

# Prescription Drugs and Intellectual Property Protection

## Finding the Right Balance Between Access and Innovation



NIHCM  
FOUNDATION

*Over the last decade, U.S. spending on prescription medications has surged. Policy makers have cited an aging population, expensive new drugs, expanded insurance coverage, an increase in the number of prescriptions and extensive promotion by drug manufacturers as the primary factors driving this trend. Less understood is the relationship between higher drug costs and the federal laws which protect the pharmaceutical industry from competition in the making and marketing of drugs.*

This brief examines the major pieces of legislation that have increased intellectual property protection for pharmaceuticals during the past 20 years. In addition, it considers the effects of this enhanced protection on technological innovation and the marketplace for prescription drugs. As spending on prescription drugs continues to rise and Congress contemplates drug coverage for the Medicare program, the repercussions of current patent laws and other protections for pharmaceuticals now warrant scrutiny.

## Overview

Intellectual property protection (IPP) aims to provide incentives for innovation. Patents and other forms of protection eliminate direct competition to a product for a fixed period of time. During this period the inventor can often charge premium prices, which ensure an attractive return on what might have been a considerable investment in research and development. However, these higher prices can slow the diffusion of new technology by making the product more expensive for some who would benefit. Thus, IPP usually entails a tradeoff between consumers' having easier access to the most advanced technology and better products in the future.

Over the past two decades, Congress has enacted a series of laws that have greatly increased the "effective patent life" enjoyed by brand name prescription drugs. The effective patent life is the number of years remaining in a drug's patent term after

the Food and Drug Administration (FDA) approves the drug for market. These statutes have either (1) extended the term of the original patent; (2) shortened the period of time consumed by clinical testing and regulatory review; and/or (3) granted "market exclusivity" to drugs under certain circumstances (**See Figure 2**).

Considered individually, each of the laws offers a reasonable approach to stimulate pharmaceutical innovation and ensure broad access to new medications. Viewed collectively, the laws have conferred multiple and additive protection on prescription drugs.

No research assesses the cumulative effect of all of the laws on the patent life of new drugs. But a review of the evidence available suggests that the average effective patent life of many new drugs has increased by at least 50 percent between the early 1980s and today (**See Figure 1**). For companies able to take advantage of the full array of changes in IPP, the effective patent life of some drugs may have doubled.

Understanding the consequences of the dramatic increase in intellectual property protection is important for a number of reasons:

### ***IPP Contributes to Prescription Drug Spending***

When the patent on a brand name drug is extended or a drug is granted a period of market exclusivity, consumers pay more for the product over a longer period. The result is increased overall spending on prescription drugs. Recent discussion about a

*Drugs have experienced dramatic increases in effective patent life from multiple, additive patent extensions.*

Medicare prescription drug benefit has focused public interest on moderating the increase in drug costs. The debate over how to control spiraling costs has often been posed as a choice between price controls and market competition. However, the role of IPP and its direct effect on price competition, consumer choice and timely access to generic drugs deserves examination as a key factor in ensuring access to affordable medications.

## A TIMELINE & BRIEF SYNOPSIS

### LAWS THAT AFFECT THE PATENT LIFE OF PRESCRIPTION DRUGS

**2000 Pipeline Drug Proposals** are being considered by Congress to provide up to three years patent extension to selected drugs.

**1999 The Patent Term Guarantee Authority Act** requires the federal Patent and Trademark Office (PTO) to compensate for delays of over three years in processing patents.

**1997 The Food and Drug Administration Modernization Act (FDAMA)** enables firms to reduce clinical study time and offers six months of additional IPP to drugs that companies test in children.

**1994 The Uruguay Round Agreements Act (URAA)** changes term of all patents in U.S. from 17 years from the date of issue to 20 years from date of application. Allows longer of the two terms for some drugs already on the market.

**1992 The Prescription Drug User Fee Act (PDUFA)** authorizes user fee support for FDA's premarket review program, and sets performance goals to reduce approval time.

**1986 The Federal Technology Transfer Act** authorizes federal agencies doing research to enter into formal cooperative agreements with private industry to help develop, market, and manufacture government inventions.

**1984 The Drug Competition and Patent Term Restoration Act (Waxman-Hatch)** authorizes patent extensions of up to five years for new drugs and up to two years for drugs in development at the time. Provides three years of market exclusivity for qualifying drugs. Streamlines FDA review process for generic drugs.

**1983 The Orphan Drug Act** provides seven years of market exclusivity to drugs for rare diseases, and tax credits for 50% of the cost of researching and developing such drugs.

### IPP Fosters Both Breakthrough and Incremental Innovation

The conventional wisdom is that IPP stimulates mostly breakthrough discoveries which modify treatment or prevention of disease. But current IPP laws just as frequently encourage companies to derive new products from compounds or drugs already patented.

In the 1990s, the FDA approved a total of 857 new drug applications.<sup>1</sup> Of these, over a third (311) were new molecular entities (NMEs), which by definition are compounds that have never been sold on the U.S. market. Some NMEs constitute important clinical improvements; they provide treatments for diseases that formerly lacked them, or are significantly safer or more effective than existing drugs (**See Figure 3**).

However, nearly half (426) of the drugs approved by the FDA in the 1990s were "new formulations" or "new combinations" of compounds already approved. New formulations consist of active ingredients already on the market but have been modified, e.g., to improve dosing or reduce side effects. A new combination contains two or more previously approved active ingredients in a new single medicine. Aventis' Allegra-D is an example of a new combination product.

### IPP Encourages Industry to Bring to Market Drugs Developed in Collaboration with Federal Laboratories

IPP also applies to drugs developed at public expense, enabling private companies to secure patent and other types of IPP from discoveries funded in part by taxpayers. Under law, government inventions must be transferred to the private sector for commercialization. Pharmaceutical companies have been willing to help develop, manufacture and distribute these drugs under exclusive licensing agreements which, in combination with IPP, enable them to sell their products at relatively high prices. Consequently, the public enjoys access to these drugs though often at a premium. *The Boston Globe* conducted an investigation of 50 top-selling pharmaceuticals approved by the FDA from 1992–1997 and found that 48 had received funding from the government for some phase of development.<sup>2</sup>

### IPP Shields Branded Drugs from Price Competition

IPP promotes an oligopolistic market for brand name drugs, where as few as two or three products can dominate a therapeutic category<sup>3</sup> (**See Figure 4**). Patents and market exclusivity stifle competition from other drugs. With so few competitors, companies

have more opportunity to price their products aggressively. A 1998 Congressional Budget Office (CBO) study showed that manufacturers tend to introduce new branded drugs at premium prices, and then raise these prices as the drugs become accepted.<sup>4</sup> The study found that even after similar branded products enter the market, drug companies often continue to increase the price.

**IPP Delays the Entry of Affordable Generic Drugs**

Lengthening patent terms and providing other forms of IPP to branded drugs delay the entry of generic drugs, which are usually far less expensive. As a result, branded drugs now dominate the U.S. market, where they account for about 90 percent of total dollar spending and about three-fifths of prescriptions despite the fact that they typically cost far more than generic medicines<sup>5</sup> (See Figures 7, 8).

