when other industries sag. Fortune 500 drug companies saw their year 2000 return on revenue increase 15 percent from 1999. That success came at a time when the American economy saw overall profit growth drop from 29 percent in 1999 to 8 percent last year.<sup>45</sup>
- As consistent profit-generators, drug companies tend to outperform other industries during economic downturns, and investors know it. Not surprisingly, they boosted the stocks of Fortune 500 drug companies 38 percent while selling off other industries during last year's stock market turbulence.<sup>46</sup>

**Figure 1**



Source: Public Citizen update of Stephen W. Schondelmeyer calculation, *Competition and Pricing Issues in the Pharmaceutical Market*, PRIME Institute, University of Minnesota based on data found in *Fortune* magazine, 1958 to 1999; *Fortune* magazine, April 2000, Fortune 500 ([www.fortune.com](http://www.fortune.com)).

## VI. What Risk? A High Percentage of New Drugs Are “Me-Too” Drugs

Evidence also suggests that a significant amount of industry R&D does not concern new treatments for serious and life-threatening conditions, but instead goes into “me-too” drugs. These are drugs that have little or no therapeutic gain over drugs that already exist; also known as “copycat” drugs.

Until 1992, the U.S. Food and Drug Administration classified every new drug approved according to its significance for human health. The ranking system:

1A = Important therapeutic gain: a breakthrough drug

1B = Modest therapeutic gain: e.g., change in formulation so that the drug can be taken once instead of three or four times a day

1C = Little or no therapeutic gain: “me-too” or “copycat” drug – for all practical purposes a duplicate of products already available

**Table 5**  
**More than Half of New Drugs Approved from 1982-1991 Were “Me-Too” Drugs**

FDA Category	Number	Percent
1A - Important Therapeutic Gain	41	16%
1B - Modest Therapeutic Gain	80	31%
<b>1C - Little or No Therapeutic Gain</b>	<b>137</b>	<b>53%</b>
Total New Drugs Approved 1982-91	258	100%

Source: Donald Drake and Marian Uhlman, *Making Medicine, Making Money* (1993), p. 72.

As seen in Table 5, more than one-half (53%) of the newly discovered drugs had “little or no therapeutic gain” compared to drugs already on the market – and only 16 percent of new drugs represented an “important therapeutic gain.”

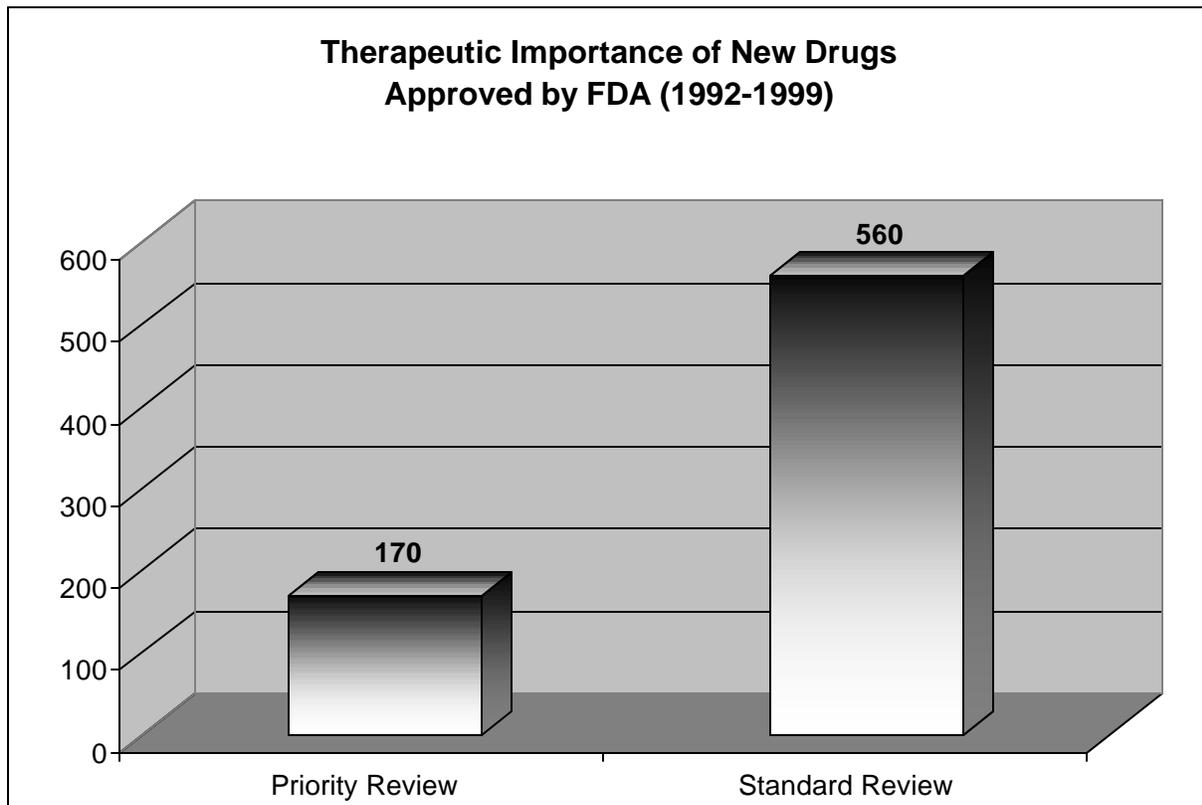
The pharmaceutical industry abhorred this system, because it provided objective information to the public and medical practitioners about the true value of a majority of their products. In response to industry pressure, the Bush I Administration eliminated these rankings in 1992.<sup>47</sup> Industry executives were grateful and glad. “To put [the 1A-1B-1C system] into well-deserved oblivion was a PMA priority for a very long time,” said John R. Stafford, chief executive officer of American Home Products at the 1992 annual convention of the Pharmaceutical Manufacturers Association (PhRMA’s former name). “Now it is accomplished.”<sup>48</sup>

Although our ability to track the exact proportion of “me-too” drugs ceased with the demise of this ranking system, more recent evidence still confirms that a relatively small proportion of the

drug industry's claimed R&D expenditures are directed at the discovery of innovative treatments for serious and life-threatening illnesses:

- While the FDA dumped the 1A-1B-1C rankings, its new system still shows that the vast majority of new drugs did not represent significant therapeutic improvements. From 1992 through 1999, the FDA rated 170 drug approval applications for “priority review” and 560 for “standard review.” (See Figure 2) “Priority review” is for drugs that represent “significant improvement compared to marketed products in the treatment, diagnosis, or prevention of a disease.” “Standard review” is for drugs that “appear to have therapeutic qualities similar to those of one or more already marketed drugs.”<sup>49</sup> (Critics claim that the FDA’s “priority” category is far too liberal, giving drugs like Celebrex – which is no more effective than naproxen at relieving arthritis pain – priority status. Nevertheless, if the results from Figure 2 are combined with those in Table 5, only 22 percent of the drugs approved by the FDA from 1982-1999 represented important therapeutic gains.)

**Figure 2**



Source: FDA/Center for Drug Evaluation and Research, “NDAs Approved in Calendar Years 1990-1999,” December 31, 1999.

