

COMMENT

THE HATCH-WAXMAN SYSTEM: SUFFERING A
PLAGUE OF BAD BEHAVIOR*

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* 2005 J.D. Candidate from the University of Houston Law Center; M.S. in Chemical Engineering from University of Tulsa; M.S. in Chemistry from Oklahoma State University; B.S. in Chemistry and B.S. in Mathematics from University of North Dakota. She worked for fifteen years in research and development. This paper was selected for the 2004 Writing Award for Distinguished Paper in Intellectual Property. This paper is dedicated to the author's husband, Jeffrey, and son, Dustin.

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I. INTRODUCTION

In 1984, Congress passed the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act.¹ The Amendments sought to strike a balance between two conflicting policy objectives: inducing pioneer drug companies to invest in the research, development and approval of new prescription drugs, while simultaneously encouraging generic manufacturers to market cheaper, generic copies of those drugs. Twenty years later, the Hatch-Waxman system is out of balance due to the aggressive manipulation by the health care industry.

1. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended at 35 U.S.C. §§ 271(e), 156 (2000) and 21 U.S.C. § 355(j) (2000)). The Hatch-Waxman Act is named for its congressional sponsors.

This article explores the abuses of the Hatch-Waxman Act system. It explains the operation of the three-part system in today's health care market. Both pioneer drug companies and generic manufacturers seek to increase their drug profits through aggressive, legal, and sometimes illegal strategies. In December 2003, Congress passed the Medicare, Prescription Drug Improvement, and Modernization Act of 2003, which includes provisions to tighten the loopholes of the Hatch-Waxman system and expedite generic market entry.² This article discusses those recent changes.

II. CURRENT ECONOMIC SITUATION

In the United States, many people have shifted from conventional to managed care plans as a result of an increasingly competitive market for health insurance.³ Managed care plans have a competitive advantage because they negotiate better rates from doctors, hospitals, and other health care providers.⁴ An important trend in most health care plans, including conventional plans, is the management of outpatient prescription drug benefits through pharmaceutical benefit management companies or (PBMs).⁵ PBMs are an important intermediary in limiting drug costs because 60% of prescription drugs are sold through pharmacies and other retail outlets.⁶ Having considerable leverage, PBMs negotiate lower prices from both manufacturers and pharmacies.⁷

2. Medicare, Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003); see also S. 1225, 108th Cong. (2003), available at <http://thomas.loc.gov/home/c108query.html>.

3. CONG. BUDGET OFFICE STUDY, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 5 (1998), available at <http://www.cbo.gov/showdoc.cfm?index=655&sequence=0> [hereinafter CONG. BUDGET OFFICE STUDY 1998]. According to the Bureau of Labor Statistics, the proportion of full-time employees with health insurance who were enrolled in managed care plans increased from approximately 26% in 1988 to 61% in 1995. *Id.* (citing Press Release, Dept. of Labor, Bureau of Labor Statistics, *BLS Reports on Employee Benefits in Medium and Large Private Establishments 1995* (July, 25, 1997), available at <http://stats.bls.gov/special.requests/ocwc/oct/ebs/ebnr0003.txt>).

4. CONG. BUDGET OFFICE STUDY 1998, at 5.

5. *Id.* at 6.

6. *Id.*

7. *Id.* PBMs also negotiate rebates from brand-name manufacturers based on their ability to direct their members toward a particular drug by using a formulary. *Id.* at 6-7. Using a computerized network, a pharmacist checks the plan's list of preferred drugs as a guide in filling the prescription. *Id.* at 7. Such lists often require substitution of a generic drug for a brand-name drug or suggest substitution of a lower-cost brand-name drug. *Id.* The patient's physician must approve any substitution between brand-name drugs. *Id.*

A. *Changing Drug Market*

In the next couple of years, the pharmaceutical industry will be undergoing significant change.⁸ The driving forces are the patent expirations of blockbuster brand-name drugs, the presence of managed-care and cost-containment programs throughout the United States, and the number of prescriptions being filled with lower-cost generic drugs.⁹ Considering generic drug sales can account for 50% of drug sales within six months of generic introduction, the following table illustrates the huge incentives to manipulate the Hatch-Waxman system.¹⁰ Since the adoption of the act, the generic share has grown to approximately 50% of the domestic prescription drug market.¹¹ The generic market is projected to grow 9.8% annually and anticipated to reach \$43 billion in 2003.¹²

8. Stephanie E. Piatt, Note, *Regaining the Balance of Hatch-Waxman in the FDA Generic Approval Process: An Equitable Remedy to the Thirty-Month Stay*, 59 N.Y.U. ANN. SURV. AM. L. 163, 181 (2003) (citing Ron Winslow & Barbara Martinez, *Efforts to Switch Patients to Generic Prozac Advance*, WALL ST. J., Aug. 20, 2001, at A3).

9. Taren Grom, *Generics: Best Years to Come*, MED. AD. NEWS, Oct. 1, 1999, at 1.

10. Piatt, *supra* note 8, at 181-82 (citing Frank Scussa, *Patent Games*, MED. AD. NEWS, June 1, 2002, at 1) (table partially provided below).

Drug Brand-Name	Pioneer Company	Patent Expiration	Global Sales, 2001 (Millions)
DIFLUCAN	Pfizer	Jan. 2004	1,066
PARAPLATIN	Bristol-Meyers Squibb	Apr. 2004	702
XENICAL	Roche Labs.	Jun. 2004	570
LAMISIL	Novartis Pharms.	Jul. 2004	832
LIPRON	Tap Pharm.	Oct. 2004	833
LOVENOX	Aventis Pharms.	Dec. 2004	1,301
BIAXIN	Abbott Labs.	May 2005	1,159
ZOFRAN	GlaxoSmithKline	Jun. 2005	865
PREVACID	Tap Pharm.	Jul. 2005	2,951
AREDIA	Novartis Pharms.	Aug. 2005	752
ZOLADEX	AstraZeneca	Sep. 2005	728
PRAVACHOL	Bristol-Meyers Squibb	Dec. 2005	2,173
ZOCOR	Merck & Co.	Dec. 2005	6,670
ZOLOFT	Pfizer	Dec. 2005	2,366
Total			22,968

11. PHARM. RES. & MFRS. OF AM., PhRMA INDUSTRY PROFILE 61-62 (2003), available at <http://www.phrma.org/publications/publications/profile02/index.cfm> [hereinafter PhRMA INDUSTRY PROFILE 2003].

12. Grom, *supra* note 9, at 1.

B. Managed-Care and Cost-Containment Programs

Both public and private policy makers are striving to contain rising health-care costs. A “major—and disproportionate—focus of their efforts emphasizes strategies to control prescription drug costs.”¹³ In the United States, “90 cents of every dollar spent on health care is on items other than prescription drugs.”¹⁴ The 10 cents spent on prescription medicines includes brand-name drugs, generic copies, pharmacy services and distribution-chain costs.¹⁵

As prescription drug usage has increased, medical “plans have relied increasingly on the use of pharmacy benefit managers, or PBMs, to manage prescription drug programs.”¹⁶ These cost-containment “tools include drug utilization review, generic substitution, prior authorization, step-care protocols, therapeutic interchange, restrictive formularies, and three-tier co-payment structures.”¹⁷ Today, about 92% of HMOs and 78% of PPOs manage their outpatient prescription drug benefits.¹⁸

Another cost-control strategy focuses on the beneficiaries’ out-of-pocket payments for prescription drugs.¹⁹ “[S]ome insurance companies. . . are launching aggressive plans to switch consumers from brand-name to generic drugs.”²⁰ They are seeking to increase their profits by spending less on prescription drugs.²¹ The most common approach is to require various co-payments for different groups of prescription drugs.²² In a three-tier formulary, patients would pay one price for generic drugs, a higher price for some brand-name drugs, and an even higher price for the remaining brand-name drugs.²³ About 2% of plans

13. PhRMA INDUSTRY PROFILE 2003, *supra* note 11, at 42.

14. *Id.* (citing CTRS. FOR MEDICARE AND MEDICAID SERVS., THE NATION’S HEALTH DOLLAR: 2001 (Jan. 8, 2003), available at <http://cms.hhs.gov/statistics/nhe/historical/chart.asp>).

15. *Id.*

16. *Id.*

17. *Id.*

18. *Id.* (quoting KAISER FAMILY FOUND. AND HEALTH RESEARCH AND EDUC. TRUST, EMPLOYER HEALTH BENEFITS: 2002 ANNUAL SURVEY (Menlo Park, Cal.: KFF and HRET, 2002)).

19. PhRMA INDUSTRY PROFILE 2003, *supra* note 11, at 42.

20. Piatt, *supra* note 8, at 183 (citing David Barkholz, *Blue’s Plan’s Ad Campaign Touts Generic Drugs*, BUS. INS., Aug. 27, 2001, at 14).

21. *Id.* (citing Ron Winslow & Barbara Martinez, *Efforts to Switch Patients to Generic Prozac Advance*, WALL ST. J., Aug. 20, 2001, at A3). According to Blue Cross, switching a mere 3% of its Michigan customer’s prescriptions to generic drugs would save the company approximately \$100 million. Ron Winslow & Barbara Martinez, *Efforts to Switch Patients to Generic Prozac Advance*, WALL ST. J., Aug. 20, 2001, at A3.

22. PhRMA INDUSTRY PROFILE 2003, *supra* note 11, at 42.

23. *Id.*

are instituting a fourth tier requiring patients to pay a percentage of the retail cost of specified brand-name drugs.²⁴

C. Disease Management Programs

The health-care plans have begun using disease management programs to improve patient care and reduce treatment costs.²⁵ Disease management programs are “especially important for chronic, expensive conditions such as asthma, diabetes, and congestive heart failure.”²⁶ Nearly “1.5 million people in the United States are covered by disease management programs,” according to the Tufts Center for the Study of Drug Development.²⁷

“In a survey of HMO medical directors, 67[%] believed disease management program lower costs, and 96[%] believed the programs reduced morbidity and mortality.”²⁸ In a study of 1100 patients with congestive heart failure, the “pharmacy costs increased by 60[%], while the hospital costs decreased by 78[%]. The net savings were \$9.3 million.”²⁹ Contrary to popular opinion, increased spending on prescription drugs for treatment of chronic conditions reduces overall healthcare cost.³⁰

D. Prescription Drug Sales

The mail-order sales represent 12% of the total domestic prescription drug sales.³¹ They have doubled from \$10.4 billion in 1998 to \$20.7 billion in 2001.³² This growth is due to pharmacy benefit managers (PBMs) urging their consumers to order prescriptions by mail.³³ A distributor supplies the prescription drug at prices that are less expensive for the consumer and the PBM’s client (such as an employer).³⁴ The PBM has an incentive

24. *Id.*

25. *Id.* at 43.