**IPP Supports Pharmaceutical Industry Profits**

The pricing power provided by IPP has helped the pharmaceutical industry maintain its position as the nation's most profitable for the past 20 years, notwithstanding efforts by both the private and public sector to control health care spending. In fact, the profitability gap between the pharmaceutical

industry and other Fortune 500 companies has grown dramatically since the mid-1980<sup>6</sup> (See Figure 5).

**IPP Will Expire for Many Branded Drugs Over the Next Few Years**

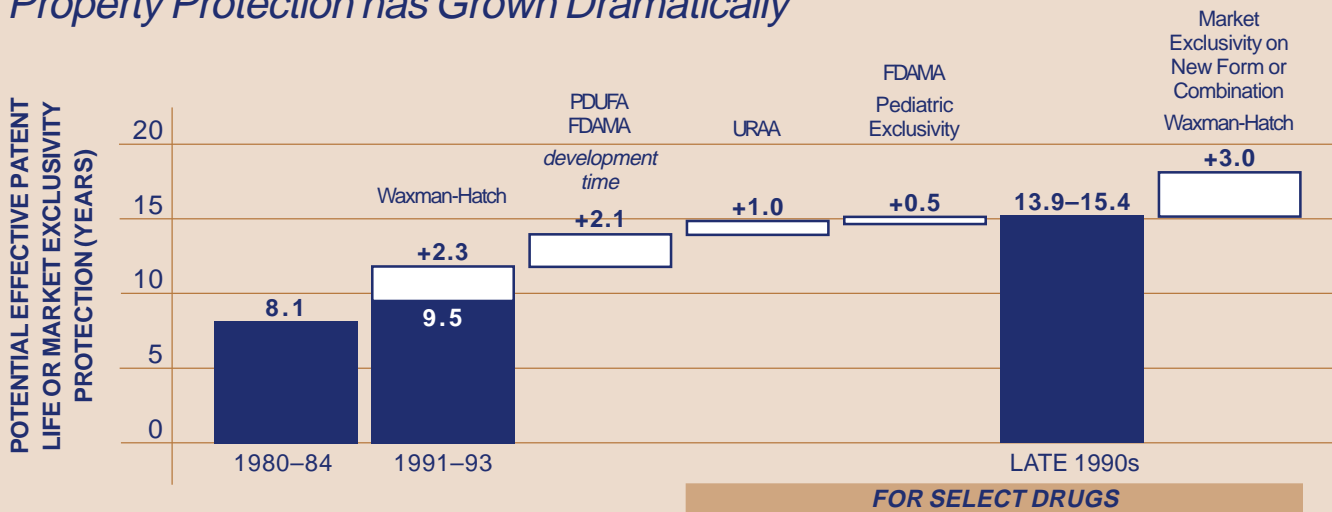
Over the next five years, brand name drugs with combined U.S. sales approaching \$20 billion will go off patent<sup>7</sup> (See Figure 6). This will provide an enormous opportunity for the generic industry and a commensurate threat to the brand-name pharmaceutical industry. Manufacturers seeking to protect the sales of branded drugs are increasing their efforts to extend the period of IPP.

**IPP is Being Applied Amid Rapidly Changing Technology**

Pharmaceutical companies are taking advantage of new technology to protect the franchises on their lucrative brand name drugs. Most recently, companies have begun seeking patents on "purified" forms of some drugs. Through manipulation of a compound's molecular structure, a company can create a purified product eligible for a patent of its own. After clinical testing and approval by the FDA, this new patent may lengthen the life of an existing active ingredient for a decade or more. During this time, the company can encourage doctors to switch their patients from the "old" drug to the new purified form.

*The pricing power provided by IPP has helped the pharmaceutical industry maintain its position as the nation's most profitable for the past 20 years.*

FIGURE 1  
*The Potential Time Period During Which a Drug Can Enjoy Intellectual Property Protection has Grown Dramatically*



**PDUFA:** The Prescription Drug User Fee Act  
**FDAMA:** The Food and Drug Administration Modernization Act  
**URAA:** The Uruguay Round Agreements Act

SOURCES: Kaitin and Trimble, 1987; Grabowski and Vernon, 1996; PRIME Institute, University of Minnesota, 1995; Tufts Center for the Study of Drug Development 2000; FDA 2000; NIHCM Foundation analysis

## Major Legislation Affecting IPP of Pharmaceuticals

Under the Patent Act of 1952, all inventors may obtain U.S. patents giving them the right to exclude others from making, using and selling their inventions for a fixed term. Drug manufacturers usually acquire patents on promising new compounds as well as other inventions connected with their products,

support the prices of pharmaceuticals which have been developed partly at public expense.

### *The Waxman-Hatch Act of 1984*

The Drug Price Competition and Patent Term Restoration Act of 1984 (the “Waxman-Hatch Act”) was a legislative compromise between an expedited approval process for generic prescription drugs and the restoration of patent life “lost” during the clinical testing and FDA review period for innovative branded drugs, also called “originator” or “pioneer” drugs.

Because drug manufacturers usually apply for patents while promising compounds are still under development, the process of clinical testing and FDA review consume several years of the patent term. Hence, the effective patent life may be too short for the manufacturer to earn an acceptable return. Increasing development time reduced the effective patent life for new compounds from an average of 12.4 years in the 1970s, to just 8.1 years in the early 1980s.<sup>8</sup>

Congress attempted to balance the interests of branded drug companies and the public’s need for affordable medications by (1) providing financial incentives for companies to invest in the development of new drugs, with a view to improving medicines for the future; and (2) enabling generic drug companies to bring products to market faster and cheaper, with a view to expanding consumers’ access to less expensive alternatives.

**To increase incentives for research and development, the Act offers both patent extensions as well as market exclusivity, a special form of IPP extended only to prescription drugs:**

- For each new compound, Waxman-Hatch allows one patent term extension equal to the “regulatory review period,” that is, the sum of clinical study and FDA review time. The extension may not exceed five years, or result in an effective patent life of more than 14 years.
- So-called “pipeline” drugs, that is, promising compounds already undergoing clinical trials or under FDA premarket review, were limited to a maximum patent extension of two years, rather than five. (Congress is now considering proposals which would allow some of these drugs to receive additional patent extensions of up to three years.)
- The Act created “data exclusivity,” which bars competing manufacturers from relying upon a branded drug company’s clinical data to gain FDA approval for a specified period of time: (1) five

FIGURE 2

### *Intellectual Property Terms*

#### **PATENT**

Granted by the U.S. Patent and Trademark Office (PTO) and gives the owner the right to exclude others from making, using or selling an invention for a fixed period of time.

#### **PATENT LIFE**

The period of time during which a patent is in effect, currently 20 years, beginning on the date of application to the PTO.

#### **EFFECTIVE PATENT LIFE**

Portion of the patent term that remains after clinical testing and FDA review.

#### **MARKET EXCLUSIVITY**

A special form of IPP conferred only on qualifying prescription drugs, which generally prevents the FDA from approving the same new use of a drug for a competing manufacturer for a specified period of time. Sometimes called data exclusivity.

#### **EVERGREENING**

In general, a strategy for renewing the IPP of a popular drug’s franchise as the drug’s patent nears expiration, by patenting additional features of a product or introducing a “purified” form of the drug (which may have its own patent).