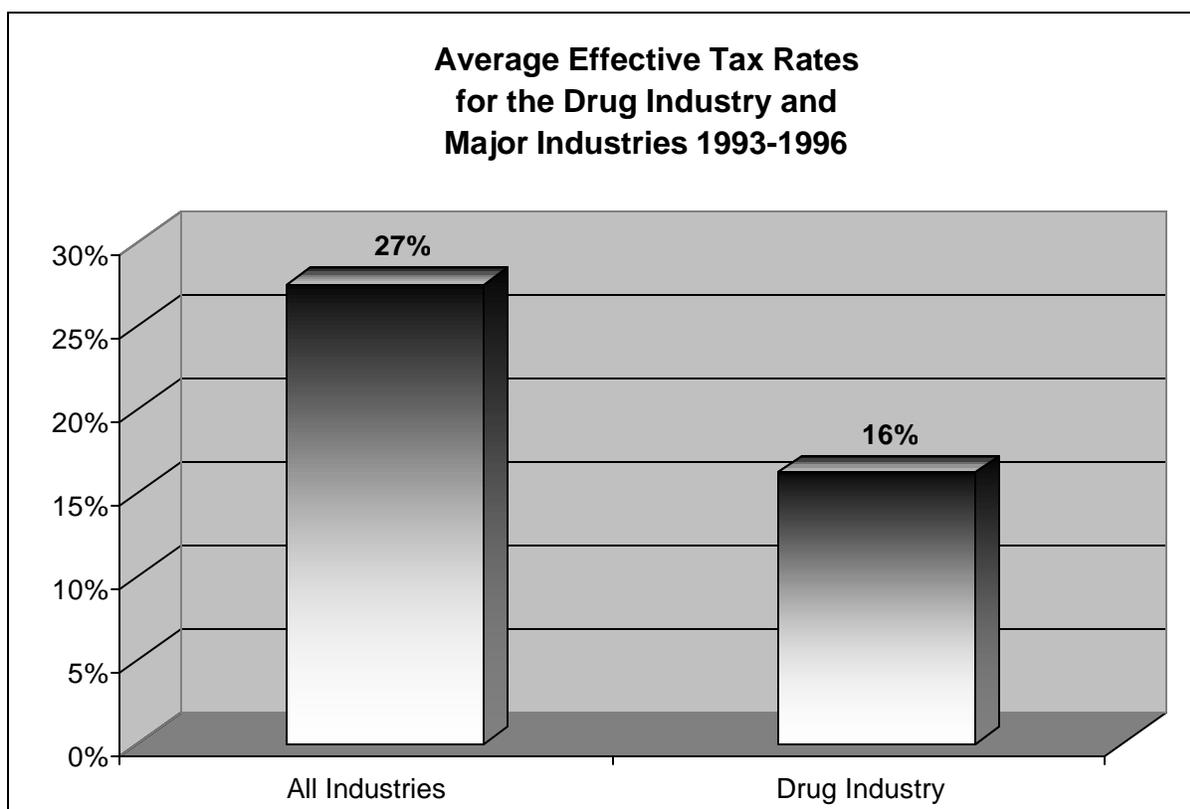
Note: According to the FDA, “priority review” is for drugs that represent a “significant improvement compared to marketed products in the treatment, diagnosis, or prevention of a disease.” “Standard review” is for drugs that “appear to have therapeutic qualities similar to those of one or more already marketed drugs.”

## VII. What Tax Burden? The Drug Industry Is Lightly Taxed

The drug industry has historically realized significant savings from four tax credit provisions: the foreign tax credit, possessions tax credit, research and experimentation tax credit, and the orphan drug tax credit (all of these are in addition to deductions for research expenditures which are worth 34 cents on the dollar). Combined, these tax credits have allowed the drug industry to save \$4 billion a year in taxes, according to the Congressional Research Service.<sup>50</sup>

- In all, the industry used tax credits to save almost \$28 billion from 1990 through 1996.<sup>51</sup>
- The drug industry has also taken advantage of a tax break for companies that build factories in Puerto Rico. From 1980 through 1990, the GAO estimated that 26 pharmaceutical companies had tax savings of \$10.1 billion thanks to this tax credit.<sup>52</sup>
- The drug industry's effective tax rate has been lower – much lower in some cases – than that of almost every major industry, despite its very high profitability. The drug industry's effective tax rate averaged 16 percent from 1993 through 1996 compared to 27 percent for all major industries over the same period.<sup>53</sup> (See Figure 3)

**Figure 3**



Source: Congressional Research Service Memorandum, "Federal Taxation of the Drug Industry from 1990 to 1996," December 1999.

Note: An industry's effective tax rate differs from its statutory corporate tax rate. Hence, the industry deducts R&D expenses at the 34 percent corporate tax rate, yet also pays at the same time an effective tax rate of 16 percent. This is not inconsistent in any way. It's very similar to what many Americans experience when they itemize their personal taxes. The 34 percent deduction is on a firm's taxable income and it reduces a firm's taxable income. The effective tax rate is a calculation based on tax credits, which are applied to reduce the tax liability, or taxes owed, after determining taxable income. For more details, see Appendix D.

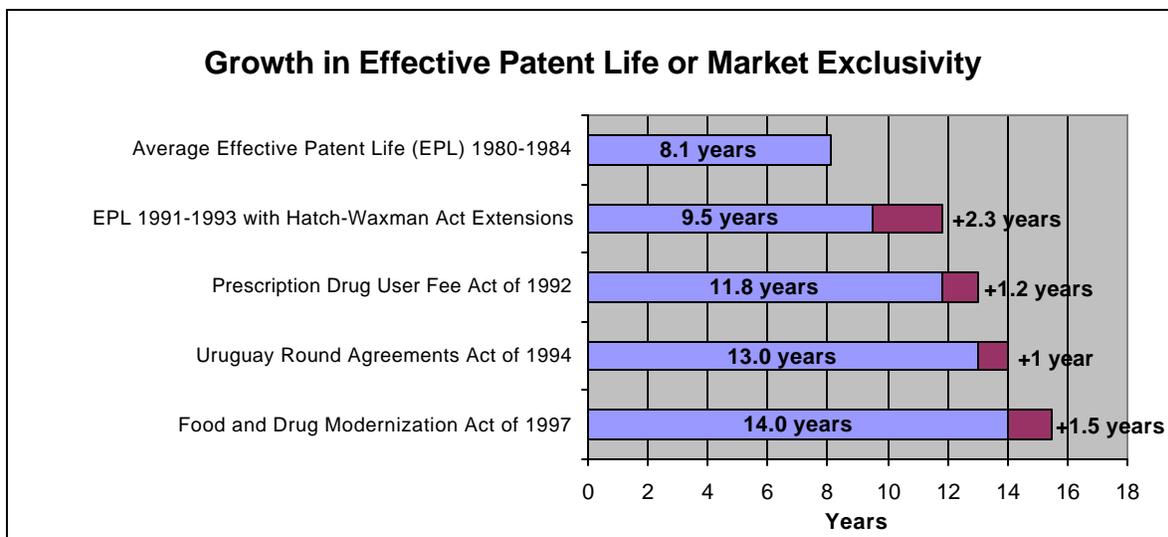
### VIII. More Public Aid: Monopoly Patents and Research Incentives

In addition to research subsidies and tax credits, the drug industry enjoys other forms of government assistance, including patent extensions and lucrative incentives for testing the safety of drugs in children.

The federal government grants drug companies monopoly patents on new products that last 20 years, from date of patent application to expiration. More important is the "effective patent life" of a drug, which is the number of years remaining in a drug's patent term after the U.S. Food and Drug Administration approves the drug for market.

Starting in the mid-1980s, the federal government adopted several laws that extended the effective lives of drug patents. Combined, various laws of the 1980s and 1990s (Hatch-Waxman Act of 1984, Prescription Drug User Fee Act of 1992, the Uruguay Round Agreements Act of 1994, and the Food and Drug Modernization Act of 1997) have added 4.4 to 5.9 years of effective patent life. Effective patent life now averages 13.9 to 15.4 years.<sup>54</sup> (See Figure 4)

**Figure 4**



Source: National Institute for Health Care Management, "Prescription Drugs and Property Rights," 2000.

These patent extensions create a windfall for drug companies. For example, a pediatric exclusivity provision contained in the Food and Drug Modernization Act of 1997 gives six months of extra monopoly patent protection, or exclusivity, to a drug in return for the manufacturer conducting studies on the safety of the drug for children. Critics of the provision complain that it creates a lucrative incentive for companies to test their most valuable drugs on children, rather than those drugs most needed by children.