26. *Id.*

27. *Id.* (citing *Disease Management Cuts Inpatient Costs via Greater Drug Spending*, 4:2 IMPACT REPORT (2002)).

28. PhRMA INDUSTRY PROFILE 2003, *supra* note 11, at 44 (citing W.P. Welch ET AL., *Disease Management Practices of Health Plans*, 8:4 AM. J. MANAGED CARE 353-61 (2002)).

29. *Id.* (citing *Provide Education About Congestive Heart Failure and Pump Up Your Savings*, 8:4 MANAGED HEALTHCARE 42-44 (1998)).

30. *Id.* at 31.

31. NAT’L INST. FOR HEALTH CARE MGMT., A PRIMER: GENERIC DRUGS, PATENTS AND THE PHARMACEUTICAL MARKETPLACE 24, (2002), available at <http://www.nihcm.org/pharm.htm> [hereinafter NAT’L INST. 2002].

32. *Id.*

33. *Id.*

34. *Id.*

to encourage the sale of brand-name drugs over generics because brand-name drugs net larger rebates, which is a major source of PBM revenue.³⁵ In addition, consumers with chronic conditions are more likely fill the same prescription repeatedly because they will not have access to a pharmacist who might recommend the generic alternative.³⁶ The “brick and mortar” pharmacies have financial incentives to switch patient to generics because the retail mark-up is higher for generic than brand-name drugs.³⁷ As a result, the chain stores fill approximately 50% of prescriptions with generics while the mail-order stores fill only 28%.³⁸

III. DRUG DEVELOPMENT COSTS

A. *Research and Development Risks*

Pharmaceutical companies gamble their profits in the research, development and approval of new prescription drugs. It takes ten to fifteen years to bring a new drug from concept to market.³⁹ The lengthy process “reflects the greater complexity of target diseases,⁴⁰ the longer clinical trials required by the Food and Drug Administration (FDA), and the medical system’s growing demand for more complex data on new drugs.”⁴¹ As a result, the “average cost to develop a new drug has grown from \$138 million in 1975 to \$802 million in 2000.”⁴²

The risks involved in developing new prescription drugs are substantial.⁴³ As scientific pioneers, pharmaceutical researchers suffer failure more often than they enjoy success.⁴⁴ Of 5,000 to 10,000 screened compounds, only 250 enter pre-clinical testing, five enter clinical testing and one is approved by the FDA.⁴⁵ The pharmaceutical companies need to develop highly profitable drugs not only to recover the development costs of the successful

35. *Id.*

36. *Id.* at 24-25.

37. NAT’L INST. 2002, *supra* note 31, at 25.

38. *Id.*

39. PHARMA INDUSTRY PROFILE 2003, *supra* note 11, at x, 2-3.

40. *Id.* at x, 3-4 (citing data from Center for the Study of Drug Development, Tufts University, 1995).

41. *Id.*

42. *Id.* (citing J.A. DiMasi, R.W. Hansen, & H.G. Grabowski, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151-185 (2003)).

43. *Id.* at 3.

44. *Id.*

45. PHARMA INDUSTRY PROFILE 2003, *supra* note 11, at 3.

drug but also to recover the costs of the numerous unsuccessful drugs.⁴⁶

A recent Congressional Budget Office Committee evaluated the return on investment of sixty-seven proprietary drugs.⁴⁷ Of these drugs, the “top six collectively earned \$1 billion, but only the top twenty earned enough to exceed the average cost of . . . development of a single new drug.”⁴⁸ Statistics demonstrate only one of three new drugs actually earns a profit in the current market.⁴⁹ Many drugs are not profitable as a result of increased development costs, shorter effective patent terms, and risk of liability.⁵⁰

B. Food and Drug Administration Approval

One factor distinguishing prescription drugs from other products is the FDA’s requirements established by the Federal Food, Drug and Cosmetic Act (FFDCA).⁵¹ Prior to marketing a new prescription drug, the pharmaceutical company must obtain FDA approval.⁵² To obtain FDA approval, the pharmaceutical company must complete extensive testing on its new prescription drug.⁵³ The applicant must generate drug data including the chemical structure, safety, efficacy, and toxicology analyses in vitro and in animals.⁵⁴

46. Mandy Wilson, Note, *Pharmaceutical Patent Prosecution: More Generic Favored Legislation May Cause Pioneer Drug Companies to Pull the Plug on Innovation*, 90 KY. L.J. 495, 498-99 (2002) (citing CONG. BUDGET OFFICE STUDY, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 48, (1998)).

47. *Id.* at 499.

48. *Id.*

49. PhRMA INDUSTRY PROFILE 2003, *supra* note 11, at 3 (citing H. Grabowski ET AL., *Returns on Research and Development for 1990s New Drug Introductions*, 20 PHARMACOECONOMICS Supp. 3, 11-29 (2000)); *see also* Wilson, *supra* note 46, at 499 (citing CONG. BUDGET OFFICE STUDY 1998, at 45).

50. *See, e.g.*, PhRMA INDUSTRY PROFILE 2003, *supra* note 11, at 3 (citing H. Grabowski, J. Vernon, and J. DiMasi, *Returns on Research and Development for 1990s New Drug Introduction*, 20 PHARMACOECONMICS Supp. 3, 11-29 (2000)).

51. Federal Food, Drug, and Cosmetics Act, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301-395 (2000)).

52. 21 U.S.C. § 355(a) (2000). “No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application...is effective with respect to such drug.” *Id.*

53. W. Kip Viscusi ET AL., *Deterring Inefficient Pharmaceutical Litigation: An Economic Rationale for the FDA Regulatory Compliance Defense*, 24 SETON HALL L. REV. 1437, 1442-43 (1994).

54. 21 C.F.R. § 312.23 (2003).

1. Clinical Trials of New Prescription Drugs

The FDA may request further testing or allow the clinical trials to begin.⁵⁵ The Phase 1 trials are “designed to determine the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.”⁵⁶ These trials involve giving different dosages of the new drug to twenty to eighty “ill patients whose disease is the target of the particular new chemical.”⁵⁷ The Phase 2 trials designed to demonstrate the drug’s effectiveness in treating the target condition and determine common short-term side effects of the drug.⁵⁸ The second phase is conducted on “several hundred patients for the clinical effectiveness of the drug.”⁵⁹ Lasting one to four years, the Phase 3 trials determine the overall effectiveness of the new drug.⁶⁰ The final clinical trials involve a much larger population of adults having the targeted condition.⁶¹

2. New Drug Applications

After the completion of the Phase 3 trials, the pharmaceutical company files a New Drug Application (NDA) with the FDA.⁶² An NDA “include[s] detailed reports of all animal studies and clinical testing done with the drug, reports of any adverse reactions, and any other pertinent information from worldwide scientific literature.”⁶³

55. Viscusi, *supra* note 53, at 1443.

56. 21 C.F.R. § 312.21(a)(1) (2003); *see also* Viscusi, *supra* note 53, at 1443.

57. 21 C.F.R. § 312.21(a)(1); *see also* Ronald L. Desrosiers, *The Drug Patent Term: Longtime Battleground in the Control of Health Care*, 24 NEW ENG. L. REV. 115, 120 (1989).

58. 21 C.F.R. § 312.21(b). Phase 2 trials “include[] the controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug.” *Id.*

59. Desrosiers, *supra* note 57, at 120.

60. 21 C.F.R. § 213.21(c). Phase 3 trials are “intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall [risk-benefit] relationship of the drug and to provide an adequate basis for physician labeling.” *Id.*

61. 21 C.F.R. § 312.21(b)-(c).

62. 21 U.S.C. § 355(a)-(b) (2000); 21 C.F.R. § 314.50 (2003).

63. Pennington Parker Landen, *Federal Preemption and the Drug Industry: Can Courts Co-Regulate?*, 43 FOOD DRUG COSM. L.J. 85, 100 (1988); *see also* 21 U.S.C. § 355(b)(1). The NDA shall include

(A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the

The FDA closely scrutinizes the data contained in the NDAs.⁶⁴ The new drug approval process takes approximately five to seven years.⁶⁵ The FDA determines the health benefits with a risk-assessment of the new drug and ensures the safety and efficacy with establishment of scientific data.⁶⁶ After market approval, the FDA conducts extensive post-market surveillance.⁶⁷ The FFDCA requires drug manufacturers to monitor drug effects and to conduct ongoing research.⁶⁸

C. Product Liability Suits

Even after clinical trials and FDA approval of a new drug, certain individuals are susceptible to adverse side effects because of their personal variations in biochemical pathways.⁶⁹ “There are some products which, in the present state of human knowledge, are quite incapable of being made safe [for all people] for their intended and ordinary use. These are especially common in the field of drugs.”⁷⁰ A pharmaceutical company must consider the risks of a product liability suit based on a design defect in a new drug.⁷¹ The potential for a design defect suit can adversely affect the return on investment calculation for new drug development.⁷²

methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (F) specimens of the labeling proposed to be used for such drug.

21 U.S.C. § 355(b)(1).

64. Viscusi, *supra* note 53, at 1444.

65. *Id.*

66. Wilson, *supra* note 2, at 499.

67. Viscusi, *supra* note 53, at 1447.

68. 21 C.F.R. § 314.80 (2004).

69. Wilson, *supra* note 2, at 499.

70. *Id.* (citing RESTATEMENT (SECOND) OF TORTS § 402A, cmt. k (1965)). “The same is true of many other drugs, vaccines, and the like, many of which for this very reason cannot legally be sold except to physicians, or under the prescription of a physician.” *Id.* Note the following example:

[T]he vaccine for the Pasteur treatment of rabies, which not uncommonly leads to very serious and damaging consequences when it is injected. Since the disease itself invariably leads to a dreadful death, both the marketing and the use of the vaccine are fully justified, notwithstanding the unavoidable high degree of risk which they involve. Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it unreasonably dangerous.

Id.