#### **“PURIFIED” FORMS OF DRUGS**

Drugs whose molecular structure have been manipulated either to reduce side effects and dangerous interactions or to enhance effectiveness. A purified version may be eligible for a patent of its own.

such as methods of manufacture. In addition, Congress has granted special forms of IPP which apply only to pharmaceuticals, such as market exclusivity.

The material below examines the series of laws enacted over the past two decades that have had the most pronounced effect on pharmaceutical IPP. Rather than presenting them in chronological order, the section begins with a landmark bill that fundamentally changed the framework of IPP for prescription drugs. In addition to describing other laws, this section briefly considers the use of IPP to

years for new compounds; and (2) three years for new uses of an existing compound, such as new indications, formulations or combinations. Since most new compounds have more than five years of effective patent life, data exclusivity offers more significant protection to new uses of drugs.<sup>9</sup> Although a generic company may perform its own clinical studies, doing so is often very expensive. Thus, data exclusivity, sometimes called “market exclusivity,” provides an effective barrier to generic market entry against a new use of the drug. Branded drug manufacturers may sustain a popular drug’s franchise for three more years by introducing new uses of their products just as the patent on the original drug expires and encouraging doctors to switch patients to the new form.

To balance these concessions to branded manufacturers, Waxman-Hatch created a new, streamlined system allowing generic manufacturers to file an “abbreviated new drug application” (ANDA) with the FDA. The ANDA must document only that the generic product is “bioequivalent” to the originator drug: that is, the extent and rate of its absorption are the same or almost the same as the branded medication. By contrast, previous law required the manufacturer to conduct expensive clinical trials to prove the product’s safety and effectiveness. In addition, the Act permits ANDA applicants to make or use a patented product, perform all necessary testing, submit an application and even receive tentative approval before the relevant patents on the originator drug expire. Thus, a manufacturer can bring its product to market on the very day that the branded drug loses its protection.

The Waxman-Hatch Act has succeeded in its goal of restoring nearly all of the patent life consumed by clinical research and FDA review. According to a Duke University study, by the early 1990s the average effective patent life of new compounds was 11.8 years, 2.3 years longer than the 9.5 year period applicable to a drug without Waxman-Hatch extensions<sup>10</sup> (See Figure 1). Because no study has examined the consequences of the three-year market exclusivity provision, the total effect of Waxman-Hatch on the additional periods of IPP enjoyed by branded drugs is unknown.

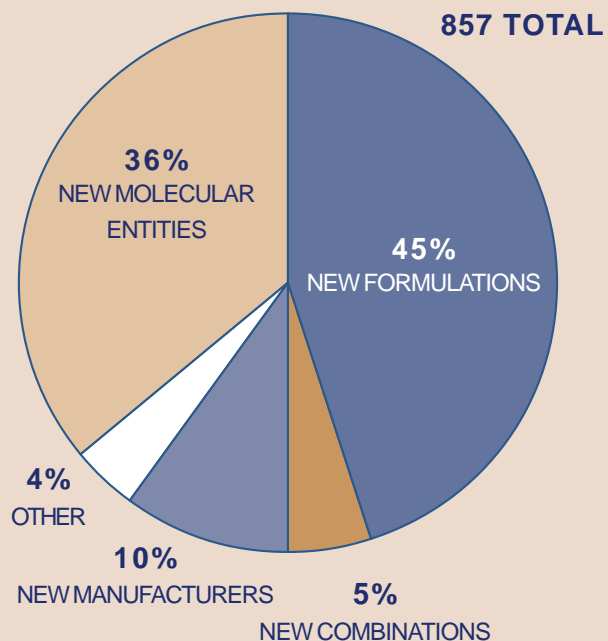
Waxman-Hatch spurred immediate growth in the generic drug industry, but its longer term effect on access to less expensive medications is unclear. In the first few years following its enactment, generic market penetration grew rapidly as many branded drugs went off patent and cost containment efforts encouraged consumers to switch to this affordable alternative. Over the past few years, however, generic drugs have suffered a significant loss of market

share in terms of dollars and a modest one in terms of prescriptions<sup>11</sup> (See Figure 7). Moreover, studies from the CBO and others have shown that increased competition from generics to date has not reduced the profitability of the pharmaceutical industry.<sup>12</sup>

Furthermore, the Act’s effect on pharmaceutical innovation merits examination. Both the public and private sectors have increased their investment in research and development over the past decade, resulting in some important new medicines. However, it is unclear whether the most advanced technology has resulted primarily from public or private investment, and whether the incremental improvements fostered by the Act justify the increased costs to consumers.

FIGURE 3

*60% of New Drug Applications Approved by FDA in 1990–1999 Were for Drugs Containing Existing Active Ingredients*



**NEW FORMULATION:** new dosage or new formulation of active ingredients for drug already on the market.

**NEW COMBINATION:** drug containing two or more compounds which have been marketed before, but have not been marketed together in a product.

**NEW MANUFACTURER:** company creating product with the same active ingredients or formulation as marketed by another manufacturer.

**NEW MOLECULAR ENTITY:** new compound which has never been sold before on the U.S. market.

SOURCE: FDA/Center for Drug Evaluation and Research 2000

**The Uruguay Round Agreements Act (URAA) of 1994**

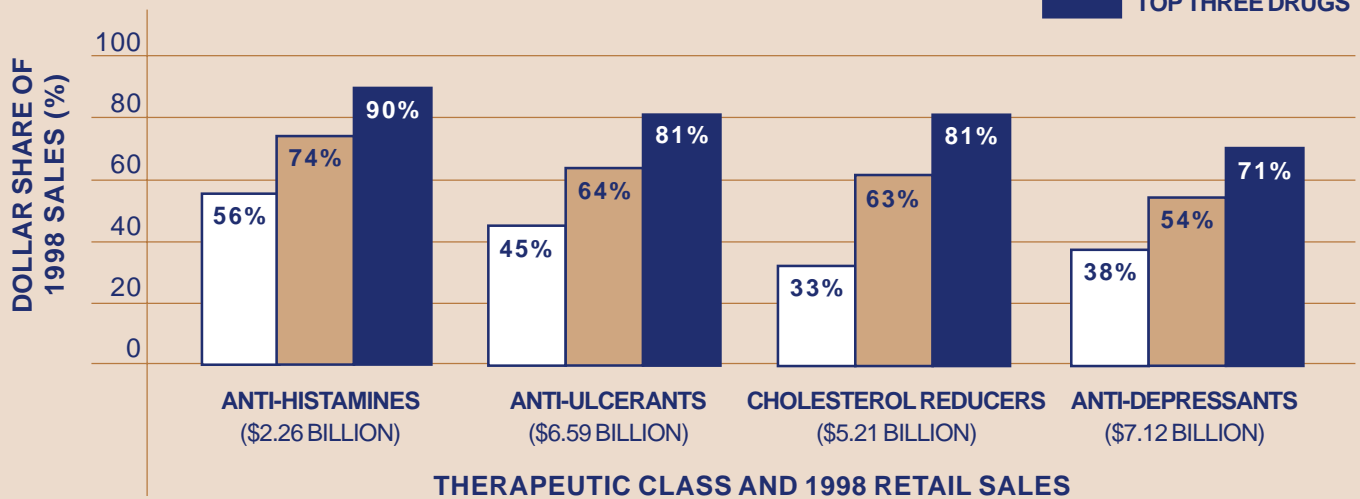
The 1994 Uruguay Round Agreements Act (URAA) brought U.S. patent law into conformance with rules adopted under the General Agreement on Tariffs and Trade (GATT) and by the World Trade Organization (WTO).<sup>13</sup> To that end, the Act stipulated that any patents filed after

companies received *de facto* patent extensions delaying the entry of generic competitors to many of their products.<sup>16</sup> According to a 1995 study, the additional IPP that URAA inadvertently provided branded drugs has cost consumers more than \$6 billion that faster access to generic drugs would have spared them.<sup>17</sup>