Indeed, drug companies are gaining the six-month bonus by testing some drugs that treat conditions uncommon in children, such as arthritis, ulcers and hypertension. For instance, pediatricians wrote less than 1 percent of the prescriptions for Glucophage, an adult-onset diabetes drug, and Vasotec, a hypertension medicine. The six months of extra exclusivity won by these drugs is worth nearly \$1 billion in sales.<sup>55</sup>

Because the pediatric incentive delays the introduction of lower-priced generic drugs, the FDA estimates that it will reward drug companies with \$592 million per year in additional profit and cause consumers to pay an additional \$14 billion over 20 years in higher prices.<sup>56</sup> (For more complete analysis of pediatric exclusivity, see <http://www.citizen.org/congress/drugs/pediatricexclusivity.html>)

## **IX. High U.S. Drug Prices Don't Necessarily Mean More R&D**

The pharmaceutical industry is a global industry dominated by large multinational companies. Since the 1980s, U.S. pharmaceutical companies have merged with or acquired significant stakes in European firms, and vice versa. All drug companies, regardless of where their national headquarters are located, charge higher prices in the U.S. market. That doesn't mean, however, that R&D will diminish if U.S. prices are moderated, as PhRMA President Alan Holmer has declared.

There are several reasons why. For one, profit margins are large enough that reducing them will still leave plenty of money for research. For another, cutting research is anathema to a drug company. It means walking away from new and potentially lucrative drugs. And that seems an odd course to take at a time when research is becoming quicker because of advances in technology and thus, cheaper.

“A decade ago, a good research chemist could produce 50-100 new compounds a year. Today with standard combinatorial chemistry, the same chemist can turn out a couple of thousand compounds a year,” according to industry analysts at PricewaterhouseCoopers. “Meanwhile, high-throughput screening has massively accelerated the speed at which compounds can be tested to identify the most promising molecules.”<sup>57</sup>

The upshot of this move towards “e-R&D”? New technologies “will enable drug manufacturers to accelerate the selection process, reduce the costs of preclinical and clinical studies, and increase their overall chance of success. We estimate that they could collectively save at least \$200 million and two to three years per drug.”<sup>58</sup>

In addition, the drug industry will soon enjoy a “demographic tailwind” as the Baby Boom generation hits retirement age and consumes more prescription drugs. “The fundamentals are massively positive,” said Tom McKillop, head of AstraZeneca, the company that makes the world’s best-selling drug, Prilosec. “We’ve got huge increases in the number of elderly. And we’re at a new phase of pharmaceuticals. Discoveries now involve the chronic degenerative diseases like Alzheimer’s...The science has never been more exciting.”<sup>59</sup>

Price and profit controls – which exist in virtually all European countries – haven’t hurt the thriving drug industry in Europe where companies such as Glaxo Wellcome, Novartis, Aventis, AstraZeneca and Roche all have revenues that put them in the top 10 companies in global drug sales. (There are five American and five European companies in the top 10.)<sup>60</sup>

While it is true that many European companies have substantial sales in the U.S., they still maintain robust R&D activities, despite the price controls in the European market.

A recent study by the Tufts Center for the Study of Drug Development notes that 49 percent of 107 new chemical entities it reviewed were first approved for market in the U.S.<sup>61</sup> This suggests that a majority of new NCEs are developed outside the U.S. If that’s the case, then it appears that R&D operations of European companies are indeed healthy despite price controls.

This conclusion is supported by data concerning new drugs and the home-base of the companies that are bringing them to market. As Figure 5 shows, European-based companies have produced more new molecular entities (NMEs, which are similar to NCEs) in the last decade than American companies. While some important facts are not reflected in this data – such as where the European companies actually conducted their research and sold these drugs – the numbers do support the assertion that European companies have strong R&D activities, while operating under price controls.

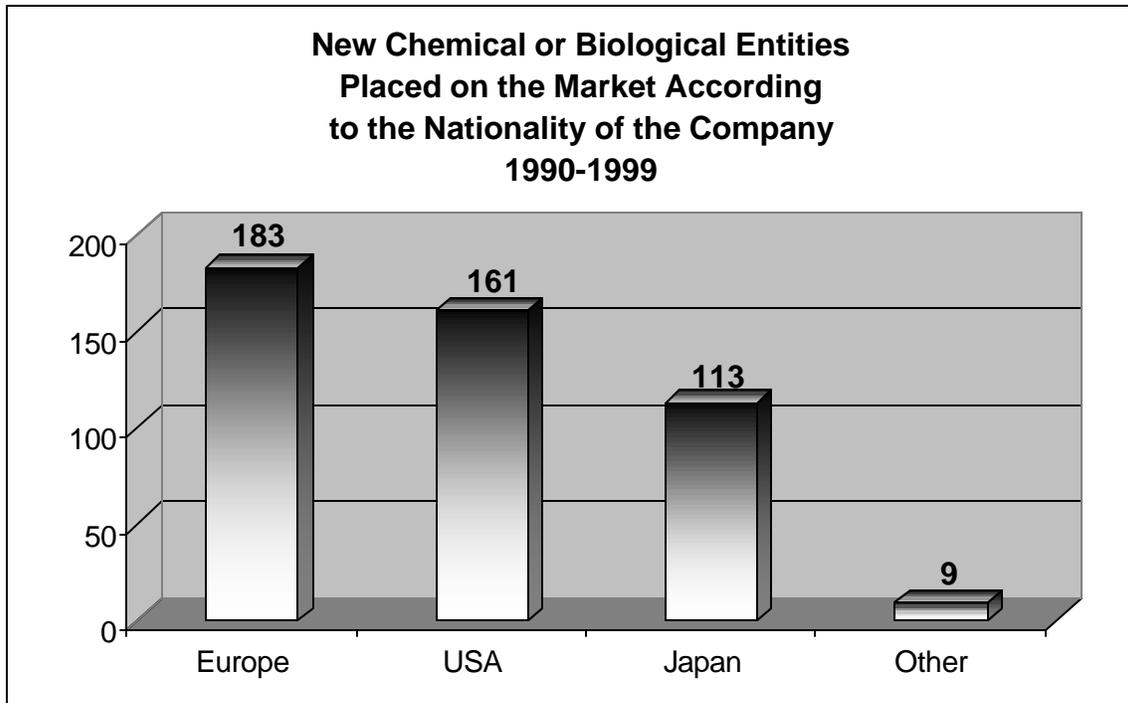
There are many factors that shape R&D and government regulation of prices is just one of them. As a GAO report concluded: “[D]rug prices are only one of many factors that influence pharmaceutical R&D. Therefore, pharmaceutical spending control policies can coexist with a strong research-based industry, even though by themselves such policies would decrease R&D spending.”<sup>62</sup>

Any debate about prices and R&D must address not just the average cost of R&D per drug, but also the more important question of whether prices are already too high or are increasing too fast. In addition, any debate should look at whether dollar returns on R&D investments are more than enough to continue to induce investment in drug research.

On this last point, the OTA study was clear and unequivocal – returns were more than enough to stimulate investment. Specifically, the OTA found: “Each new drug introduced to the U.S. market between 1981 and 1983 returned, net of taxes, at least \$36 million more to its investors than was needed to pay off the R&D investment.”<sup>63</sup>

Furthermore, the OTA said, “The long-run persistence of higher dollar returns... than the amount needed to justify the cost and risk of R&D is evidence of unnecessary pricing power for ethical pharmaceuticals.”<sup>64</sup>

**Figure 5**



Source: European Federation of Pharmaceutical Industries and Associations, *The Pharmaceutical Industry in Figures*, 2000. A drug is defined as a new chemical or biological entity if it has never before been marketed regardless of dosage form.