71. *Id.*

72. *Id.*

D. *Effective Patent Life*

Pioneer drug companies rely on pharmaceutical patents to protect their huge investments in developing new prescription drugs.⁷³ Due to the lengthy development and approval process, the effective patent life of a prescription drug is only eleven or twelve years, compared to eighteen and half years for other patented products.⁷⁴ Furthermore, “patents do not guarantee a return on investment,” or prevent someone else from developing a competing product.⁷⁵

The possession of a pharmaceutical patent does not provide the protection one might expect.⁷⁶ The exclusivity period granted to the pioneer drug company under the patent act does not provide a monopoly on a given treatment.⁷⁷ “Since a patent applies to a specific chemical or production process, other companies can patent] similar competing drugs based on the same innovative principle.”⁷⁸ More than one compound can produce similar results because the biochemical pathways involve complex, multi-step reactions.⁷⁹ A competitor can design around a pharmaceutical patent by targeting a different step in the biochemical pathway.⁸⁰ If the subsequent developer is successful, the competing drug would eliminate the original drug’s “monopoly” on a treatment.⁸¹

When a drug is released on the market, competitors can analyze the drugs composition and copy its formulation.⁸² By obtaining patent protection, pioneer drug companies have a

73. PhRMA INDUSTRY PROFILE 2003, *supra* note 11, at 6.

74. *Id.* at 61-62; *see also* Press Release, PHARM. RES. & MFRS. OF AM. (June 17, 2003), available at <http://www.phrma.org/mediaroom/press/releases/17.06.2003.747.cfm>.

75. PhRMA INDUSTRY PROFILE 2003, *supra* note 11, at 59.

76. *See* 35 U.S.C. § 154 (2000); PhRMA INDUSTRY PROFILE 2003, *supra* note 11, at 58. Before the Hatch-Waxman Act, pharmaceutical “[p]atent holders had the right to prevent a competitor from making, using, or selling a patented invention for the entire term of a patent.” PhRMA INDUSTRY PROFILE 2003, at 58. Today, they “have only the right to prevent a competitor from selling a product protected by an [effective] patent.” *Id.*

77. CONG. BUDGET OFFICE STUDY 1998, *supra* note 3, at 3.

78. *Id.* In 1977, Tagamet was the first drug to relieve ulcers by blocking the H2 receptors from stimulating acid production. *Id.* at 19. By 1989, three slightly different drugs (Zantac, Pepcid and Axid) using the same therapeutic mechanism (blocking the H2 receptor) were also patentable. *Id.* As a result, Tagamet, “the breakthrough drug had only six years of market exclusivity before being challenged by a competitor using a similar compound.” *Id.* In addition, “drug therapies often compete with non-drug therapies.” *Id.* at 3.

79. Wilson, *supra* note 46, at 500 (citing PHARM. RES. & MFRS. OF AM., PhRMA INDUSTRY PROFILE 102 (2000)).

80. *Id.*

81. *Id.*

82. *Id.*

defense against forfeiting their development investment to generic manufacturers who can cheaply copy the pioneer drug.⁸³ The decreased effective patent term of pioneer drugs expedites generic market entry.⁸⁴ The loss of the pioneer drug's monopoly creates a risk the development costs may not be recovered.⁸⁵ Regardless of the negative incentives, the current approach in reducing drug costs is to further expedite generic competition.⁸⁶ As pioneer drugs become less profitable, pharmaceutical companies may be reluctant to develop drugs for the more complex diseases.⁸⁷

IV. PATENT LAW—FDA APPROVAL RELATIONSHIP

A. Patent Act Protection for New Drug Manufacturers

In 1952, Congress passed a Patent Act based on review of new inventions by the United States Patent and Trademark Office (USPTO).⁸⁸ The USPTO has the authority to grant inventors limited monopolies in exchange for full disclosure of their inventions.⁸⁹ An inventor is required to submit a specification,⁹⁰ which is a “written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same.”⁹¹ In the specification, the inventor is also required to provide his opinion of the preferred embodiment, or “best mode

83. *Id.*

84. *Id.* (citing PhRMA INDUSTRY PROFILE 2000, at 100-04).

85. Wilson, *supra* note 46, at 500.

86. *Id.* (citing 21 U.S.C. § 355(j) (1994 & Supp. V 2000)).

87. CONG. BUDGET OFFICE STUDY 1998, *supra* note 3, at 46. After the Hatch-Waxman Act, the pioneer drug company's profits erode rapidly because of increased generic competition. *Id.* The erosion rate depends upon the occurrence of generic market entry and size of the generic market. *Id.* “[T]he effect of increased generic [competition] on the returns from marketing a new drug is less than one might expect because generic entry occurs at the end of a drug product's life, when profits are more heavily discounted.” *Id.* at 46-47.

88. 35 U.S.C. §§ 1-293 (2000). The Congress receives its power to legislate patent protection from the Patent & Copyright clause of the United States Constitution. U.S. CONST. art. I, § 8, cl. 8. “To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.” *Id.* The Framers of the Constitution believed inventors should be rewarded for their discoveries with a limited monopoly “to promote the Progress of Science and useful Arts.” *Id.*

89. *See generally*, 35 U.S.C. §§ 1-293 (2000).

90. 35 U.S.C. §§ 111(a)(2) (2000).

91. *Id.* § 112; *see also* Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1209 (Fed. Cir. 1991) (construing 35 U.S.C. § 112).

contemplated by the inventor of carrying out his invention.”⁹² The patent application will be scrutinized to determine whether the invention satisfies the statutory requirements of subject matter, utility, novelty, and non-obviousness.⁹³ Many of the recent exceptions to this incentive-based program are directed towards the pharmaceutical industry.⁹⁴

B. *Federal Food, Drug and Cosmetic Act*

The Congress passed the Pure Food and Drugs Act to prohibit manufacturers from introducing misbranded products into interstate commerce.⁹⁵ In 1938, Congress passed the Federal Food, Drug, and Cosmetic Act to impose quality standards on food and drugs and to require safety data for FDA approval.⁹⁶ The Act gave the FDA authority over the labeling of prescription drugs and over-the-counter pharmaceutical drugs but not over drug advertising.⁹⁷

In 1962, Congress passed the Kefauver-Harris Amendments to enhance safety standards, encourage generic competition and transfer authority over prescription drug advertisements to the FDA.⁹⁸ Prior to 1962, a new drug was automatically approved if the FDA failed to reject it within 180 days.⁹⁹ After 1962, the stricter safety requirements for new drugs included substantial data of efficacy and clinical trials to demonstrate effectiveness.¹⁰⁰

These amendments made generic competition feasible through the creation of the Abbreviated New Drug Applications (ANDAs).¹⁰¹ Any pre-1962 generic products could obtain FDA approval based on literature demonstrating drug safety if the

92. 35 U.S.C. § 112.

93. *Id.* §§ 101-103.

94. Drug Price Competition & Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 35 U.S.C. §§ 271(e), 156 (2000) and 21 U.S.C. § 355(j)(2000)).

95. See THOMAS SZASZ, *OUR RIGHT TO DRUGS: THE FOOD AND DRUGS ACT OF 1906* (Praeger Publishers 1992), available at www.druglibrary.org/schaffer/Library/szasz1.htm (discussing the Pure Food and Drugs Act of 1906, Pub. L. No. 59-384, Chap. 3915, 43 Stat. 768 (1906)).

96. See Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301-395 (2000)).

97. 21 U.S.C. §§ 360 (j)(1)(A)-(B).

98. Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962) (codified as amended at 21 U.S.C. § 301-381 (2000)). The Kefauver-Harris Amendments are named for their congressional sponsors.

99. 21 U.S.C. § 355 (i)(5)(A).

100. *Id.* § 355(d).

101. Elizabeth Powell-Bullock, *Gaming the Hatch-Waxman System: How Pioneer Drug Makers Exploit the Law to Maintain Monopoly Power in the Prescription Drug Market*, 29 J. LEGIS. 21, 25 (2002).

generic product was a bioequivalent to the patented drug.¹⁰² Any post-1962 generic product had to complete a full NDA before obtaining FDA approval.¹⁰³ By 1984, only fifteen NDAs for post-1962 generic products existed in the market for 150 prescription drugs with expired patents.¹⁰⁴

In 1978, President Carter initiated a review of industrial innovation and patent term restoration.¹⁰⁵ Three years later, the Senate passed the Patent Term Restoration Act to achieve the president's goals of extending the patent terms to a seven-year limitation.¹⁰⁶ The act failed to become law because the same bill was placed on the House Suspension Calendar where it garnered a simple majority of votes.¹⁰⁷ As a result, no substantive changes were made to the drug approval process between 1962 and 1984.¹⁰⁸

C. *Drug Price Competition and Patent Term Restoration Act of 1984*

1. History of Hatch-Waxman Act

(a) Pre-1984 Drug Approval Process

During the twentieth century, Congress increased its oversight of the development and marketing of pharmaceutical products.¹⁰⁹ "In 1906, Congress passed the Pure Food and Drugs Act to prohibit manufacturers from introducing misbranded and adulterated foods and drugs into interstate commerce."¹¹⁰ In 1938, the Congress passed the FDCA to impose quality

102. *Id.* at 24.

103. *Id.* (citing Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962) (codified as amended at 21 U.S.C. §§ 301-381 (2000))); *see also* United States v. Generix Drug Corp., 460 U.S. 453, 461 (1983) (concluding a post-1962 generic product was still a new drug under the FDCA even though the patented drug was FDA-approved).

104. *See* Gerald J. Mossinghoff, *Striking the Right Balance Between Innovation and Drug Price Competition: Understanding the Hatch-Waxman Act*, 54 FOOD AND DRUG L.J. 187, 187 (1999).

105. Mossinghoff, *supra* note 104, at 188.

106. *Id.* (citing S. 255, 98th Cong., 2d Sess. 25 (1984)).

107. *Id.* The Suspension Calendar requires a two-thirds majority for passage. *Id.* (citing Charles W. Johnson, HOW OUR LAWS ARE MADE, S. DOC. NO. 105-14 (1997)).

108. Powell-Bullock, *supra* note 101, at 24 (citing Gerald H. Mossinghoff, *Striking the Right Balance Between Innovation and Drug Price Competition: Understanding the Hatch-Waxman Act*, 54 FOOD AND DRUG L.J. 187, 187 (1999)).

109. *Id.* at 22.

110. *Id.* at 23. (citing Pure Food and Drugs Act, Pub. L. No. 59-384, 34 Stat. 768 (1906)).

standards and to require evidence of safety for FDA approval.¹¹¹ “The Act gave the FDA authority over the labeling of both prescription and over-the-counter pharmaceutical drugs but not over drug advertising, which remained with the Federal Trade Commission (FTC).”¹¹²

In 1962, the Congress enacted the Kefauver-Harris Amendments to the original FDCA, which enhanced safety standards, encouraged generic competition, and transferred authority over prescription drug advertisement to the FDA.¹¹³ Prior to 1962, a new drug was automatically approved if the FDA failed to reject it within 180-days.¹¹⁴ After 1962, the enhanced safety standards required substantial evidence of efficacy and extensive clinical trials ensuring the pharmaceutical product was effective in treating the ailment for which it was prescribed.¹¹⁵ After enactment of the Amendments, the FDA approval process took approximately nine to thirteen years.¹¹⁶ The Kefauver-Harris Amendments drastically increased the FDA approval time for new drugs, severely reduced the effective life of drug patents, and diminished the pioneer company’s return on investment for developing drugs to treat serious illnesses.¹¹⁷

111. *Id.* (citing Federal Food, Drug, and Cosmetic Act, Pub. L. No. 752 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301-395 (2000))).