Yet there is no evidence that Congress intended to exclude generic drug manufacturers from the protected infringer rules.<sup>18</sup> Further, the courts have ruled that origi-

FIGURE 4

**A Few Top-Selling Drugs Dominate a Therapeutic Class**



SOURCE: Factors Affecting the Growth of Prescription Drug Expenditures, The Barents Group LLC/NIHCM Foundation 1999

*IPP activity will increase as manufacturers seek to protect the \$20 billion worth of drugs coming off patent over the next five years.*

June 8, 1995 would have a term of 20 years from the date of application, rather than 17 years from the date of grant.<sup>14</sup> The URAA also contained transitional rules for patents either in force or filed prior to that date, enabling the inventor to choose the longer of the 17 or the 20-year term.<sup>15</sup> Branded drugs which had received their patents in less than three years following application stood to gain extensions under these rules. As a result, pharmaceutical companies elected the 20-year term for many of their products.

Congress recognized that generic manufacturers in many industries had already made “substantial investments” in developing copies of branded products. To protect the interests of such manufacturers, URAA contained “protected infringer” provisions. These rules allowed generic companies to bring their products to market when the original patent term expired without the threat of legal action, so long as they paid the patent owner “equitable remuneration.”

After URAA was implemented, however, courts barred generic drug manufacturers from using these protected infringer rules because of a technicality in the ANDA process. As a result, originator drug

manufacturer may obtain both URAA and Waxman-Hatch patent extensions<sup>19</sup> (See box on Claritin).

A recent statute ensures that pharmaceuticals will have patent terms under URAA which are the same length as those under previous law. In 1999, Congress enacted the Patent Term Guarantee Authority Act. In general, this new law stipulates that if the Patent and Trademark Office takes more than three years to process a patent application, the patent holder will receive a day for day extension in patent term for the extra time consumed.

**Prescription Drug User Fee Act (PDUFA) of 1992**

In 1992, Congress passed the Prescription Drug User Fee Act (PDUFA) authorizing the collection of user fees from the pharmaceutical industry in order to increase the resources available for the FDA’s premarket review program. In exchange, PDUFA required that the FDA meet annual performance targets, which were chosen to ensure that the agency would significantly reduce its

premarket review times. With a September 1997 sunset provision looming, the FDA faced the prospect of losing this important source of new funding unless it performed well enough to justify reauthorization.

From 1993–1997, the agency made a strenuous and successful effort to increase its efficiency. Both FDA review time for all NDAs and total approval time declined significantly.<sup>20</sup> According to the Tufts Center for the Study of Drug Development, the average total time required for FDA approval declined from 2.6 years for the cohort of drugs approved in 1990–1992, to 1.4 years for those approved in 1996–1998.<sup>21</sup> As a result, patients now have faster access to new technology. However, industry profits will increase since new drugs' effective patent lives have lengthened (See Figure 9).

**Food and Drug Administration Modernization Act (FDAMA) of 1997**

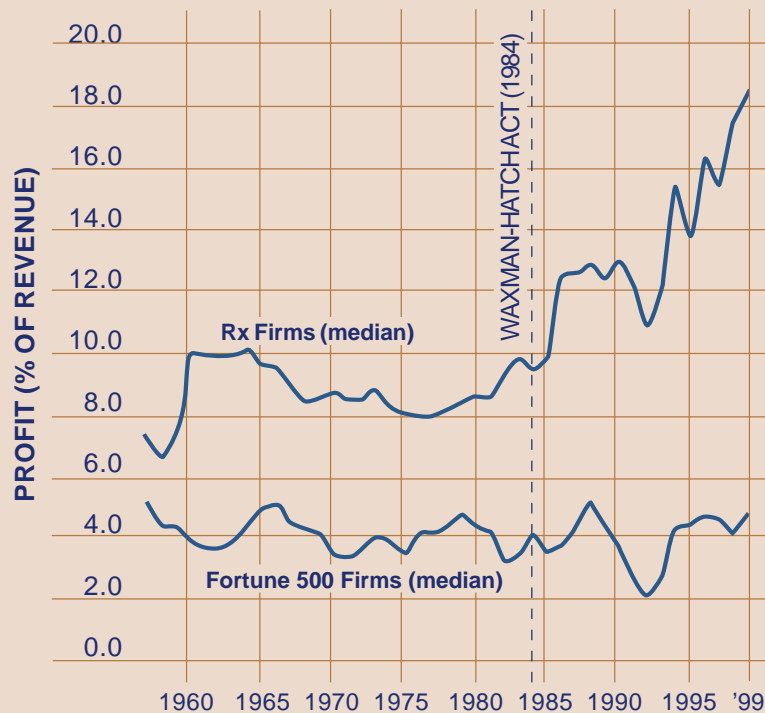
Congress passed the landmark Food and Drug Administration Modernization Act (FDAMA) of 1997 in order to make the U.S. regulatory framework more conducive to the flow of new technology. FDAMA renewed user fee support for the premarket review program and provided the FDA with a “fast track authority” to process applications for priority drugs quickly. It also contains several provisions designed to reduce clinical study time for new drugs.

Implementation of FDAMA has reduced the average number of years for clinical study from 6.8 years, for the cohort of new drugs approved in 1990–1992, to 5.9 years for those approved in 1996–1998.<sup>22</sup>

The combination of FDAMA (affecting clinical study time) and PDUFA (reducing FDA approval time) has decreased total development time by about 2.1 years from 1993 to 1999, resulting in a corresponding gain of effective patent life (See Figures 1, 9).