Finally, the OTA said it’s not clear whether a reduction in R&D spending would necessarily be harmful. “Whether a decrease in R&D would be good or bad for the public interest is hard to judge. It is impossible to know whether today’s level of pharmaceutical R&D is unquestionably worth its cost to society [in high prices].”<sup>65</sup>

It could very well be that some research can wither without significant consequence. Section VI showed that the majority of drugs that companies bring to market are not drugs that represent important therapeutic advances. Rather, most are me-too drugs that replicate already successful drugs so that different companies can gain a cut of a burgeoning market. Some industry critics argue that less research on me-too drugs would improve the overall quality of industry research and decrease clutter in the market.

## **X. Advertising, Not R&D, Is the Drug Industry’s Fastest Growing Expenditure**

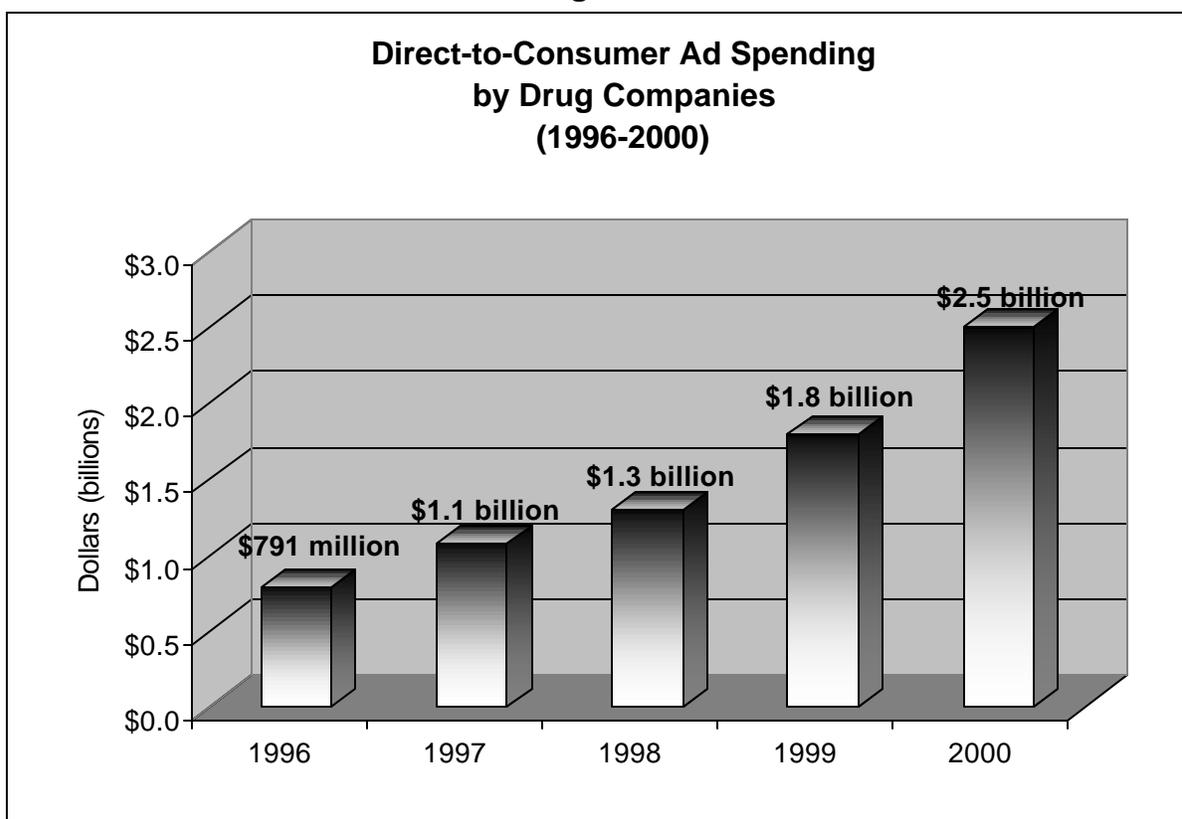
Since Senator Estes Kefauver’s groundbreaking hearings into the business practices of U.S. pharmaceutical companies in the late 1950s, the industry’s investment in marketing to gain and

maintain market share has been well documented. Public Citizen's Health Research Group has exposed the negative impact on consumer and patient health that the industry's slick and all-but-unregulated marketing practices produce (see [www.citizen.org/hrg/publications/drugs.htm](http://www.citizen.org/hrg/publications/drugs.htm) then scroll down to "promotion" for a list of publications). Since the FDA relaxed standards for Direct-to-Consumer (DTC) TV ads in 1997, drug advertising – and its negative consequences – have escalated rapidly.

As a result, promotion and advertising have driven drug expenditures higher and higher. And while it's impossible to pinpoint (because of industry secrecy) how much of the industry's R&D costs are actually market research, we do know the following:

- In 2000, the 11 Fortune 500 drug companies devoted nearly three times as much of their revenue to marketing and administrative costs (30 percent of revenue) as to research and development (12 percent of revenue).<sup>66</sup>
- Drug industry spending on DTC advertising increased at a far greater rate (38 percent) in 1999 than spending on research and development (14 percent).<sup>67</sup>
- One blockbuster drug was hyped more than Coke and Bud: After the FDA relaxed its rules on TV advertising in 1997, Schering-Plough spent \$136 million in 1998 advertising its allergy drug Claritin. That's more than Coca-Cola Co. spent advertising Coke, or Anheuser-Busch spent advertising Budweiser that year.<sup>68</sup>
- Prior to the FDA's relaxation of the DTC standards the drug industry spent \$791 million on advertising in 1996. It is estimated that DTC spending totaled \$2.5 billion for the year 2000, an increase of 216 percent over 1996 and 39 percent over 1999.<sup>69</sup> (See Figure 6)
- Increased advertising seems to be playing a big part in increased spending on drugs. The 25 most-advertised drugs accounted for 41 percent of the increase in overall 1999 drug spending.<sup>70</sup>
- It's clear why drug companies are spending more and more on advertising – it works. In a 1998 IMS Health survey of physicians, 97 percent of allergists said their patients were influenced by DTC advertising.<sup>71</sup>
- In a UCLA survey, 92 percent of consumers said they had heard of Claritin; 25 percent said that if their doctor advised against prescribing a particular drug they would switch doctors.<sup>72</sup>
- Advertising is becoming more important to drug companies: The drug industry is shifting the core of its business away from the often unpredictable task of creating drugs and toward the steadier business of marketing them. Marketing of Viagra to healthy young men is an example of how the industry is pinning its future less on new products and more on persuading people to buy the pills already being sold.<sup>73</sup>

Figure 6



Source: IMS Health figures made available to Public Citizen on April 18, 2001.

Note: 2000 figure estimate based on DTC spending through October.

## XI. Conclusion and Recommendations

The prescription drug industry is arguably America's most government-coddled industry. It receives a 20-year monopoly patent on the drugs it develops, permitting companies to charge whatever the market will bear for life-saving drugs. The industry is one of the least taxed in America, yet it has the highest profit margin of all industries – three times the average of all industries. It claims to be a high-risk industry, yet for almost two decades it has topped the profit charts by a factor of two and more recently three. Taxpayers fund significant amounts of the research that results in new drug discoveries, but demand next to nothing in return – not even a simple accounting of our investment. It is time to form a new relationship on behalf of America's consumers between our government and the drug industry.

The financial outlook for the prescription drug industry has never been healthier. In 2000, the 11 largest drug companies netted \$28 billion in profits – a 15 percent increase in their return on revenue over 1999. (See Public Citizen's report at: <http://www.citizen.org/congress/drugs/factshts/mostprofitable.htm>). The profits of one drug company, Merck (\$6.8 billion), were larger than the combined profits of all the Fortune 500

companies in each of the following industries: airline, entertainment, metals, food production and hotel/casino/resort industries.