112. *Id.*

113. *Id.* (citing Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962) (codified as amended at 21 U.S.C. §§ 301-381)).

114. Powell-Bullock, *supra* note 101, at 23 (citing Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended at 21 U.S.C. §§ 301-395)).

115. *Id.* (citing Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962) (codified as amended at 21 U.S.C. §§ 301-381)).

116. *Id.* at 23-24 (citing COMM’N ON THE FED. DRUG APPROVAL PROCESS, FINAL REPORT PREPARED BY THE SUBCOMM. ON NATURAL RES., AGRIC. RESEARCH AND ENV’T AND THE SUBCOMM. ON INVESTIGATION AND OVERSIGHT OF SCI. AND TECH., 97th Cong., 2d Sess. 2 (1982) (explaining that the FDA approval process took approximately nine to thirteen years from the synthesis of the new chemical entity (NCE) to FDA approval of a new drug)); *see also* FDA’s DRUG REVIEW AND APPROVAL TIMES, CTR. FOR DRUG EVAL. & RES., 1 (stating that new drug approval times have been dramatically reduced from a median of twenty-two-months in 1992 to less than twelve-months in 1999, although there was a slight increase in 2001), *available at* <http://www.fda.gov/cder/reports/reviewtimes/default.htm> (last updated July 30, 2001).

117. Lisa C. Will, Note, *Accelerated FDA Approval of Investigational New Drug: Hope for Seriously Ill Patients*, 94 DICK. L. REV. 1037, 1046 (1990).

Although they were designed to provide greater protection to the American public by requiring proof of both safety and efficacy, the [Kefauver-Harris Amendments] have created an unacceptably large increase in approval time, a decrease in incentive for drug innovation, and a barrier to the acquisition of necessary drugs for seriously ill patients.

The Amendments encouraged generic competition through the creation of Abbreviated New Drug Applications (ANDAs).¹¹⁸ For drugs approved before 1962, the FDA could approve generic drugs based upon literature demonstrating the chemical's safety if the generic product was a bioequivalent to the patented drug.¹¹⁹ For drugs approved after 1962, the generic manufacturer was required to submit a full NDA including clinical studies for FDA approval.¹²⁰ In 1984, there was Congressional testimony there were no generics for 150 post-1962 drugs with expired patents because generic manufacturers refused to invest in clinical trials required for FDA approval, and there were only fifteen generics for pre-1962 drugs.¹²¹

(b) Experimental Use Exception

Under 35 U.S.C. § 102(b), an invention may not be patented if it was "in public use or on sale in this country more than one year prior to the date of the application for patent in the United States."¹²² A defense to the "public use bar" is evidence the use of the invention was for the purpose of research and development rather than for the commercialization of the product.¹²³ In *T.P. Labs*, an orthodontist had designed an orthodontic device for positioning teeth.¹²⁴ Before the patent application was filed, the orthodontist used the device on three patients free of charge.¹²⁵ In a challenge to the resulting patent, the Federal Circuit found the use of the device did not violate the public use bar because the "inventor was testing the device not the market."¹²⁶

Before the Hatch-Waxman Act, an experimental use was not a viable defense to patent infringement.¹²⁷ Roche Products, Inc.

Id.

118. Powell-Bullock, *supra* note 101, at 25.

119. *Id.* at 23 (citing Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962) (codified as amended at 21 U.S.C. §§ 301-381 (2000))).

120. *Id.* at 24. (citing Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962) (codified as amended at 21 U.S.C. §§ 301-381 (2000)); *see* United States v. Generix Drug Corp., 460 U.S. 453, 461 (1983) (holding a generic version of a drug approved after 1962 constituted a new drug under the Federal Food, Drug, and Cosmetics Act).

121. Mossinghoff, *supra* note 104, at 187.

122. 35 U.S.C. § 102(b) (2000).

123. *T.P. Labs, Inc. v. Profl Positioners, Inc.*, 724 F.2d 965, 973 (Fed. Cir. 1984).

124. *Id.* at 967.

125. *Id.* at 967-68.

126. *Id.* at 973.

127. *Embrex, Inc. v. Serv. Eng'g Corp.*, 216 F.3d 1343, 1346 (Fed. Cir. 2000) (stating the experimental use and *de minimus* exceptions should not allow a violation of patent laws when the scientific inquiry has a commercial purpose); *Roche Prod., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858, 863 (Fed. Cir. 1984) (holding the experimental use exception should not allow a violation of patent laws when the scientific inquiry has a definite

(Roche) filed an infringement lawsuit to protect its successful brand-name sleeping pill, Dalmane.¹²⁸ Bolar Pharmaceutical Company (Bolar) wanted to satisfy FDA testing requirements to market the generic version immediately after the patent's expiration.¹²⁹ Since FDA approval can delay introduction by more than two years, Bolar decided to use the patented product in their experiments.¹³⁰ The Federal Circuit found Bolar infringed the patent because their "'experimental' use [was] solely for business reasons and not for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry."¹³¹ The unlicensed experiments conducted to adapt the patented product to Bolar's business violated the patent holder's right to exclude others.¹³² In response to *Roche*, the Congress enacted the Drug Price Competition and Patent Term Act of 1984, which includes an experimental use exception.¹³³

2. Hatch-Waxman Act

(a) New Drug Applications

For new drugs, the Hatch-Waxman Act maintained the rigorous New Drug Application (NDA) process and required the "Approved Drug Products with Therapeutic Equivalence Evaluations," which is commonly known as the "Orange Book."¹³⁴ When an NDA is filed, the applicant submits a list of patents

commercial purpose), superseded on other grounds by 35 U.S.C. § 271(e) (1984). In *Embrex*, a government scientist developed a patented technology for inoculating birds against disease by injecting vaccines into a specified region of the egg before hatching. *Embrex*, 216 F.3d at 1346. Upon receiving an exclusive license, Embrex, Inc. (Embrex) designed machines to perform the claimed method in large scale chicken farms. *Id.* Embrex filed an infringement lawsuit against Service Engineering Corp. (SEC) for attempting to market a similar in ovo injection device. *Id.* In post trial motions, the district court denied SEC's motion for JMOL, and awarded treble damages and attorney's fees under the terms of a previous settlement agreement as well as under 35 U.S.C. §§ 284-285. *Id.* The Federal Circuit affirmed-in-part the denial of SEC's motion for JMOL on the infringement verdict because substantial evidence supports the jury's verdict of patent infringement. *Id.* at 1352. The court also reversed-in-part because, "as a matter of law, an offer to sell a device cannot infringe a method patent without evidence of the device's actual use to carry out the method." *Id.*

128. *Roche*, 733 F.2d at 860.

129. *Id.* (stating the FDA required stability data, dissolution rates, bioequivalency studies and blood serum studies for a NDA application).

130. *Id.*

131. *Id.* at 863.

132. *Id.*

133. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 35 U.S.C. §§ 271(e), 156 (2000) and 21 U.S.C. § 355(j) (2000)).

134. Powell-Bullock, *supra* note 101, at 26 (citing 21 U.S.C. § 355(j)).

claiming the drug (active ingredient, formulation, or preparation) or method of using the drug.¹³⁵ The FDA publishes the patent listings along with the expiration dates in the Orange Book to notify future generic applicants such patents may prohibit the sale of infringing products.¹³⁶

(b) Abbreviated New Drug Applications

“To resolve the discrepancy between pre-1962 and post-1962 generic drugs, the Hatch-Waxman Act created” abbreviated New Drug Applications (ANDAs) for generic products equivalent to pioneer drugs approved shortly after 1962.¹³⁷ A generic manufacturer could use the original pioneer drug company’s NDA to prove safety and efficacy in its ANDA provided the generic drug was a bioequivalent to the patent listed in the Orange Book,¹³⁸ and it completed one of four ANDA certifications.¹³⁹ The four possible certifications are determined

135. Terry G. Mahn, *Patenting Drug Products: Anticipating Hatch-Waxman Issues During the Claims Drafting Process*, 54 FOOD DRUG COSM. L.J. 245, 249 (1999) (citing 21 U.S.C. § 355(b)(1)(F) (1994); 21 C.F.R. § 314.53 (1998)).

136. *Id.* at 249-50. When submitting an generic application for which one or more patents exist, the generic manufacturer must certify for each patent listed:

1. that such patent information has not been filed;
2. that such patent has expired;
3. that such patent will expire on specified date; or
4. that such patent is invalid or will not be infringed by the manufacture, use, or sale of the generic drug.

Id. (citing 21 C.F.R. § 314.94(a)(12)(i)(A) (1998)).

137. Powell-Bullock, *supra* note 101, at 26 (citing Elizabeth H. Dickenson, *FDA’s Role in Making Exclusivity Determinations*, 54 FOOD DRUG COSM. L.J. 195, 195-96 (1999)).

138. FOOD AND DRUG ADMIN., CTR. FOR DRUG EVALUATION AND RESEARCH, APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, available at <http://www.fda.gov/cder/ob/default.htm> (last updated Dec. 22, 2003). The “Orange Book” is named for the publication’s orange cover.

139. *Id.* (citing 21 U.S.C. § 355(j) (2000)). A generic drug is the bioequivalent to a listed drug if the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses.

21 U.S.C. § 355(j)(8)(B)(i). Alternatively, a drug is the bioequivalent if the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

Id. § 355(j)(8)(B)(ii).

by: Paragraph I if no patent information on the on the drug product is subject of the ANDA has been submitted to the FDA;¹⁴⁰ Paragraph II if the patent has expired;¹⁴¹ Paragraph III if the patent will expire on a stated date;¹⁴² or Paragraph IV if the patent is invalid or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA applicant seeks approval.¹⁴³

If the generic applicant files a Paragraph IV ANDA and the patent holder files an infringement suit within forty-five days of the required notice, the Hatch-Waxman [Act] prohibits FDA approval of the ANDA until the end of a thirty-month stay or on the date the court decides the patent is invalid or not infringed.¹⁴⁴ Regardless of the merits, the mere filing of an infringement lawsuit can provide additional years of a generic-free market.¹⁴⁵ This provision encourages generic manufacturers to wait until the patent expires before entering the market to avoid the automatic thirty-month stay and the possibility of costly lawsuits.¹⁴⁶

(c) First ANDA Applicant Exclusivity

The Hatch-Waxman Act established 180-day market exclusivity for the first ANDA applicant, five-year new chemical entity (NCE) exclusivity, and three-year new clinical study exclusivity.¹⁴⁷ The Congress has enacted two additional

140. FOOD AND DRUG ADMIN., *supra* note 138 (citing 21 U.S.C. § 355(j)(2)(A)(vii)(I) (2000)).

141. *Id.* (citing 21 U.S.C. § 355(j)(2)(A)(vii)(II)).