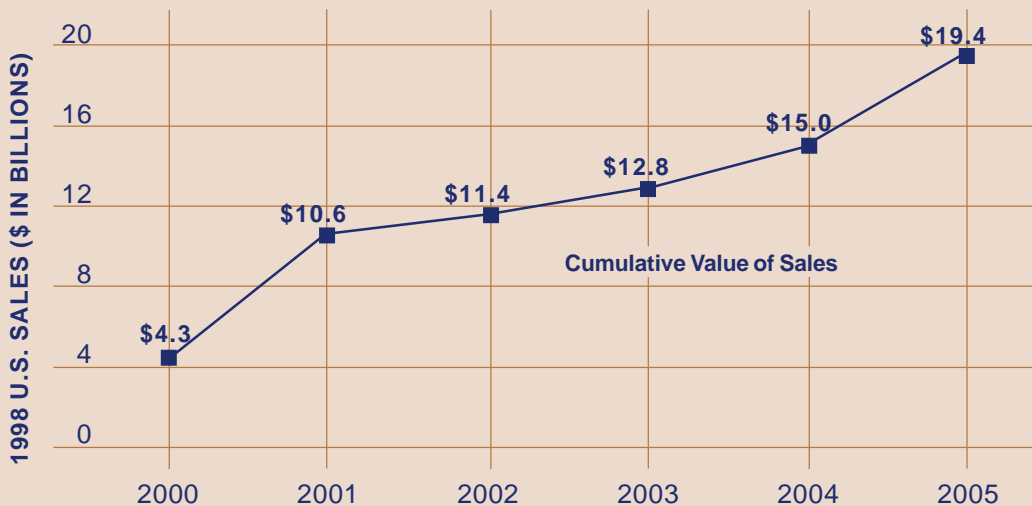
In order to encourage manufacturers to study the performance of drugs in children, FDAMA also allows the agency to confer six months of market exclusivity on a drug if a manufacturer submits satisfactory pediatric studies. This period of “pediatric exclusivity” is added to the end of a drug's existing

**FIGURE 5**  
*Profitability Gap Between Rx Firms and Fortune 500 Firms Grows*



SOURCE: PRIME Institute 1999; Stephen Schondelmeyer, Data from *Fortune* Magazine 1958–2000

**FIGURE 6**  
*Nearly \$20 Billion in Drugs Go Off Patent 2000–2005*



SOURCE: GPIA; FDA Orange Book; IMS Health; Physician's Desk Reference; Warburg Dillon Reed

patent term, or of the term of any other market exclusivity in effect, whichever expires last (See Figure 1). To date, pediatric exclusivity has been granted to 17 drugs.<sup>23</sup>

Whether the usefulness of the data generated from such studies justifies the increased costs associated with pediatric exclusivity is unknown. However, the FDA has issued study requests for 12 drugs with more than \$1 billion in worldwide sales, half of which are facing imminent patent expiration.<sup>24</sup> The Tufts Center for the

Study of Drug Development has estimated that the additional period of market exclusivity would be worth nearly \$2 billion collectively for these drugs.<sup>25</sup>

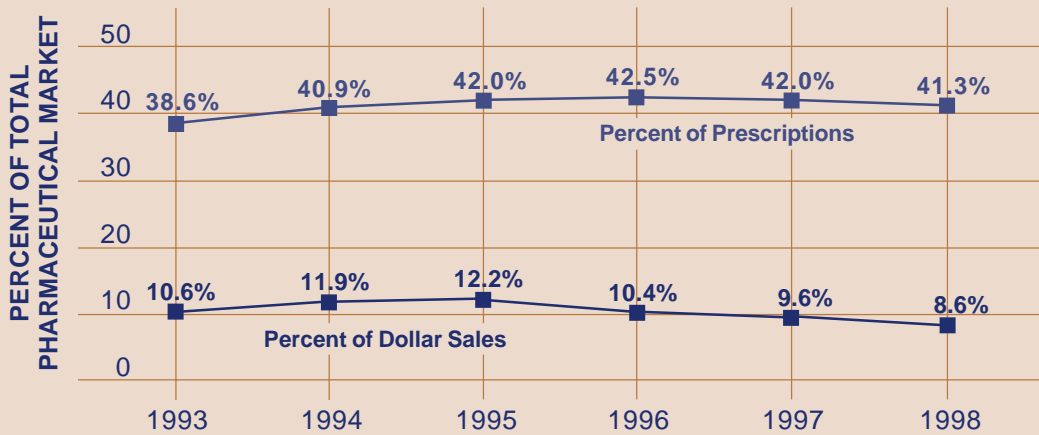
**The Orphan Drug Act (ODA) of 1983**

An estimated 20 million Americans suffer from one of about 5,000 rare diseases. Twenty years ago, few effective drugs were available to treat such conditions. In the belief that small patient populations made it impossible for companies to recover their research and development costs, Congress offered a rich array of incentives through the 1983 Orphan Drug Act (ODA) in a humanitarian effort to stimulate the flow of new medications. Following a 1984 amendment, "orphan drugs" were defined as medicines which treat diseases or conditions affecting fewer than 200,000 patients in the U.S.

As its most potent stimulus, the ODA provides seven years of market exclusivity for any drug that the FDA designates as an orphan product and approves for marketing. The FDA can confer this protection on compounds not patented, or on those for which the patent has already expired.

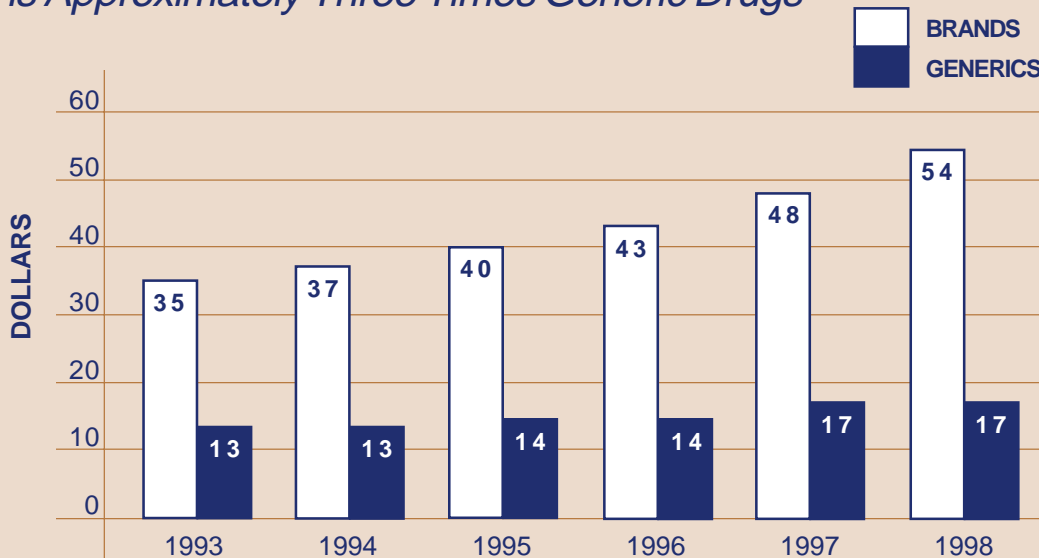
By March 2000, the FDA had approved 201 orphan products. The majority alleviate suffering and do not generate high sales or profits for their sponsors.<sup>26</sup> In a few cases, however, manufacturers have been able to use market exclusivity to support high prices for medicines achieving blockbuster sales. This has occurred when the drugs

FIGURE 7  
*Generic Drugs Market Share in Dollars is Low and Declining*



SOURCE: IMS Health from Generic Pharmaceutical Industry Association

FIGURE 8  
*Average Price Per Prescription for Brand Name is Approximately Three Times Generic Drugs*



SOURCE: IMS Health from Generic Pharmaceutical Industry Association



were found to be effective treatments for prevalent diseases or when the targeted patient population expanded, as in the case of the AIDS epidemic. Some believe that lack of a mechanism to withdraw market exclusivity after the drug reaches a certain threshold of sales or profits has resulted in consumers' paying higher prices for drugs than necessary.<sup>27</sup> Further, market exclusivity may be used to support monopolistic pricing of drugs developed at public expense.