And the picture looks just as rosy, if not rosier, for the future. As Fortune magazine noted in a recent issue, “Never has an industry had brighter long-term prospects...pharma is highly likely to match or exceed the past decade’s performance, in which it generated average annual returns of 25 percent. In a queasy economy, that’s powerful medicine indeed.”

Public Citizen believes that it is essential that America maintain a strong and vibrant prescription drug industry – one that provides healthy but reasonable profits to attract investors. However, this report shows that there is no essential connection between high prices and revenues for the industry and the invention of new medications. The industry has massively overstated the amount it spends inventing new drugs. It devotes much more of the revenue it takes in to paying dividends to its stockholders and to promoting drugs it has already created than it does to inventing new drugs. It leaves much of the truly pioneering research into deadly diseases to publicly funded researchers at the National Institutes of Health and universities around the world. And the drugs the industry “invents” are more likely to be knock-offs of drugs already on the market than they are to be new cures for a deadly disease.

In light of this situation, Public Citizen makes the following recommendations to Congress:

#### **A. Drug Price Cost Containment**

- 1. Medicare cost containment:** As Congress debates enacting Medicare prescription drug coverage there is a deafening silence about giving Medicare the authority to negotiate drug prices as it already negotiates hospital and physician payments. If the Departments of Defense and Veterans’ Affairs can negotiate deep price cuts there is no rationale for prohibiting Medicare from doing the same. Yet no major bill proposes such authority because of the power of the drug industry over lawmakers. As recent Congressional Budget Office projections show, given the rising cost of drugs and the budgetary limits placed on a drug benefit, it will be very difficult to construct a benefit that is generous enough along with premiums and cost sharing that are low enough to attract a sufficient number of Medicare beneficiaries to make the program viable. The logical solution is to reduce the cost of drugs. There are different ways to allow for Medicare negotiated prices – the bottom line could be a savings that is 30 percent to 40 percent greater than that anticipated under current Democratic reform proposals using a pharmacy benefit manager model. The Merrill Lynch investment company noted in a 1999 report that such savings would result in a net revenue loss to the drug industry of only 3.3 percent because lower prices would stimulate greater demand.<sup>74</sup>
  
- 2. Reasonable pricing of drugs developed with taxpayer support:** Drug companies should be required to sell drugs that have benefited from taxpayer-funded research at reasonable prices to all, including the Medicare program.

Reasonable prices would be determined in a fashion similar to that used in other advanced industrialized countries. Drug companies would be required to submit price applications in which they would propose a price at which they planned to sell their drug along with a justification for that price. The justification would include a listing of the research and development expenses by the company, a detailed accounting of the role of federally-funded research in the development of the drug, and the anticipated therapeutic benefit of the drug. The reasonable price would be set such that the company would receive a healthy but reasonable profit above and beyond its expenses. In determining a reasonable price for a drug, an examination would also be made of the price of drugs in the same therapeutic class in the U.S. and other advanced industrialized countries. The reason that taxpayers fund government research through the National Institutes of Health (NIH) is to develop cures for dread diseases. Clearly, NIH research does little good if consumers cannot afford the drugs that were developed with our tax dollars. This proposal would benefit all those who rely on essential medications, not just Medicare beneficiaries.

3. **Payment based on the value of drugs:** As discussed in this report, much of the research and development and advertising by the drug industry is for the production and marketing of me-too drugs, which represent little or no therapeutic improvement over existing drugs. FDA should require studies of the comparative efficacy and safety of drugs as a condition of their approval. Medicare should not cover new drugs unless there is scientific documentation of a therapeutic advantage over older approved drugs. For drugs that show a genuine therapeutic advance, Medicare would cover the drug and negotiate a fair price based on the new innovation. If Medicare were to do this, then a Medicare drug benefit would not hinder genuine innovation, as the drug industry has asserted, but might act as an inspiration to innovation. In the event that Medicare were unable to create a system of negotiated payments based on a drug's value, then studies of drugs' comparative value could be conducted through the Centers for Education Research and Training (CERT) created under Food and Drug Administration Modernization Act of 1997 (FDAMA). CERT sites are independent, academic centers that given adequate funding could evaluate the comparative value of drugs. Private payers should use the work of the CERT sites to set their coverage policies for new drugs as a way of controlling costs in the private sector and creating an incentive for innovative research.

## **B. Industry Transparency & Preventing Conflicts of Interest**

1. **Better tracking of taxpayer developed drugs:** Legislation must be enacted that requires the NIH to maintain a public record detailing the extent of federally-funded support towards the research and development of new drugs. By forcing the NIH to formally track the role of research it funds in the creation of new drugs, the public will be better able to hold the industry accountable for how it

uses the research it is given and be able to seek compensation for such public assistance in the form of reasonable prices for drugs.

2. **Require disclosure of the cost of R&D:** Since drug industry claims about the cost of R&D play such a prominent role in its campaign to oppose Medicare drug coverage and Medicare-negotiated drug prices it would be very valuable for the government and private sector to be able to determine how much it costs for the industry to develop new medicines. Currently, only Congress may subpoena drug company financial records to determine what the industry spends on R&D – authority it has not used. The General Accounting Office also should be given such authority in order to determine if the numerous government programs that purchase drugs are being defrauded.
3. **Require disclosure of best prices:** The public debate over what can be done about the high price of prescription drugs for U.S. seniors and other consumers has been stymied by a lack of information about the discounts that the industry offers its most favored domestic and foreign purchasers. Legislation should be enacted that would force the industry to reveal to policy makers the lowest prices it charges to purchasers here and abroad.
4. **Prohibit drug researcher conflicts of interest:** Oftentimes, researchers use non-profit institutions to apply for government research grants, but then enrich themselves by funneling the results of that research to for-profit companies that they control or are employed by. Congress should enact legislation to prevent such abuse of the taxpayer trust. Or, if Congress is unwilling to prohibit such conflicts of interest, it should require grant recipients to fully disclose them.

## C. Ending Corporate Welfare

1. **End the pediatric incentive for all new drugs:** Pediatric exclusivity is a provision in current law that gives drug companies an additional six months of monopoly marketing protection for testing drugs in children. If this provision is reauthorized this year it will mean \$29 billion in additional revenue for the brand-name drug industry over the next 20 years. This provision should not be reauthorized. Instead, Congress should grant the FDA authority to require that all new drugs likely to be used in children be studied for safety and efficacy in children as a pre-condition of marketing approval. The FDA has estimated the annual cost of conducting those studies if they had been required between 1993 and 1997 at \$80 million.<sup>75</sup> This is a modest cost in exchange for lucrative monopolies granting the rights to market a prescription drug. The amount represents less than one-half-of-one-percent of the \$28 billion in profits earned by the top 11 drug companies in 2000. For more on this go to: <http://www.citizen.org/congress/drugs/pedexclusivityfactsheet.html>.

2. **No patent extensions/no patent abuses:** The Hatch-Waxman Act, which was passed in 1984, has been described as legislation that balanced the public's need for access to lower-priced generic drugs and the brand name drug industry's need for adequate revenues to fund the research and development it uses to invent medications. However, in the years since the Act was passed the drug industry has exploited loopholes in the law to extend their lucrative patents on drugs in ways that were not intended by the Act. One of the loopholes in the law is a provision that prevents a generic from coming to market for 30 months after a lawsuit for patent infringement has been filed against them by a brand name company. The industry exploits this loophole by filing frivolous lawsuits against generics -- thus delaying the entry of competing products by at least 30 months. This provision in the Hatch-Waxman Act should be revised so that brand name drug companies can only receive protection from competition if they can prove in a court of law that there is a good reason that a competing generic ought to be kept off of the market. This change is contained in legislation pending before the U.S. House and Senate, the Greater Access to Affordable Pharmaceuticals Act, Schumer-McCain/Brown-Emerson, S. 812/H.R.1862.