142. *Id.* (citing 21 U.S.C. § 355(j)(2)(A)(vii)(III)).

143. *Id.* (citing 21 U.S.C. § 355(j)(2)(A)(vii)(IV)).

144. *Id.* (citing 21 U.S.C. § 355(j)(5)(B)(iii)). If the generic applicant prevails in the trial court and the patent holder appeals, the generic manufacturer may not want to risk liability by introducing a generic product before the patent litigation is resolved. Elizabeth H. Dickenson, *FDA's Role in Making Exclusivity Determinations*, 54 FOOD & DRUG L.J. 195, 198 (1999).

145. Powell-Bullock, *supra* note 101, at 26-27 (citing 21 U.S.C. § 55(j)(4)(B)(iii)(I)(II)(III)(c)(3)(C)(2000); *see also* CONG. BUDGET OFFICE STUDY 1998, *supra* note 3, at 68. As a result of the Hatch-Waxman Act, more pioneer drugs experience generic competition after their patents expire. CONG. BUDGET OFFICE STUDY 1998, at 37. On the average, pioneer drugs lose 40% of their market to generic drugs. *Id.*

146. Dickenson, *supra* note 144, at 198.

147. Powell-Bullock, *supra* note 101, at 27 (citing Drug Price Competition & Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 35 U.S.C. §§ 271(e), 156 (2000) and 21 U.S.C. § 355(j) (2000)). The five-year NCE exclusivity is granted to innovative drug containing no active moiety previously approved by the FDA. Dickenson, *supra* note 144, at 200. The three-year clinical investigation exclusivity is granted for changes to the drug product such as changes in dosage form, in new indications and for switches from prescription to over-the-counter drug products, which require reports of new clinical investigations. *Id.* at 201.

exclusivity provisions: seven-year orphan drug exclusivity,¹⁴⁸ and a six-month pediatric exclusivity.¹⁴⁹ If a pioneer drug company can satisfy a combination of the exclusivity provisions, it can anticipate a longer period of market exclusivity and sell its products at higher prices without generic competition.¹⁵⁰ “If a generic manufacturer secures the 180-day market exclusivity where its only competition is the brand-name drug. . .” it can anticipate considerable profits as health insurance companies modify their plans to include the less-expensive generic alternative.¹⁵¹ The 180-day market exclusivity for the first ANDA applicant provides an incentive to challenge invalid patents and develop alternative forms of patent drugs.¹⁵²

Some generic manufacturers file a non-final ANDA merely to secure the 180-day market exclusivity for the first ANDA applicant.¹⁵³ In June 1998, Andrx Pharmaceuticals, Inc. (Andrx)

148. Orphan Drug Act, Pub. L. No. 97-414, 96 Stat. 2049 (1983) (codified in scattered sections of 21 U.S.C.). The Orphan Drug Act grants a seven-year exclusivity period for new drugs that are developed for the treatment of rare diseases with fewer than 200,000 afflicted patients. Dickenson, *supra* note 144, at 201-02. The Act prevents approval of the same drug for the same disease or condition, even from a second NDA submitted by another applicant. *Id.* at 202.

149. Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (1997) (codified as amended in scattered sections of 21 U.S.C.). The Act grants six-months of additional exclusivity for new drugs that are tested for use by children. Dickenson, *supra* note 144, at 203. The Act does not require new labeling or evidence of safety in children’s studies because its purpose is to inform the public. *Id.* If an innovator has three-years of exclusivity, the pediatric exclusivity will provide six-months of additional protection. *Id.* If the innovator has a patent, the six-months of exclusivity will be added to the end of the patent term. *Id.* If the innovator has five-year NCE exclusivity, the pediatric exclusivity will provide six-months of additional NCE exclusivity. *Id.*

150. Powell-Bullock, *supra* note 101, at 27.

151. *Id.*

152. *Id.* 27-28. (citing Grautec, Inc. v. Shalala, Nos. 97-1873, 97-1874, 1998 WL 153410, at *10 (4th Cir. Apr. 3, 1998)). In *Shalala*, the Fourth Circuit held the FDA’s regulations are inconsistent with the statute and are invalid. Shalala, 1998 WL 153410, at *10. The court confirmed FDA approval cannot be denied when a generic manufacturer complies with all applicable FDA regulations and is entitled to a final approval effective on that date. *Id.*

153. Robert D. Bajefsky & Gregory Chopskie, *Biting the Hand that Feeds?: Generic Drugs and the Abuse of the Hatch-Waxman Law*, 10 No. 14 ANDREWS INTELL. PROP. LITIG. REP. 27 (2003) (citing Bill Alpert, *Dirty Tricks in the Land of Generic Drugs*, BARRON’S TECH. WEEKLY, Mar. 11, 2002, at T1). Some generic manufacturers rush an incomplete ANDA application to the FDA, in a strategy of “submit first, and fix later.” Bill Alpert, *Dirty Tricks in the Land of Generic Drugs*, BARRON’S TECH. WEEKLY, Mar. 11, 2002, at T1. Only twenty-four out of 812 generic drug approvals had more than twelve ANDA amendments. *Id.* Half of the approved ANDAs had less than four amendments, while three-quarters had less than six. *Id.* A mere handful of generic manufacturer’s are guilty of extreme amending: Andrx Pharmaceuticals, Inc., Mylan Pharmaceuticals, Inc., Teva Pharmaceutical Industries, and Watson Pharmaceuticals, Inc. *Id.*

filed an ANDA for a generic version of Tiazac.¹⁵⁴ In October 1998, Biovail filed a Paragraph IV ANDA infringement lawsuit against Andrx.¹⁵⁵ Andrx denied infringement of the Tiazac patent and counterclaimed the patent was invalid.¹⁵⁶ After the close of discovery, Andrx filed eleven amendments to the ANDA, which were not disclosed to Biovail until shortly before appellate argument.¹⁵⁷ The Federal Circuit stated “[i]t is an abuse of the judicial role for Andrx to ask [them] to review on appeal what should have been made known, and adequately explored, at trial.”¹⁵⁸ After reviewing the amendments, they affirmed the district court’s judgment that Andrx’s product does not infringe the Tiazac patent.¹⁵⁹

(d) Patent Term Extensions

The Hatch-Waxman Act allows patent term extensions to compensate the pioneer drug company for the lengthy regulatory review process.¹⁶⁰ The patent term extension is equal to one-half the time of the investigational new drug trial (IND) period plus the NDA review period.¹⁶¹ The extension cannot exceed five-years if the patent issued after the enactment date or if the patent issued before the enactment date and no clinical testing has been conducted.¹⁶² If the patent was issued for a drug before the enactment date and clinical test had begun, the extension was limited to two-years for pipeline drugs to encourage development of future products.¹⁶³ Any product which had not begun clinical testing or FDA review was eligible for the five-year extension.¹⁶⁴

In 1994, the patent term was lengthened following the

154. Biovail Corp. Int’l v. Andrx Pharms., Inc., 239 F.3d 1297, 1299 (Fed. Cir. 2001). Biovail Corp. and Biovail Labs. Inc. are the exclusive licensee for Tiazac, a diltiazem salt used to treat hypertension and angina. *Id.* Andrx’s product consists of a bead containing a diltiazem salt and sugar encapsulated in a microporous membrane. *Id.*

155. *Id.* at 1299-1300.

156. *Id.*

157. *Id.* at 1304. The parties litigated for three years over Andrx’s original ANDA even though Andrx modified the application repeatedly during the course of the litigation. Bajefsky, *supra* note 153, *Filing Non-Final ANDAs to Ensure “First-Filer” Status*.

158. *Id.*

159. *Id.* at 1304-05.

160. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 35 U.S.C. §§ 271(e), 156 (2000) and 21 U.S.C. § 355(j) (2000); *see also* Mossinghoff, *supra* note 104, at 192 (stating the FDA reviews an NDA in approximately 15-16 months).

161. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 35 U.S.C. §§ 271(e), 156 and 21 U.S.C. § 355(j)).

162. 35 U.S.C. § 156(g).

163. *Id.*

164. *Id.*

ratification of the Agreement on Trade-Related Aspects of Intellectual Property Rights¹⁶⁵ and the enactment of pending legislation.¹⁶⁶ The Uruguay Round Agreements Act (URAA) provided a drug with a patent in effect or pending on June 8, 1995, a twenty-year patent-term from the patent application date, or a seventeen-year patent-term from the patent issue date, whichever was longer.¹⁶⁷ The difference between these two time-periods, named the Delta period, defined a safe-harbor when no generic manufacturer could compete in the market.¹⁶⁸ In 1996, a pioneer drug with a patent-term of twenty-years from its filing date was allowed an additional extension under the Hatch-Waxman patent restoration due to unnecessary delays in the FDA approval process.¹⁶⁹

(e) Limitations of Safe-Harbor Provision

The Hatch-Waxman Act provides an experimental use exception.¹⁷⁰ The statute states the patented invention should be used “solely for [purposes] reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs. . .”¹⁷¹ This exception protects generic manufacturers whose use of patented

165. General Agreement on Tariffs and Trade: Multilateral Trade Negotiations Final Act Embodying the Results of the Uruguay Round of Trade Negotiations, Annex 1C to WTO Agreement, 33 I.L.M. 1125, 1197 (1994), available at http://www.wto.org/english/docs_e/legal_e/27-trips.wpf.

166. Uruguay Round Agreements Act, Pub. L. No. 103-465, 108 Stat. 4809 (1994) (codified at 35 U.S.C. § 154 (2000)).

167. 35 U.S.C. § 154(c)(1) (2000). The patent term “that is in force on or that results from an application filed before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act shall be the greater of the 20-year term . . . , or 17-years from grant, subject to any terminal disclaimers.” *Id.*

168. Powell-Bullock, *supra* note 101, at 29 (citing Bristol-Meyers Squibb Co. v. Royce Labs., 69 F.3d 1130, 1132 (Fed. Cir. 1995)). In *Royce Labs.*, the Federal Circuit stated that a generic drug can be approved if the patented drug did not have a patent in effect or pending on June 8, 1995. *Royce Labs.*, 69 F.3d at 1132.