**The Federal Technology Transfer Act of 1986**

A series of laws ensures that inventions discovered in federal laboratories are assigned to the private sector for commercial development. In 1986, the Federal Technology Transfer Act authorized federal laboratories to enter into formal cooperative research and development agreements (CRADAs) with private industry. As a collaborator with federal partners on an invention, the pharmaceutical industry has been able to use CRADAs to secure exclusive rights to federal technology.

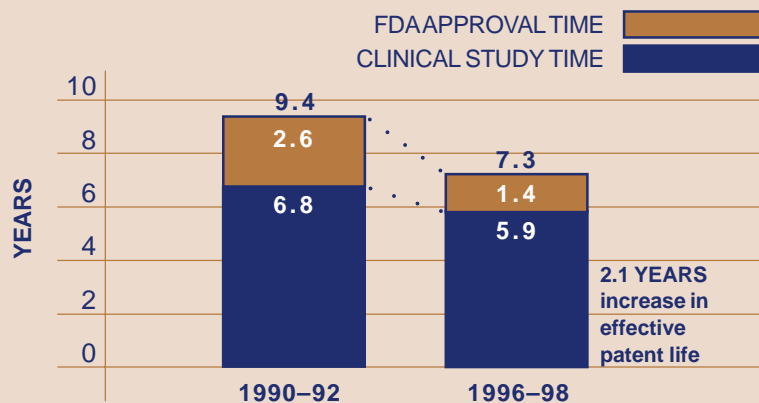
From 1993 to 1999, the National Institutes of Health (NIH) executed a total of 619 CRADAs.<sup>28</sup> Of these, 515 occurred after 1995 when NIH repealed a requirement for a "reasonable pricing clause" on the view that it was discouraging industry interest in CRADAs. This policy had required that products developed in part through research at NIH should reflect a "reasonable relationship between the pricing of the licensed product, the public investment in the product, and the health and safety needs of the public."<sup>29</sup>

In recent years, some have expressed concern that without a reasonable pricing clause, CRADAs do not protect public investment in research and may enable companies to reap high profits from advanced technology developed partly at public expense. For example, a 1994 study found that half of the 30 clinically most important drugs approved by the FDA from 1987 to 1991 had federal support at some stage of their development, and 11 had federal support at every stage. Moreover, the median wholesale cost of the new drugs developed with federal funding was \$4,854, almost three times the price (\$1,626) for drugs developed without federal support.<sup>30</sup>

Taxol, Bristol-Myers Squibb's (BMS) treatment for breast and ovarian cancer, has become a controversial illustration of how the private sector profits from federally developed technology as well as makes use of orphan drug market exclusivity. NIH discovered and developed Taxol in the 1970s and 1980s. In 1991, NIH entered into a CRADA with BMS with a view to bringing this important new cancer drug to market and granted BMS exclusive rights to all NIH funded research on Taxol. In March 1997, BMS was able to

obtain orphan drug approval of Taxol as a treatment for Kaposi's sarcoma, an AIDS related disease. As a result, it received seven years of market exclusivity

FIGURE 9  
*Effect of PDUFA and FDAMA on Development Time for NMEs*



**PDUFA:** The Prescription Drug User Fee Act  
**FDAMA:** The Food and Drug Administration Modernization Act  
**NMEs:** New Molecular Entities

SOURCE: Tufts CSDD 2000; FDA 2000

FIGURE 10  
*Top Selling Brand Name Drugs with Patents Expiring 2000-2005*

BRAND NAME	PATENT EXPIRES	1998 U.S. SALES	COMMENTS
VASOTEC (Hypertension)	2/22/00	\$1.0 billion	• Recently received 6 months of pediatric exclusivity from FDA
PROZAC (Depression)	2/2/01	\$2.3 billion	• Patent on "purified" form expires in 2015
PRILOSEC (Ulcers)	4/01/01	\$2.9 billion	• Dominant drug with 44% of 1998 sales in therapeutic class
CLARITIN (Allergies)	4/21/04	\$1.8 billion	• Patent on "purified" form expires in 2014
PRAVACHOL (Cholesterol)	10/20/05	\$1.0 billion	• Accounted for almost a fifth of 1998 sales in therapeutic class
ZOCOR (Cholesterol)	12/24/05	\$2.2 billion	• Accounted for 30% of 1998 sales in therapeutic class

SOURCE: Generic Pharmaceutical Industry Association; NIHCM Foundation analysis of data provided by the Barents Group LLC; Merck 1999 Annual Report

for Taxol and has been able to use this protection to keep generic copies off the U.S. market.<sup>31</sup>

Today, the typical course of treatment for breast cancer runs \$20,000; for ovarian cancer, the cost is \$10,000.<sup>32</sup> In 1999, Bristol-Myers Squibb had sales of \$1.5 billion from Taxol.<sup>33</sup>

## Cumulative Effects of Changes in IPP Law

Although no research has assessed the cumulative impact of the numerous increases in IPP afforded pharmaceuticals, it is possible to make a rough and qualified estimate from available sources.

New drugs that were approved between 1980–1984 had effective patent lives of only 8.1 years, with no possibility of reformulating the drug to take advantage of market exclusivity provisions.

By contrast, new molecular entities approved in the late 1990s typically benefited not only from extensions under Waxman-Hatch, but also from the combined consequences of PDUFA and FDAMA. Assuming a “base” effective patent life before extensions of 9.5 years, as indicated by the Duke University study mentioned above, it appears that some new drugs approved in the late 1990s could expect to add 4.4 to 5.9 years to their effective patent lives, for a total of 13.9 to 15.4 years.

To determine how a drug company would have extended the life of a product, one must apply the various laws granting patent term extensions and market exclusivity. Accordingly, these drugs will receive a combined increase in their effective patent lives due to the following:

- Under Waxman-Hatch: these drugs could obtain patent extensions averaging 2.3 years;<sup>34</sup>

# CLARITIN AND IPP

A NEW FORM  
OF CLARITIN  
WILL ENJOY  
INTELLECTUAL  
PROPERTY  
PROTECTION  
UNTIL 2014

Claritin, an oral antihistamine, has enjoyed spectacular success in the U.S. market with sales topping \$1.9 billion last year. Schering-Plough Corporation, the drug’s manufacturer, has achieved this success through product innovation, extensive promotion and aggressive pricing:

- In 1998, Schering-Plough spent approximately \$267 million to promote the drug to American consumers and doctors;<sup>1</sup>
- Americans pay almost four times as much for Claritin as Canadians (\$1.94 versus \$.54 per pill) who purchase it over the counter, as do many Europeans.<sup>2</sup>

To defend this lucrative franchise, Schering-Plough has found numerous ways to extend intellectual property protection on new uses of Claritin for the next 14 years. The following illustrates both the range and the cumulative impact of IPP afforded branded drugs:

### ACQUIRED OR LICENSED PATENTS ON DIFFERENT COMPOUNDS

- In 1981, Schering-Plough acquired a patent on loratadine, the active ingredient in Claritin. The loratadine patent was due to expire in August 1998 but has been extended twice (see sequence of events below.)
- When humans take loratadine, the body produces descarbethoxylopratadine or DCL, the principal active metabolite of loratadine. In 1987, Schering-Plough was granted a patent on a form of DCL which expires in 2004.
- Schering-Plough has licensed patent rights from Massachusetts based Sepracor Inc. on desloratadine, a purified form of DCL. Desloratadine is the active ingredient in a new product, commonly referred to as “super Claritin.” The desloratadine patent will not expire

until 2014. The FDA will probably approve “super Claritin” this year, giving the company two years to persuade doctors to switch their patients to it from Claritin before the loratadine patent expires in 2002. If Schering-Plough is successful, the franchise will be protected for an additional 12 years.