### C. Comparative Drug Information

1. **Require the FDA to estimate the therapeutic value of new drugs:** In order for the public and private sectors to be better equipped to negotiate lower drug prices, better information is needed about whether new products may offer a therapeutic advantage over older drugs or are simply me-too drugs. This would be similar to the system used by the FDA prior to 1992 in which it distinguished between drugs that represented an "important therapeutic gain, a "modest therapeutic gain," and "little or no therapeutic gain."
2. **Analyze the comparative value of all currently-approved prescription drugs:** Congress should require the FDA or else establish a private entity to study the comparative value of all prescription drugs so that consumers, payers, and doctors can be better informed. If funding for the Centers for Education, Research and Training (CERT) established under FDAMA were increased, they could do this research. As a condition of federal support, academic medical centers could be required to use this unbiased information in educating medical students and in continuing medical education so that doctors can make distinctions between "me-too" and breakthrough drugs in their prescribing decisions. Also, such information would be made available to medical insurance payers so that they could make better decisions about which drugs to cover.

### E. Regulate Drug Company Advertising and Promotion

1. **Require FDA to promulgate regulations for direct-to-consumer (DTC) advertising:** As this report shows, drug company advertising to consumers plays

a role in rising prescription drug costs. But currently there is limited FDA authority to regulate such advertising. Congress should require the FDA to issue regulations concerning DTC advertising by a date certain. These regulations should require that drug companies provide consumers with scientifically accurate, useful, comparative information about the value of drugs in their advertisements and in the packaging of the drugs they manufacture.

2. **Assure adequate FDA funding to monitor both professional and DTC advertising:** The FDA office charged with overseeing drug advertising, the Division of Drug Marketing Advertising and Communication (DDMAC), is woefully understaffed. While the dollar value of DTC advertising and promotion has more than tripled from \$791 million in 1996 to \$2.5 billion in 2000, and other advertising, to professionals, also increased, the number of FDA staff assigned to review and investigate all prescription drug advertising during this same period has increased from 11 to only 14. Clearly, in order for FDA to protect consumers from misleading claims in advertisements by the drug industry that help to fuel double-digit spending increases, additional staff for DDMAC is essential.
3. **Strengthen FDA enforcement:** To give FDA stronger enforcement powers, Congress should give the agency the authority to level civil monetary fines for misleading drug advertising. The FDA has asked for such authority in the past. (See *American Journal of Law and Medicine*, 1999, p. 149.).

## **Appendix A**

### **Chapters on R&D Costs for New Drugs from the Office of Technology Assessment Report “Pharmaceutical R&D: Costs, Risks and Rewards”**

See attached

Chapter One: Summary

Chapter Three: The Costs of Pharmaceutical R&D

## Appendix B

### Methodology for Section II ("PhRMA's Own Data Contradicts the \$500 Million Claim")

The aggregate analysis in Section II is roughly modeled after a study by S.N. Wiggins ("The Cost of Developing A New Drug," Washington, D.C., Pharmaceutical Manufacturers Association, 1987).

This aggregate analysis is not perfect, for several reasons explained below, but it has been reviewed by three economists with acknowledged expertise in the pharmaceutical industry and they have found it sound.

The first imperfection in Public Citizen's analysis is that it relies on PhRMA data, which has not been verified for accuracy.

The second imperfection is that PhRMA reports R&D spending in two categories – 1) "domestic" (which includes all spending by American and foreign-based companies in the U.S.) and 2) "abroad" (which only includes overseas spending by U.S.-based companies). Neither of these categories is ideal for this particular analysis, as explained below.

Public Citizen's aim was to show simply the amount PhRMA reported that the industry spent on R&D, and then divide that spending by new drugs approved for market (over a time frame that corresponded to R&D spending). That simple division ought to produce a spending-per-new drug figure derived from the industry's own data. This figure would not include the opportunity cost of capital, so it would reveal how much drug companies actually spent on R&D for each new drug – on average – including failures.

Here's how Public Citizen arrived at the figures:

To get an accurate apples-to-apples analysis, one would need to know all R&D (both here in the U.S. and abroad) that led to the discovery and development of drugs approved for market in the U.S. over an appropriate time frame.

The problem is, these numbers don't exist in public records and PhRMA doesn't report its data in such fashion. The FDA records how many new drugs are approved for market each year, but it does not identify the location of spending that connects directly to each new drug approved.

For example, consider PhRMA's reported spending in two categories – "domestic" and "abroad." These two categories do not necessarily capture all relevant spending pertaining to drugs approved for market in the U.S. In some cases, these two categories might underestimate spending; in other cases, they could overestimate.

It could be that foreign-based companies conducted R&D overseas for a drug that was approved in the U.S. and such spending would not be evident in PhRMA's data. Conversely, PhRMA's reported spending might include R&D costs here and abroad that had nothing to do with new drugs approved in the U.S.

Public Citizen considered identifying those new drugs approved by the FDA that were developed only by U.S.-based companies, and then comparing those drugs to spending (both here and abroad) by U.S. companies. But such an analysis might be left counting U.S. company spending that did not pertain to these drugs; or it might not capture overseas spending by foreign-based companies on these drugs; or it might not account for the licensing deals by which foreign-based companies perform contract work on specific drugs for U.S.-based companies and vice versa.

Given those limitations, it did not make sense to winnow the list of FDA-approved drugs down to those that were mainly developed by U.S.-based companies. So Public Citizen was left with PhRMA's reported annual R&D spending and the FDA's annual tally of new drugs approved for market. Economists advised that a comparison of these numbers would provide a rough estimate of R&D spending per new drug (including failures).

Public Citizen then wanted to account for the roughly seven-year lag between R&D spending and new drug approval. Thus, this measure compares R&D spending for 1994 to new drug approvals for the year 2000.

To be even more accurate, this measure accounts for years in which spending on new drugs was extraordinarily high or low. It compares spending over seven-year periods with new drug approvals over seven-year periods. An annual average was calculated for each period, which has the effect of smoothing out peaks and valleys.

The results? From 1988 through 1994, PhRMA reported total R&D (domestic and abroad) spending of \$69.7 billion. Adjusted for inflation, it is \$88.0 billion in year 2000 dollars, for an average of \$12.56 billion per year (See Table B-1). During the period 1994-2000, the FDA reported that 667 new drugs were approved for market, or 95.3 new drugs approved each year, on average.

Dividing the average annual spending by average annual new drug approvals, we see that average R&D spending per new drug in this period was \$87.0 million (after accounting for R&D tax deductions).

**Table B-1**  
**Average R&D Cost per New Drug Approval During the 1990s**  
**(Rolling 7-Year Average with 7-Year Lag, \$ in millions)**

**Domestic + Foreign R&D Spending**

7-Year R&D Period	Average Annual R&D Spending	7-Year NDA Period	Average Annual New Drugs Approved	Pre-Tax R&D Spending per New Drug	After-Tax R&D Spending per New Drug
1988-1994	\$12,564.3	1994-2000	95.3	\$131.9	\$87.0
1987-1993	\$11,523.2	1993-1999	91.3	\$126.2	\$83.3
1986-1992	\$10,417.6	1992-1998	92.4	\$112.7	\$74.4
1985-1991	\$9,339.1	1991-1997	88.6	\$105.4	\$69.6
1984-1990	\$8,433.5	1990-1996	80.4	\$104.9	\$69.2

Source: Spending data comes from Pharmaceutical Research and Manufacturers of America, PhRMA Annual Survey, 2000; NDA data comes from U.S. Food and Drug Administration, Center for Drug Evaluation and Research, December 31, 2000. (All spending figures have been inflated to year 2000 dollars.)

Note: Domestic R&D includes expenditures within the United States by research-based pharmaceutical companies. Foreign R&D includes expenditures outside the United States by U.S.-owned research-based pharmaceutical companies.