169. Merck v. Kessler, 80 F.3d 1543, 1553 (Fed. Cir. 1996). In *Kessler*, the Federal Circuit held the URAA patent extension did not apply to patents that were still in effect on June 8, 1995 due to the Hatch-Waxman patent restoration. *Id.*

170. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 35 U.S.C. §§ 271(e), 156 and 21 U.S.C. § 355(j)).

171. 35 U.S.C. § 271(e)(1) (2003). “It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention . . . solely for uses reasonably related to development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.” *Id.*

drugs is required to obtain FDA approval.¹⁷² The courts are struggling to define the limits of the safe-harbor provision.

(i) Scope of “Patented Invention”

Under the safe harbor provision, the courts have defined the scope of “patented invention.”¹⁷³ The Supreme Court has stated the phrase “patented invention” in the safe harbor provision is defined to include all inventions, not drug-related inventions alone.¹⁷⁴ The Court decided the safe harbor applies to all products eligible for the patent-term extension because they are subject to FDA approval.¹⁷⁵ The Federal Circuit held that all classes of medical devices fall within the safe harbor provision.¹⁷⁶ One district court stated the safe harbor applies only to patents covering drug products, medical devices, food additives and color additives subject to FDA approval.¹⁷⁷

In *Eli Lilly, Medtronic, Inc.* (Medtronic) allegedly infringed patents for ventricular defibrillation devices.¹⁷⁸ Medtronic defended on the ground that its activities were related to obtaining FDA approval.¹⁷⁹ The district court concluded the safe harbor provision did not apply to medical devices.¹⁸⁰ The Federal Circuit reversed on the ground that Medtronic’s activities would not constitute infringement under the section 271(e)(1) if they were reasonably related to FDA approval.¹⁸¹ The Supreme Court stated the phrase “patented invention” in the safe harbor provision is defined to include all inventions, not drug-related

172. See *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 664, 678-79 (1990) (holding that alleged infringer’s use of patented invention to submit application for FDA approval was not infringement).

173. 35 U.S.C. § 271(e)(1); see e.g., *Eli Lilly*, 496 U.S. at 665 (holding the phrase “patented invention” in section 271(e)(1) includes all products eligible for patent-term extension, not merely drug products); *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019, 1029 (Fed. Cir. 1997) (holding the phrase “patented invention” includes all medical devices including Class II medical devices); *Bristol-Meyers Squibb Co. v. Rhone-Poulec Rorer, Inc.*, No. 95 Civ. 8833(RPP), 2001 WL 1512597, at *3, (S.D.N.Y. Nov. 28, 2001) (holding the phrase “patented invention” includes all patented products or discoveries, not merely those within the patent-term extension provision); *Infigen, Inc. v. Advanced Cell Tech., Inc.*, 65 F. Supp. 2d 967, 980 (W.D. Wis. 1999) (holding the phrase “patented invention” includes patented products actually eligible for patent-term extension).

174. *Eli Lilly*, 496 U.S. at 665 (citing 35 U.S.C. § 100(a) (1999)).

175. *Id.* at 670-71.

176. *Abtox*, 122 F.3d at 1029.

177. *Infigen*, 65 F. Supp. 2d at 979-80.

178. *Eli Lilly*, 496 U.S. at 664.

179. *Id.* at 661.

180. *Id.*

181. *Id.*

inventions alone.¹⁸² The Court decided the safe harbor applies to all products eligible for the patent-term extension because they are subject to FDA approval.¹⁸³ These patent extensions protect drug products, medical devices, food additives, and color additives that are subject to FDA approval.¹⁸⁴

Similarly, Rhone-Poulenc Rorer, Inc. (RPR) alleged infringement of patents for a semi-synthesis of taxol, a cancer chemotherapeutic agent.¹⁸⁵ The district court decided patented intermediaries fall within the safe harbor provision because the phrase “patented invention” includes all inventions, not drug-related inventions alone.¹⁸⁶ The court denied RPR’s motion for summary judgment because Bristol-Meyer’s use of the patented intermediaries was reasonably related to obtaining FDA approval.¹⁸⁷ After substantial litigation, the district court held RPR’s patent was unenforceable because they obtained it by inequitable conduct.¹⁸⁸ The Federal Circuit affirmed the decision because the patent agent drafted the claims more broadly than warranted by the inventor’s Journal of the American Chemical Society (JACS) article and failed to disclose the JACS article with the intent to mislead the patent office.¹⁸⁹

MDT Corporation (MDT) alleged infringement of patents that disclosed devices to sterilize medical instruments in plasma, a partially ionized gas.¹⁹⁰ In a counterclaim, Abtox, Inc. (Abtox)

182. *Id.* at 665 (citing 35 U.S.C. § 100(a) (2000)). “When used in this title unless the context otherwise indicates ... [t]he term ‘invention’ means invention or discovery.” 35 U.S.C. § 100(a) (2000).

183. *Eli Lilly*, 496 U.S. at 670-71. The Court reasoned if patent-term extensions were available for a broad range of patented products while the safe harbor applied only to patented drugs, the Hatch-Waxman Act would increase distortions of the patent-term for patented products that were advantaged by the extension, but not disadvantaged by the safe harbor provision. *Id.* at 671.

184. *Id.* at 672. Under the patent term extension section, “[t]he term ‘product’ means: (A) A drug product [or] (B) Any medical device, food additive, or color additive subject to regulation under the Federal Food, Drug, and Cosmetic Act.” *Id.* at 670-71 (citing 35 U.S.C. § 156(f) (2000)).

185. *Bristol-Meyers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, 326 F.3d 1226, 1229 (Fed. Cir. 2003).

186. *Bristol-Meyers*, 2001 WL 1512597, at *3 (citing *Abtox.*, 122 F.3d at 1028; *Chartex Int’l PLE v. M.D. Pers. Prod. Corp.*, 5 F.3d 1505 (Fed. Cir. 1993)).

187. *Bristol-Meyers*, 2001 WL 1512597, at *8. Bristol-Meyer’s use of clinical data obtained through its experiments for filing patent applications of its analogs and preparation of a SAR database would not violate the safe harbor provision. *Id.*

188. *Bristol-Meyers*, 326 F.3d at 1229.

189. *Id.* at 1230 (referring to a scientific article written by the inventors of the patents, entitled “A Highly Efficient, Practical Approach to Natural Taxol,” which was published in the Journal of the American Chemical Society (JACS)).

190. *Abtox*, 122 F.3d at 1020-21. Because the high-energy charged particles damage delicate medical instruments, the devices must sterilize with neutral active components by using a Faraday shield, a metal barrier that blocks charged particles. *Id.* at 1021.

alleged MDT infringed one of its patents.¹⁹¹ In a separate opinion, the district court granted MDT's motion for partial summary judgment and certified for appeal the question of whether section 271(e)(1) precluded infringement.¹⁹² Under *Eli Lilly's* broad holding, the Federal Circuit concluded all classes of medical devices, including Class II devices, fall within the safe harbor provision because it does not distinguish between the different FDA classes.¹⁹³ The court decided MDT's activities were either non-infringing or reasonably related to FDA approval.¹⁹⁴

Advanced Cell Technology, Inc. (ACT) infringed patents for activating bovine oocytes (unfertilized eggs) for use in cloning cattle.¹⁹⁵ The district court stated the safe harbor provision applies only to patents covering drug products, medical devices, food additives and color additives subject to FDA approval.¹⁹⁶ The court decided the safe harbor provision did not apply to the media or method patents because neither covered drug products nor products which are eligible for the patent-term extension.¹⁹⁷ Furthermore, the common law experimental use exception did not apply because the experiments were part of ACT's ongoing

191. *Id.* at 1027.

192. *Id.* (citing *Abtox, Inc. v. Exitron Corp.*, 888 F. Supp. 6, 9 (D. Mass. 1995)). At the time of the litigation, MDT had neither filed an application for FDA approval nor marketed the device. *Id.*

193. *Abtox*, 122 F.3d at 1029 (stating that only Class III devices fall within the safe harbor provision under *Eli Lilly's* narrower justification of statutory symmetry). In *Eli Lilly*, the Supreme Court explicitly accepted a statutory interpretation "in which a patentee will obtain the advantage of the [patent-term] extension but not suffer the disadvantage of the [safe harbor] provision, and others in which he will suffer the disadvantage without the benefit." *Id.* (citing *Eli Lilly*, 496 U.S. at 671-72). In other words, they indicated that statutory symmetry is desired but not required. *Id.*

194. *Id.* at 1030.

195. *Infigen*, 65 F. Supp. 2d at 969.

196. *Id.* at 980-81 (cataloging patented products falling within the safe harbor provision); see e.g., *Eli Lilly*, 496 U.S. at 664 (implantable cardiac defibrillator); *Abtox*, 122 F.3d at 1020 (medical device for sterilizing plasma); *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1563-64 (Fed. Cir. 1997) (active ingredient in anti-ulcer medication); *Teletronics Pacing Sys., Inc. v. Ventritex, Inc.*, 982 F.2d 1520, 1522 (Fed. Cir. 1992) (implantable defibrillator); *Ortho Pharm. Corp. v. Smith*, 959 F.2d 936, 937 (Fed. Cir. 1992) (oral contraceptive); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104, 106 (D. Mass. 1998) (hormone for stimulating red blood cell growth); *Key Pharms., Inc. v. Hercon Labs. Corp.*, 981 F. Supp. 299, 302 (D. Del. 1997) (transdermal patch); *NeoRx Corp. v. Immunomedics, Inc.*, 877 F. Supp. 202, 204 (D.N.J. 1994) (product for labeling proteins for cancer detection and treatment); *Infinitech, Inc. v. Vitrophage, Inc.*, 842 F. Supp. 332, 333 (N.D. Ill. 1994) (perflorocarbon used in retinal surgery); *Baxter Diagnostics, Inc. v. AVL Scientific Corp.*, 798 F. Supp. 612, 613-14 (C.D. Cal. 1992) (medical devices).

197. *Infigen*, 65 F. Supp. 2d at 980.

business activities.¹⁹⁸ ACT intended to develop transgenic cattle to be commercialized along with other transgene products.¹⁹⁹

(ii) Reasonably-Related Activities

The courts have also defined the scope of the phrase “solely for uses reasonably related to the development and submission of information under [a Federal law].”²⁰⁰ The statute specifies only the making, using or selling of a patented invention as potentially infringing activities.²⁰¹ Clearly, potentially infringing activities are exempt if they are performed solely for FDA approval.²⁰²

To recruit clinical investigators, advertising the availability of the product on the company website, in medical and scientific journals, at academic conferences, and at trade shows does not constitute infringement.²⁰³ In fund raising efforts, the description of clinical trials to investors, analysts, and journalists is exempt because it falls under the category of dissemination of data developed for FDA approval.²⁰⁴

If the clinicians are willing to apply for investor-sponsored Investigational Device Exemption (IDE), providing an opportunity for clinicians to test the product is reasonably related to FDA approval, even without FDA pre-market approval.²⁰⁵ The decision to continue clinical trials after submitting an application is reasonably related to FDA approval because the FDA may require more information.²⁰⁶

If the data is first submitted for FDA approval, the subsequent submission of the same data for foreign regulatory

198. *Id.* at 981.