### OBTAINED MULTIPLE PATENT EXTENSIONS

- Under Waxman-Hatch, Schering-Plough sought and received its first extension for two years on the loratadine patent, thus moving its expiration date to August 2000.
- The company also obtained a second extension for 22 months under URAA, which moved the expiration date forward again to June 2002. Thus, loratadine has benefited from almost four years (46 months) in patent extensions and enjoys a patent life of 21 years.<sup>3</sup>

### LOBBIED FOR FUTURE PATENT EXTENSIONS

- Over the past few years, Schering-Plough has continued to urge Congress to pass specific legislation to extend loratadine’s patent even further. Even if such attempts fail, the company can still count on the desloratadine patent to protect a form of Claritin until 2014.

1. “U.S. Pharmaceutical Industry Spent More than \$5.8 Billion on Product Promotion in 1998: Direct to Consumer Advertising Expenditures Exceed \$1.3 Billion,” accessed June 27, 2000 from <http://www.imshealth.com>.

2. “Why Allergy Drugs Cost So Much,” *USA TODAY* (April 12, 2000):1.

3. Generic Pharmaceutical Industry Association, “Claritin Patent Extension Chronology,” accessed from <http://www.gpia.org>.

- From PDUFA and FDAMA: on average, the drugs received an additional 2.1 years in effective patent life<sup>35</sup> (**See Figure 9**);
- Under URAA: drugs which qualified would have received an extension averaging one year;<sup>36</sup>
- Under FDAMA: some pharmaceuticals may have been granted six months of pediatric exclusivity.<sup>37</sup>

The second step is to estimate how a company might utilize market exclusivity to protect a new generation of its product. Thus, if a manufacturer timed the introduction of a new use, such as a more convenient dosing form, to coincide with the expiration of the “mother” drug’s patent, it could have shielded the 13.9 to 15.4 year franchise of the drug for an additional three years, for as long as 17 to 18 years overall (**See Figure 1**). During the final few years, generic manufacturers could bring copies of the “mother” drug to market, but would be barred from competing against the new use.

## Conclusion

The laws described above have greatly strengthened the intellectual property protection of branded drugs and facilitated the transfer of federal inventions to the private sector. Notwithstanding the efforts of Waxman-Hatch to balance innovation with expanded access to affordable medicine, increasing intellectual property protection has delayed the entry of some generic drugs into the U.S. market and forced consumers to incur billions of dollars in drug costs that they otherwise may not have paid. More affordable medications would be particularly welcomed by most uninsured Americans, who are keenly aware of the high cost of drugs.

Further, the effect of intellectual property protection on the quality as well as the quantity of innovation deserves examination. Since the overwhelming majority of pharmaceutical research and development efforts end in dry holes, costs must be covered by the rare “blockbuster” drug that emerges from a wide portfolio of projects. Making incremental improvements to a blockbuster and obtaining additional patent life or market exclusivity protection is a relatively safe way to maximize profits. Whether the increasing costs of prescription drugs are being proportionally rewarded by private sector efforts to bring significant new technology to market is not clear.

Policy makers must consider the sort of innovation it is in the public interest to reward. John H. Barton of the Stanford University Law School recently argued for patent reform, noting that “There is no economic value in conferring a patent monopoly except for an invention that will have a significant impact.”<sup>38</sup>

## References

1. U.S. Food and Drug Administration, “NDAs Approved in Calendar Years 1990–1999 by Therapeutic Potentials and Chemical Types,” (February 15, 2000). Accessible at <http://www.fda.gov>.
2. Alice Dember and the Boston Globe Spotlight Team, “Public Handouts Enrich Drug Makers, Scientists,” *The Boston Globe* (April 5, 1998), accessed March 18, 2000 from <http://www.boston.com>.
3. NIHCM analysis of Scott-Levin data derived from audits of 1998 retail prescription drug sales. This data was collected and prepared by the Barents Group LLC.
4. Congressional Budget Office, *How Increased Competition from Generic Drugs Has Affected Returns in the Pharmaceutical Industry* (Washington, D.C.: Congressional Budget Office, July 1998). This report may be accessed from <http://www.cbo.gov>.
5. Generic Pharmaceutical Industry Association, “Prescription Drug Facts and Figures” prepared by IMS Health. Accessible at <http://www.gpia.org>.
6. Stephen W. Schondelmeyer, Pharm.D., Ph.D., “Patent Extensions of Pipeline Drugs: Impact on U.S. Health Care Expenditures,” (PRIME Institute, College of Pharmacy, University of Minnesota: Minneapolis, Minnesota: July 1999). This analysis can be accessed from <http://www.house.gov/berry/prescriptiondrugs/schondelemeyer>.
7. Generic Pharmaceutical Industry Association 2000. Accessible at <http://www.gpia.org>.
8. Cf. M. Eisman and W. Wardell, “The decline in effective patent life of new drugs,” *Res Management*, Vol. 21, 1981: 14–18; and K.I. Kaitin and A.G. Trimble, “Implementation of the Drug Price Competition and Patent Term Restoration Act of 1984: A Progress Report,” *J Clin Res Drug Devel*, Vol. 1, 1987: 263–275.
9. 21 U.S.C. § 355(j)(4)(D)(ii),(iii).
10. Henry Grabowski and John Vernon, “Longer Patents for Increased Generic Competition in the US: The Waxman-Hatch Act After One Decade,” *PharmacoEconomics*, Vol. 10, Supplement 2 (1996): 110–123.
11. Generic Pharmaceutical Industry Association, “Prescription Drug Facts and Figures,” accessed June 21, 2000 from <http://www.gpia.org>. The market share data was prepared by IMS Health.
12. Cf. Stephen W. Schondelmeyer, Pharm.D., Ph.D., “Patent Extensions of Pipeline Drugs: Impact on U.S. Health Care Expenditures” and also Congressional Budget Office, *How Increased Competition from Generic Drugs Has Affected Returns in the Pharmaceutical Industry* (Washington, D.C.: Congressional Budget Office, July 1998). This report may be accessed from <http://www.cbo.gov>.
13. Public Law No. 103–465, 108 Stat. 4809 (1994).
14. 35 U.S.C. § 154(a)(2)(Supp. 1996).
15. 35 U.S.C. § 154(c)(1).
16. Cf. *DuPont Merck Pharmaceutical Co. v. Bristol-Myers Squibb Co.*, 62 F.3d 1397 (Fed. Cir. 1995) and *Bristol Myers Squibb Co. v. Royce Laboratories, Inc.*, 69 F.3d 1130 (Fed. Cir. 1995). Cf. also discussion in Peter O. Safir and Scott M. Lassman, “GATT Implementation and Generic Drug Approval,” *Food and Drug Law Journal*, Vol. 51, No. 2 (1996): 295–302.
17. Stephen W. Schondelmeyer, Pharm.D., Ph.D., “Economic Impact of GATT Patent Extension on Currently Marketed Drugs” (PRIME Institute, College of Pharmacy, University of Minnesota: Minneapolis, Minnesota: March 1995).
18. Cf. Sen. John Chafee and Sen. David Pryor, “Congress Should Not Squander Chance to Right Previous Wrong in GATT Legislation,” (1996) accessed November 19, 1998 from <http://www.rollcall.com>.