Some critics might find fault with the seven-year lag, arguing that in accounting terms, today's R&D expenses are paid by today's revenue. Thus, R&D spending in any year ought to be compared with drugs brought to market that same year. As mentioned earlier, this study rejects that argument because it doesn't reflect the reality that R&D spending invariably precedes the marketing of a drug, and, as noted earlier, DiMasi agrees that spending should be lagged two to 12 years. Nevertheless, Public Citizen calculated R&D spending for current drug approvals and current research expenditures and found that spending remained close to \$100 million per drug, with costs in the 1990s ranging from \$99 million to \$118 million per drug. (See Table B-2)

**Table B-2**  
**Average R&D Cost per New Drug Approval During the 1990s**  
**(Rolling 7-Year Average with No Lag, \$ in millions)**

**Domestic R&D Spending Only**

7-Year Period	Average Annual R&D Spending	Average Annual New Drugs Approved	Pre-Tax R&D Spending per New Drug	After-Tax R&D Spending per New Drug
1994-2000	\$17,054.1	95.3	\$178.98	\$118.1
1993-1999	\$15,627.1	91.3	\$171.19	\$113.0
1992-1998	\$14,289.9	92.4	\$154.60	\$102.0
1991-1997	\$13,123.4	88.6	\$148.17	\$97.8
1990-1996	\$12,025.2	80.4	\$149.51	\$98.7

Source: See above.

## Appendix C

**“NIH Contributions to Pharmaceutical Development: Case Study Analysis of the Top-Selling Drugs,” an administrative document dated February 2000. Prepared by NIH Office of Science Policy.**

See attached

## Appendix D

### Tax Methodology

Drug companies are allowed a tax deduction for all qualified research and development expenses. That means all money spent on R&D can be deducted from a company's taxable income. This generates enormous savings for drug companies and substantially lowers the cost of bringing a new drug to market.

In Example 1 (see next page), Company A has spent \$10 million on R&D and collected \$100 million in revenues. At a statutory tax rate of 34 percent, Company A would pay \$34 million in federal taxes without the R&D deduction. After the deduction, Company A's taxable income is only \$90 million, lowering its tax bill to \$30.6 million. Company A has saved \$3.4 million in taxes due to the R&D tax deduction.

In Example 1, Company A saved \$3.4 million in taxes after deducting R&D expenses, which is 34 percent of the \$10 million the company spent on R&D. Every dollar Company A spends on R&D lowers its taxable income by \$1. Put another way, every dollar Company A spends on R&D lowers its tax bill by \$0.34. In effect, every dollar Company A spends on R&D only costs the company \$0.66 because of the money it saves in taxes.

Since every dollar spent on R&D can be deducted, the net cost of R&D to drug companies will always be reduced by the statutory tax rate. This is true regardless of the tax rate or the amount spent on R&D. If Company A had spent \$20 million on R&D then it would have saved \$6.8 million, which is 34 percent (Example 2). If the statutory tax rate changed to 46 percent then Company A would have saved \$4.6 million in taxes after deducting \$10 million spent on R&D (Example 3).

This R&D tax deduction should not be confused with other tax credits the drug industry receives. The deduction of R&D expenses is different from other tax credits because it is a deduction that reduces the taxable income of a company. The drug industry enjoys several tax credits that are applied after the amount a company owes in taxes has been calculated. In other words, a tax credit reduces the amount of tax owed (or tax liability), while a deduction affects the amount of income that is subject to the statutory rate.

### Example 1

Statutory Tax Rate	34%		
Gross Income	\$100,000,000	Taxes Before Deduction	\$34,000,000
R&D Deduction	\$10,000,000		
Taxable Income	\$90,000,000	Taxes After Deduction	\$30,600,000
		Difference	\$3,400,000
		Percentage of R&D Expenditure	34%

### Example 2

Statutory Tax Rate	34%		
Gross Income	\$100,000,000	Taxes Before Deduction	\$34,000,000
R&D Deduction	\$20,000,000		
Taxable Income	\$80,000,000	Taxes After Deduction	\$27,200,000
		Difference	\$6,800,000
		Percentage of R&D Expenditure	34%

### Example 3

Statutory Tax Rate	46%		
Gross Income	\$100,000,000	Taxes Before Deduction	\$46,000,000
R&D Deduction	\$10,000,000		
Taxable Income	\$90,000,000	Taxes After Deduction	\$41,400,000
		Difference	\$4,600,000
		Percentage of R&D Expenditure	46%

## Endnotes

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<sup>1</sup> National Public Radio, “Talk of the Nation,” hosted by Juan Williams, Jan. 2, 2001

<sup>2</sup> U.S. Food and Drug Administration statistics cited by Donald Drake and Marian Uhlman, “Making Medicine, Making Money” (1993), published by Andrews and McMeel, p. 72.

<sup>3</sup> National Institutes of Health, “NIH Contribution to Pharmaceutical Development,” Administrative Document, February 2000.

<sup>4</sup> Office of Technology Assessment, U.S. Congress, “Pharmaceutical R&D: Costs, Risks and Rewards,” 1993.

<sup>5</sup> Alice Dembner, “Public Handouts Enrich Drug Makers, Scientists,” *The Boston Globe*, April 5, 1998.

<sup>6</sup> Joseph DiMasi et al., “The Cost of Innovation in the Pharmaceutical Industry,” *Journal of Health Economics* 10:107-142, 1991.

<sup>7</sup> PAREXEL’s Pharmaceutical R&D Statistical Sourcebook 2000, “Recent Estimates of the Cost of Developing New Drugs,” pg. 65, cites estimate by Boston Consulting Group that the fully capitalized pretax costs of pharmaceutical R&D had risen “to perhaps over \$500 million.”

<sup>8</sup> Center for the Study of Drug Development, Tufts University web site  
<http://www.tufts.edu/med/csdd/images/spspeak.pdf>

<sup>9</sup> *Ibid.*

<sup>10</sup> See n. 6.

<sup>11</sup> Office of Technology Assessment, U.S. Congress, “Pharmaceutical R&D: Costs, Risks and Rewards,” 1993.

<sup>12</sup> See n. 6.

<sup>13</sup> See n. 6, footnote 29. DiMasi writes: “One difference is that the FDA includes diagnostic agents and we do not. Another difference is that we include a few therapeutically significant biologics, where the FDA does not include any.”

<sup>14</sup> According to the U.S. Food and Drug Administration, only 311 of the 857 New Drug Applications (NDAs) approved for market in the 1990s were new molecular entities (NMEs), which are similar to DiMasi’s NCEs.

<sup>15</sup> Office of Technology Assessment, U.S. Congress, “Pharmaceutical R&D: Costs, Risks and Rewards,” 1993.

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<sup>16</sup> See n. 6.

<sup>17</sup> Kenneth I. Kaitin and Elaine M. Healy, “The New Drug Approvals of 1998, 1997 and 1996: Emerging Drug Development Trends in the User Fee Era,” Tufts Center for the Study of Drug Development, January 2000, published in PAREXEL’s Pharmaceutical R&D Statistical Sourcebook 2000, pg. 117.

<sup>18</sup> CenterWatch, “The Speed Demons of Clinical Drug Development: The Fastest Major Pharmaceutical Companies,” 1999. Published in PAREXEL’s Pharmaceutical R&D Statistical Sourcebook 2000, pg. 123.

<sup>19</sup> Lehman Brothers, “Drug R&D Costs, Success Rates, and Emerging Technologies: A Look at Three Future Scenarios,” 1997, published in PAREXEL’s Pharmaceutical R&D Statistical Sourcebook 2000, pg. 80.

<sup>20</sup> S.N. Wiggins, “The Cost of Developing a New Drug,” Pharmaceutical Manufacturers Association, June 1987.

<sup>21</sup> See n. 6.

<sup>22</sup> Pharmaceutical Research and Manufacturers of America, “Annual Survey 2000,” List of Tables, 2001, <http://www.phrma.org/publications/publications/profile00/>.