199. *Id.*

200. *See, e.g.*, *Intermedics, Inc. v. Ventritex, Inc.*, 991 F.2d 808, No. 92-1076, 1993 WL 87405 *5 (Fed. Cir. Feb. 22, 1993); *Teletronics Pacing Sys., Inc. v. Ventritex, Inc.*, 982 F.2d 1520, 1523-25 (Fed. Cir. 1992); *Nexell Therapeutics, Inc. v. AmCell Corp.*, 199 F. Supp. 2d 197, 204-05 (D. Del. 2002); *Nexell Therapeutics, Inc. v. AmCell Corp.*, 143 F. Supp. 2d 407, 420, 422-23 (D. Del. 2001); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104, 107-08 (D. Mass. 1998); *NeoRx Corp. v. Immunomedics, Inc.*, 877 F. Supp. 202, 206, 208-09, 211-14 (D.N.J. 1994); *Farmaceutisk Laboratorium Ferring A/S v. Solvay Pharms., Inc.*, 25 U.S.P.Q.2d (BNA) 1344, 1354, No. 1:89-CV-1972-JOF, 1992 WL 421542 (N.D. Ga. Sept. 9, 1992).

201. *Teletronics*, 982 F.2d at 1523 (citing 35 U.S.C. § 271(a)).

202. *Id.*

203. *Intermedics*, 1993 WL 87405, at *1 (citing *Intermedics*, 775 F. Supp. at 1288-89); *Teletronics*, 982 F.2d at 1521-22; *Nexell*, 143 F. Supp. 2d at 420, 422-23.

204. *Teletronics*, 982 F.2d at 1521, 1523-24.

205. *See Nexell*, 143 F. Supp. 2d at 420, 422-23.

206. *Intermedics*, 1993 WL 87405, at *1 (citing *Intermedics*, 775 F. Supp. at 1282).

approval is not an infringing activity.²⁰⁷ Sales to foreign distributors are also exempt if the product is resold to FDA-approved clinical investigators.²⁰⁸ Foreign clinical trials are reasonably related to FDA approval if the data is not submitted to any foreign regulatory agency.²⁰⁹

The production of product or the completion of tests to generate useful information is protected by the safe harbor provision, even if the results are later discarded for reasons unrelated to FDA approval.²¹⁰ One court held production of “launch-quantity inventory” is reasonably related to FDA approval if the FDA is aware of the scale-up plans.²¹¹

Ventritex, Inc. (Ventritex) developed the Cadence product, an implantable defibrillator.²¹² In 1989, Ventritex began clinical trials believing its activities were exempt under the safe harbor provision.²¹³ Intermedics alleged infringement of seven patents for implantable defibrillators.²¹⁴ Ventritex sold Cadence for use in domestic clinical trials.²¹⁵ The district court found Ventritex’s decision to continue clinical trials after submitting an application was reasonably related to FDA approval because the FDA may require more information.²¹⁶ The sales to foreign distributors were also exempt because the devices were resold to FDA-approved clinical investigators.²¹⁷ The German clinical trials were reasonably related to FDA approval because there was no evidence the data was submitted to any foreign regulatory agency.²¹⁸ The safety inspection of the Cadence programmer was reasonably related to FDA approval because the inspection was a pre-requisite for importation approval for the German clinical trials.²¹⁹ Ventritex’s demonstrations of the device at trade shows did not constitute infringement.²²⁰ The district court granted Ventritex’s motion for summary judgment of infringement, and found their manufacture, use, and sale of the patented invention

207. See *Amgen*, 3 F. Supp. 2d at 111; *NeoRx*, 877 F. Supp. at 208 (citing *Intermedics*, 982 F.2d 1520, 1524).

208. *Intermedics*, 1993 WL 87405, at *1 (citing *Intermedics*, 775 F. Supp. at 1283).

209. *Id.* (citing *Intermedics*, 775 F. Supp. at 1284).

210. *Amgen*, 3 F. Supp. 2d at 110.

211. *NeoRx*, 877 F. Supp. at 206.

212. *Intermedics*, 1993 WL 87405, at *1 (citing *Intermedics*, 775 F. Supp. at 1288-89).

213. *Id.*

214. *Id.*

215. *Id.* (citing *Intermedics*, 775 F. Supp. at 1282).

216. *Id.*

217. *Id.* (citing *Intermedics*, 775 F. Supp. at 1283).

218. *Intermedics*, 1993 WL 87405, at *1 (citing *Intermedics*, 775 F. Supp. at 1284).

219. *Id.* (citing *Intermedics*, 775 F. Supp. at 1285).

220. *Id.* (citing *Intermedics*, 775 F. Supp. at 1288-89).

were exempt under the safe harbor provision.²²¹ Upon appeal, the Federal Circuit affirmed the judgment.²²²

Teletronics Pacing Systems, Inc. (TPS) alleged infringement of patents for an implantable defibrillator.²²³ TPS claimed Ventritex engaged in activities that were not exempt under the safe harbor provision.²²⁴ In 1989, Ventritex began conducting clinical trials of its implantable defibrillator.²²⁵ At seven medical conferences, Ventritex demonstrated its defibrillator to physicians and some non-physicians.²²⁶ In fund-raising efforts, the Ventritex CEO described the ongoing clinical trials to investors, analysts and journalists.²²⁷ Ventritex also mailed a memorandum to private investors to raise funds for continuing the clinical trials and for obtaining manufacturing equipment.²²⁸ The district court granted Ventritex's motion for summary judgment because it agreed the activities were exempt under the safe harbor provision.²²⁹ On appeal, the Federal Circuit affirmed the decision because Ventritex's activities fall under the category of dissemination of data developed for FDA approval.²³⁰ The statute clearly specifies only the making, using or selling of a patented invention as potentially infringing activities.²³¹

AmCell Corporation (AmCell) produced CliniMACS, a device which permits large-scale magnetic cell separation.²³² Nexell Therapeutics Corporation (Nexell) produces the Isolex system, a magnetic cell separation device.²³³ In March 2000, Nexell alleged infringement of the Civin patents for antibodies.²³⁴ Although they

221. *Id.* at *1.

222. *Id.* at *5.

223. *Teletronics*, 982 F.2d at 1521.

224. *Id.*

225. *Id.* Pursuant to an FDA Investigational Device Exemption (IDE), Ventritex sold its device at cost for implantation in patients participating in the clinical trials. *Id.* (citing 21 C.F.R. §§ 812.1 to 812.150 (West, WESTLAW Feb. 27, 2004) (1989)). The data is required for obtaining FDA approval of the device. *See* FDA Medical Devices, *Id.* § 814.20.

226. *Teletronics*, 982 F.2d at 1521.

227. *Id.* (stating the CEO compared their defibrillator to those of other companies, reported the number of centers doing the implants and distributed a handout).

228. *Id.* at 1522.

229. *Id.* at 1521.

230. *Id.* at 1523-24.

231. *Id.* at 1523 (citing 35 U.S.C. § 271(a)). Under section 271(e)(1), these potentially infringing activities are exempt if they are performed solely for uses reasonably related to FDA approval. *Id.*

232. *Nexell*, 143 F. Supp. 2d at 409.

233. *Id.* at 408. When used in conjunction with antibodies identified in the Civin patents, a magnetic cell separation device can separate stem cells from peripheral blood cells and bone marrow for therapeutic purposes. *Id.* at 408-09.

234. *Id.* at 409.

did not have FDA pre-market approval, AmCell provided an opportunity for clinicians to use the CliniMACS device in conjunction with the antibody if the clinicians were willing to apply for investor-sponsored Investigational Device Exemption (IDE).²³⁵ To recruit clinical investigators, AmCell advertised the availability of its device on its website, in medical and scientific journals, at academic conferences, and at trade shows.²³⁶

The district court granted AmCell's motion for summary judgment of non-infringement although it did not decide whether AmCell's activities violated the safe harbor provision.²³⁷ In July 2001, the FDA responded to Nexell's letter and declined to answer the plaintiff's questions because the application of the safe harbor provision lies with the court.²³⁸ Based on the evidence, the court ultimately found AmCell's activities were exempt under the safe harbor provision.²³⁹

Hoechst Marion Roussel, Inc. (HMR) allegedly infringed several patents for a recombinant (genetically engineered) form of erythropoietin (EPO), a hormone that stimulates the production of red blood cells.²⁴⁰ In early 1997, HMR exported a quantity of GA-EPO from Batch 07 to its Japanese affiliate to be used as a standard reference to evaluate an alternative manufacturing process.²⁴¹ The court stated Amgen cannot defeat application of the safe harbor provision merely by questioning HMR's sincerity.²⁴² Although the FDA prefers the Limulus Amebocyte Lysate (LAL) test, HMR used the rabbit pyrogen test to determine their product purity.²⁴³ Even if the results were unacceptable to the FDA, the rabbit pyrogen tests were reasonably related to the FDA approval process because the safety testing involved product for the clinical trials.²⁴⁴ HMR produced at least four commercial-scale production batches of GA-GPO although the FDA only requires the consistency of three consecutive batches.²⁴⁵ The production of GA-GPO is protected by the safe harbor provision because it was "objectively likely to

235. *Id.* at 420.

236. *Id.*

237. *Id.* at 423. According to the court, the FDA is in a better position to decide which activities are reasonably related to FDA approval and which are not. *Id.*

238. *Nexell*, 199 F. Supp. 2d at 202.

239. *Id.* at 208.

240. *Amgen*, 3 F. Supp. 2d at 106.

241. *Id.* at 109.

242. *Id.*

243. *Id.*

244. *Id.* at 110.