*“There is no economic value in conferring a patent monopoly except for an invention that will have a significant impact.”*

*John H. Barton  
Stanford University  
Law School*

*Between  
1990-1999,  
50 percent of  
drugs approved  
were either new  
formulations or  
new combinations  
of drugs already  
on the market.*



**NIHCM**  
FOUNDATION

1225 19th Street, NW  
Suite 710  
Washington, DC 20036  
TEL 202.296.4426  
FAX 202.296.4319  
WEB [www.nihcm.org](http://www.nihcm.org)

19. Cf. discussion in Peter O. Safir *et al.*

20. Food and Drug Administration, Center for Drug Evaluation and Research, *Improving Public Health Through Human Drugs, 1999 Report to the Nation*: 8–9. Accessed June 21, 2000 from <http://www.fda.gov>.

21. Tufts Center for the Study of Drug Development, "Clinical development times for new drugs drop 18%, reversing 12-yr trend," *Tufts CSDD Impact Report*, Volume 1 (July 1999): 1–3. Accessed June 18, 2000 from <http://www.tufts.edu/med/research/csdd>.

22. *Ibid.*

23. Tufts Center for the Study of Drug Development, "Drug firms embrace pediatric study program during first 2 years of FDAMA," *Tufts CSDD Impact Report*, Volume 2 (April 2000): 2. Accessed June 18, 2000 from <http://www.tufts.edu/med/research/csdd>.

24. The trade names of these drugs are: Losec; Prozac; Vasotec; Prilosec; Norvasc; Claritin; Zolof; Paxil; Cipro; Mevacor; Imitrex; and Zestril. Of this group, Losec, Prozac, Vasotec, Prilosec, Mevacor and Zestril are facing patent expiration in 2000 or 2001. Cf. Tufts Center for the Study of Drug Development, "Drug firms embrace pediatric study program during first 2 years of FDAMA," *Tufts CSDD Impact Report*, Volume 2 (April 2000): 3.

25. Tufts Center for the Study of Drug Development, "Clinical development times for new drugs drop 18%, reversing 12-yr trend," *Tufts CSDD Impact Report*, Volume 1 (July 1999): 1–3.

26. Cf. S.R. Shulman, B. Bienz-Tadmor, P.S. Seo *et al.*, "Implementation of the Orphan Drug Act," *Food and Drug Law Journal*, Vol. 47 (1992): 363–403.

27. Cf. Peter S. Arno, Karen Bonuck and Michael Davis, "Rare Diseases, Drug Development and AIDS: The Impact of the Orphan Drug Act," *The Milbank Quarterly*, Vol. 73, No. 2 (1995).

28. NIH, "NIH Technology Transfer Activities, FY 1993–FY 1999," accessed March 9, 2000 from <http://www.nih.gov/od/nih93-99>.

29. Cf. "Frequently Asked Questions about HR 626, the 'Health Care Research and Development and Taxpayer Protection Act,'" accessed March 17, 2000 from <http://www.cptech.org/ip/health/econ/rp-faq>. Cf. also "PHS/NIH Abandons 'Reasonable Pricing' Licensing/CRADA Policy," *Antiviral Agents Bulletin* (April 1995): 106–107. Accessed March 9, 2000 from <http://www.bioinfo.com/reasprice>.

30. James Love, "Prepared Statement of James Love, Center for the Study of Responsive Law, Taxpayer Assets Project, Before the Subcommittee on Health and the Environment of the Committee on Energy and Commerce, U.S. House of Representatives, on Prescription Drug Benefits and the Clinton Health Care Plan," February 8, 1994. Accessed March 1, 2000 from <http://www.cptech.org/pharm/waxman>.

31. James Love, "Paclitaxel (Taxol) Time-Line, version 1.0" (December 8, 1998) and "Health Registration Data Exclusivity, Biomedical Research, and Restrictions on the Introduction of Generic Drugs, Statement of James P. Love, Consumer Project on Technology, before the Subcommittee on Labor, Health and Human Services and Education and Related Agencies, Committee on Appropriations, U.S. Senate, October 21, 1997." Accessed June 18, 2000 from <http://www.cptech.org>.

32. Li Fellers, "The Medicine Market; Taxol is One of the Best Cancer Drugs Ever Discovered by the Federal Government. Why Is It Beyond Some Patients' Reach?" *The Washington Post* (May 31, 1998): W10. Accessed May 3, 2000 from <http://www.washingtonpost.com>.

33. Bristol-Myers Squibb, *1999 Annual Report*, accessed June 21, 2000 from <http://www.bms.com>.

34. Henry Grabowski and John Vernon, "Longer Patents for Increased Generic Competition in the US: The Waxman-Hatch Act After One Decade," *PharmacoEconomics*, Vol. 10, Supplement 2 (1996): 110–123.

35. Tufts Center for the Study of Drug Development, "Clinical development times for new drugs drop 18%, reversing 12-yr trend," *Tufts CSDD Impact Report*, Volume 1 (July 1999): 1–3. Accessed June 18, 2000 from <http://www.tufts.edu/med/research/csdd>.

36. Stephen W. Schondelmeyer, Pharm.D., Ph.D., "Economic Impact of GATT Patent Extension on Currently Marketed Drugs" (PRIME Institute, College of Pharmacy, University of Minnesota: Minneapolis, Minnesota: March 1995).

37. Tufts Center for the Study of Drug Development, "Drug firms embrace pediatric study program during first 2 years of FDAMA," *Tufts CSDD Impact Report*, Volume 2 (April 2000): 2. Accessed June 18, 2000 from <http://www.tufts.edu/med/research/csdd>.

38. John H. Barton, "Reforming the Patent System," *Science*, Vol. 287 (March 17, 2000): 1933.

## A PUBLICATION OF THE NIHCM FOUNDATION

### About The NIHCM Foundation

The National Institute for Health Care Management Research and Educational Foundation is a non-profit organization whose mission is to promote improvement in health care access, management and quality.

### About This Issue Brief

This brief was written by Michie I. Hunt, Ph.D., a Washington D.C.-based independent consultant who specializes in pharmaceutical industry research and policy analysis, in collaboration with Linda Kotis, J.D., and Nancy Chockley, M.B.A., of the NIHCM Foundation.

For another relevant NIHCM Foundation publication, see *Factors Affecting the Growth of Prescription Drug Expenditures* — a study conducted by The Barents Group, LLC and released in July 1999. This widely cited report explains why prescription drug spending has been rising at double digit rates in recent years.