<sup>23</sup> U.S. Food and Drug Administration, “NDAs Approved in Calendar Years 1990-1999 by Therapeutic Potentials and Chemical Types,” December 31, 1999, <http://www.fda.gov/cder/rdmt/pstable.htm>.

<sup>24</sup> PhRMA’s full definition of research expenditures is: “Every year, PhRMA surveys its member companies – the country’s leading pharmaceutical and biotechnology companies – on their individual R&D expenditures. These expenditures are defined as the total costs incurred for all pharmaceutical research and development activity, including salaries of employees who conduct, support or supervise R&D; supplies and equipment used in R&D; a fair share of overhead; contract research expenditures; the costs of synthesis and extraction of compounds; the costs of laboratory testing (pre-clinical); expenditures involved in formulating the dosage and testing the stability of compounds; the expenditures incurred in three-stage, FDA-supervised clinical trials; the costs of post-marketing studies, and bioavailability studies.” Accessed at <http://www.phrma.org/publications/backgrounders/development/invest.phtml>

<sup>25</sup> Marcia Angell (editor-in-chief), “The Pharmaceutical Industry – To Whom Is It Accountable?,” *New England Journal of Medicine*, June 22, 2000.

<sup>26</sup> See n. 6.

<sup>27</sup> Pharmaceutical Research and Manufacturers Association, “Annual Survey 2000,” List of tables, 2000

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<sup>28</sup> Dembner, see n. 5; also Public Citizen interviews with Wendy Schacht, Congressional Research Service and John Hansen, deputy director, General Accounting Office, Health Team.

<sup>29</sup> Public Citizen update of Drake and Uhlman, “Making Money, Making Medicine,” 1993.

<sup>30</sup> Iain Cockburn (University of British Columbia) and Rebecca Henderson (MIT), “Public-Private Interaction and the Productivity of Pharmaceutical Research,” National Bureau of Economic Research, April 1997.

<sup>31</sup> Dembner, see n. 5.

<sup>32</sup> National Institutes of Health, “NIH Contributions to Pharmaceutical Development,” Administrative Document, February 2000, p. 2.

<sup>33</sup> *Ibid.*

<sup>34</sup> *Ibid.*

<sup>35</sup> *Ibid.*

<sup>36</sup> See n. 4, Appendix D: Congressional Access to Proprietary Pharmaceutical Industry Data.

<sup>37</sup> *Ibid.*

<sup>38</sup> *Ibid.*

<sup>39</sup> Public Citizen analysis of lobby disclosure reports filed with the Secretary of the Senate and Clerk of the House pursuant to the Lobby Disclosure Act of 1995; Public Citizen analysis of campaign contributions reported to the Federal Election Commission and compiled by the Center for Responsive Politics; and Jamieson, et al., “Issue Advertising in 1999-2000 Election Cycle,” Annenberg Public Policy Center of the University of Pennsylvania, February 1, 2001 <http://www.appcpenn.org/issueads/1999-2000issueadvocacy.pdf>.

<sup>40</sup> Special Committee on Aging, U.S. Senate, “The Drug Manufacturing Industry: A Prescription for Profits,” September 1991.

<sup>41</sup> See n. 25.

<sup>42</sup> *Fortune* magazine, April 2001, Fortune 500 ([www.fortune.com](http://www.fortune.com)).

<sup>43</sup> Public Citizen update of Stephen W. Schondelmeyer calculation, “Competition and Pricing Issues in the Pharmaceutical Market,” PRIME Institute, University of Minnesota based on data found in *Fortune* magazine, 1958 to 1999; *Fortune* magazine, April 2000, Fortune 500 ([www.fortune.com](http://www.fortune.com)).

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<sup>44</sup> *Ibid.*

<sup>45</sup> Lee Clifford, "The Story of American Business," *Fortune*, April 16, 2001.

<sup>46</sup> Public Citizen analysis of stock prices for calendar year 2000 obtained from Commodity Systems Inc., accessed at <http://www.finance.yahoo.com>.

<sup>47</sup> Donald Drake and Marian Uhlman, "Making Medicine, Making Money," Andrews and McMeel, (1993), p. 72.

<sup>48</sup> *Ibid.*

<sup>49</sup> U.S. Food and Drug Administration, "NDAs Approved in Calendar Years 1990-1999 by Therapeutic Potentials and Chemical Types," December 31, 1999, <http://www.fda.gov/cder/rdmt/pstable.htm>.

<sup>50</sup> Congressional Research Service Memorandum, "Federal Taxation of the Drug Industry," December 1999.

<sup>51</sup> Internal Revenue Service, "Corporation Sources Book," cited in Congressional Research Service Memorandum, December 1999.

<sup>52</sup> U. S. General Accounting Office, "Pharmaceutical Industry: Tax Benefits of Operating in Puerto Rico," May 1992.

<sup>53</sup> See n. 50.

<sup>54</sup> National Institute for Health Care Management, "Prescription Drugs and Intellectual Property Protection," August 2000.

<sup>55</sup> Rachel Zimmerman, "Drug Makers Find a Windfall Testing Adult Drugs on Kids," *The Wall Street Journal*, Feb. 5, 2001, p. A1.

<sup>56</sup> U.S. Food and Drug Administration, "The Pediatric Exclusivity Provision," Status Report to Congress, January 2001.

<sup>57</sup> PricewaterhouseCoopers, "Pharma 2005 Silicon Rally: The Race to e-R&D," published in PAREXEL's Pharmaceutical R&D Statistical Sourcebook 2000.

<sup>58</sup> *Ibid.*

<sup>59</sup> Brian O'Reilly, "There's Still Gold in Them Thar Pills," *Fortune* magazine, July 23, 2001.

<sup>60</sup> Jeremy Kahn, "The World's Largest Corporations: Global 500 by the Numbers," *Fortune* magazine, July 23, 2001.

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<sup>61</sup> Kenneth I. Kaitin and Elaine M. Healy, “The New Drug Approvals of 1998, 1997 and 1996: Emerging Drug Development Trends in the User Fee Era,” Tufts Center for the Study of Drug Development, January 2000, published in PAREXEL’s Pharmaceutical R&D Statistical Sourcebook 2000, pg. 117.

<sup>62</sup> U.S. General Accounting Office, “Prescription Drugs: Spending Controls in Four European Countries,” May 1994, p. 8.

<sup>63</sup> Office of Technology Assessment, U.S. Congress, “Pharmaceutical R&D: Costs, Risks and Rewards,” 1993.

<sup>64</sup> *Ibid.*

<sup>65</sup> *Ibid.*

<sup>66</sup> Company yearly earnings reports analyzed by Public Citizen, April 2001.

<sup>67</sup> IMS Health, “IMS Health Reports...,” October 19, 2000.

<sup>68</sup> Harris, Gardiner, “Drug Firms, Stymied in the Lab, Become Marketing Machines,” *The Wall Street Journal*, July 6, 2000, citing research from Competitive Media.

<sup>69</sup> See n. 67.

<sup>70</sup> National Institute for Health Care Management, “Prescription Drugs and Mass Media Advertising,” September 2000.

<sup>71</sup> Barents Group LLC, “Factors Affecting the Growth...,” National Institute for Health Care Management, 1999.

<sup>72</sup> Michael Wilkes, et al., “Direct to Consumer Prescription Drug Advertising...,” *Health Affairs*, March/April 2000.

<sup>73</sup> See n. 68.

<sup>74</sup> Merrill Lynch, “A Medicare Drug Benefit: May not be so Bad,” June 23, 1999.

<sup>75</sup> U.S. Food and Drug Administration, “Regulations Requiring Manufacturers to Assess the Safety and Effectiveness of New Drugs and Biological Products in Pediatric Patients,” Final Rule, *The Federal Register*, December 2, 1998, p. 66661.