245. *Id.*

generate useful information, even if the results were later discarded. . . for reasons unrelated to FDA approval.”²⁴⁶ The characterization studies were also exempt because the FDA requires such characterization as part of the approval process.²⁴⁷ HMR exported GA-GPO to Scotland for stringent viral clearance tests designed to meet European standards.²⁴⁸ The viral clearance tests were exempt under the safe harbor provision because the results were submitted for FDA approval.²⁴⁹ The district court granted HMR’s motion for summary judgment of non-infringement because their activities were reasonably related to FDA approval.²⁵⁰

Immunomedics, Inc. (Immunomedics) develops products for the detection of cancer and infectious diseases, and the treatment of cancer.²⁵¹ In July 1991, NeoRx Corporation (NeoRx) alleged infringement of a patent for processes and resulting products for labeling proteins with radioactive metal isotopes to detect and treat cancer.²⁵² The district court held Immunomedics’ production of “launch-quantity inventory” of ImmuRAID-CEA was reasonably related to the FDA approval process given the FDA’s knowledge of the scale-up plans.²⁵³ The court stated if data is first submitted for FDA approval, the subsequent submission of the same data for foreign regulatory approval is not an infringing activity.²⁵⁴ The shipment of vials to foreign clinical investigators is exempt if the test results are submitted for FDA approval.²⁵⁵ The district court granted Immunomedics’ motion for summary judgment of non-infringement for the scale-up production of ImmuRAID-CEA, submission of data to foreign regulatory agencies which was first submitted for FDA approval, and shipment of vials to foreign clinical investigators whose results were submitted to the FDA.²⁵⁶

Farmaceutisk Laboratorium Ferring (FLF) alleged infringement of a method patent for treating Crohn’s disease

246. *Amgen*, 3 F. Supp. 2d at 110.

247. *Id.* at 110-11 (citing 21 C.F.R. § 610.18(c); 21 C.F.R. § 312.23(a)(7)).

248. *Id.* at 111.

249. *Id.*

250. *Id.* at 113.

251. *NeoRx*, 877 F. Supp. at 204.

252. *Id.*

253. *Id.* at 206. The “application of section 271(e) requires a two-step inquiry: (1) whether the activity at issue is a potentially infringing one; and (2) whether the exemption applies to the activity.” *Id.*

254. *Id.* at 208.

255. *Id.* at 209.

256. *Id.* at 214.

(ulcerative colitis) with 5-aminosalicylic acid (5-ASA).²⁵⁷ Although they had not filed a New Drug Application (NDA), Solvay Pharmaceuticals, Inc. (Solvay) supplied coated tablets of 5-ASA to physicians for clinical trials.²⁵⁸ Solvay indicated they planned to file an NDA for ROWASA 5-ASA No. 2 by the end of the year.²⁵⁹ The court held Solvay's activities were exempt under the safe harbor provision because they were preparing to file an NDA.²⁶⁰

(iii) Scope of Applicable Federal Laws

The courts have defined the scope of "a federal law" under the safe harbor provision. In *Eli Lilly*, the Federal Circuit found the phrase "a federal law which regulates the manufacture, use, or sale of drugs" [was] ambiguous."²⁶¹ They decided it is more natural "to refer to the entirety of any Act, including the FDCA, at least some of whose provisions regulate drugs, rather than . . . to only those individual provisions of federal law that regulates drugs."²⁶² Upon appeal, the Supreme Court commented the "phrase 'a Federal law' can be used to refer to an isolated statutory section."²⁶³ The phrase is also used to refer to an entire Act rather than an isolated provision.²⁶⁴ The Court decided "the phrase 'a Federal law which regulates the manufacture, use, or sale of drugs' summons the image of an entire statutory scheme of regulation."²⁶⁵ The Court also found "the development and submission of information under a Federal law" language seems more compatible with reference to an entire Act rather than an individual provision.²⁶⁶ The Supreme Court found the structure of the [Hatch-Waxman] Act, taken as a whole, confirmed the Court of Appeal's interpretation.²⁶⁷

257. *Solvay*, 25 U.S.P.Q.2d at 1346.

258. *Id.*

259. *Id.*

260. *Id.* at 1352.

261. *Eli Lilly*, 496 U.S. at 661.

262. *Id.*

263. *Id.* at 666.

264. *Id.*

265. *Id.* If the safe harbor provision referred to "a Federal law which pertains to the manufacture, use, or sale of drugs," it might be reasonable to apply an individual provision. . . . *Id.*

266. *Id.* If an individual provision rather than an entire statutory scheme of regulation applied, the safe harbor provision would likely state "the development and submission of information pursuant to a Federal law" or possibly "in compliance with a Federal law." *Id.* at 666-67.

267. *Eli Lilly*, 496 U.S. at 669. The Supreme Court reasoned the Act sought to eliminate the distortions that occurred at both ends of the patent term by establishing a

(iv) Infringing Activities

Although many activities are exempt, the courts have identified some activities, which violate the safe harbor provision.²⁶⁸ For example, the general biomedical research to identify candidate drugs for clinical trials is not reasonably related to FDA approval because the FDA has no interest in the identification of drugs which may or may not undergo clinical trials.²⁶⁹ Shipping products to overseas regulatory agencies is not exempt under the safe harbor provision because it is not reasonably related to FDA approval.²⁷⁰ The shipment of vials to foreign clinical investigators is exempt if the test results are submitted for FDA approval.²⁷¹ However, one court implied that the submittal of fraudulent data is not reasonably related to FDA approval even though the evidence was insufficient to support a finding of fraudulent intent.²⁷² In dicta, another court indicated a potentially infringing party leaves the protection of the safe harbor provision upon FDA approval.²⁷³ They recognized an apparent split of opinion whether filing an ANDA removes a potential infringer from the safe harbor provision.²⁷⁴

Integra Lifesciences I, Ltd. (Integra) had several patents relating to a short tri-peptide segment of fibronectin having the

patent-term extension and a safe harbor provision. *Id.* at 670. If the discovery cannot be marketed without regulatory approval, the patent term runs even though the inventor is prevented from earning any profit from the invention. *Id.* at 669-70. The combined effect of the patent law and regulatory approval created a patent-term extension that prevented competition immediately after expiration of the patent. *Id.* at 670. The Court explicitly accepted a statutory interpretation “in which a patentee will obtain the advantage of the [patent-term] extension but not suffer the disadvantage of the [safe harbor] provision, and others in which he will suffer the disadvantage without the benefit.” *Id.* at 671-72. In other words, the Court indicated that statutory symmetry is desired but not required. *Id.* at 671-73.

268. See *e.g.*, *Integra Lifesciences I, Ltd. v. Merck*, 331 F.3d 860, 867 (Fed. Cir. 2003); *NeoRx Corp. v. Immunomedics, Inc.*, 877 F. Supp. 202, 207 (D.N.J. 1994); *Farmaceutisk Laboratorium Ferring A/S v. Solvay Pharms., Inc.*, 25 U.S.P.Q.2d (BNA) 1344, 1349-50 No. 1:89-CV-1972-JOF, 1992 WL 421542 (N.D. Ga. Sept. 9, 1992); *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F. Supp. 1379, 1395 (N.D. Cal. 1987), *superseded* by *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269 (N.D. Cal. 1991)).

269. *Integra*, 331 F.3d at 866, 868.

270. *NeoRx*, 877 F. Supp. at 207.

271. *Id.* at 209.

272. *Id.* at 213.

273. *Solvay*, 25 U.S.P.Q.2d at 1350.

274. *Id.* at 1350-51 (citing *Merck & Co. v. Biocraft Labs., Inc.*, 874 F.2d 804, 806 (Fed. Cir. 1989) (filing ANDA technically constitutes patent infringement); *Zenith Labs., Inc. v. Bristol-Meyers Squibb Co.*, 24 U.S.P.Q.2d 1641, No. CIV-A-91-3423, 1991 WL 267892, at *7-8 (D.N.J. Dec 12, 1991) (filing ANDA may constitute patent infringement); *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269, 1289-90 (N.D. Cal. 1991) (filing for pre-market FDA approval without substantial departure from past activity precludes finding of infringement)).

sequence Arg-Gly-Asp (RGD peptide).²⁷⁵ The RGD sequence promotes beneficial cell adhesion by interacting with $\alpha\beta 3$ receptors on cell surfaces.²⁷⁶ A scientist at Scripps Research Institute (Scripps) discovered that blocking the $\alpha\beta 3$ receptors inhibits angiogenesis (process for generating new blood vessels).²⁷⁷ Merck hired Scripps to identify potential drug candidates for inhibiting angiogenesis and formed an agreement to fund the “necessary experiments to satisfy . . . regulatory (FDA) requirements for the implementation of clinical trials.”²⁷⁸ Integra offered Merck licenses to their RGD-related patents when they learned of the Scripps-Merck agreement.²⁷⁹ After Merck rejected the offer, Integra alleged infringement of their RGD-related patents.²⁸⁰ At trial, the jury found Merck liable for infringing four out of five patents.²⁸¹ The district court found Merck’s general biomedical research was not exempt under the safe harbor provision.²⁸² The Scripps-Merck experiments did not provide information for FDA approval, but rather identified drug candidates for future clinical testing under the FDA processes.²⁸³ The Federal Circuit stated the “Scripp [experiments] was not ‘solely for uses reasonably related’ to clinical testing for FDA [approval].”²⁸⁴ The court reasoned the FDA has no interest in the identification of drugs, which may or may not undergo clinical trials.²⁸⁵ “The safe harbor [provision] does not reach any exploratory research that may rationally form a predicate for future FDA clinical [trials].”²⁸⁶ The Federal Circuit affirmed the district court’s interpretation because the language of the safe harbor provision does not embrace general biomedical research.²⁸⁷

Immunomedics, Inc. (Immunomedics) shipped samples of its products to the Committee for Proprietary Medicinal Products

275. *Integra*, 331 F.3d at 862. “The RGD peptide sequence promotes cell adhesion to substrates in culture and *in vivo*.” *Id.*

276. *Id.*

277. *Id.* at 863. The inhibition of angiogenesis was a promising means of halting tumor growth by starvation of the rapidly dividing malignant cells. *Id.* The anti-angiogenic therapies were a possible means of treating diabetic retinopathy, rheumatoid arthritis, psoriasis, and inflammatory bowel disease. *Id.*

278. *Id.*

279. *Id.*

280. *Id.*

281. *Integra*, 331 F.3d at 863.

282. *Id.*

283. *Id.* at 865.

284. *Id.* at 866.

285. *Id.*

286. *Id.* at 867.

287. *Integra*, 331 F.3d at 868.

(CPMP) of the European Community, Hong Kong, and Canada for approval in those countries.²⁸⁸ The district court decided that shipping products overseas to regulatory agencies is not exempt under the safe harbor provision because it is not reasonably related to FDA approval.²⁸⁹ The court stated if data is first submitted for FDA approval, the subsequent submission of the same data for foreign regulatory approval is not an infringing activity.²⁹⁰ The shipment of vials to foreign clinical investigators is exempt if the test results are submitted for FDA approval.²⁹¹ However, the court implied that the submittal of fraudulent data is not reasonably related to FDA approval even though the evidence was insufficient to support a finding of fraudulent intent.²⁹² The district court denied summary judgment of non-infringement for shipment of samples to foreign regulatory agencies, which were not first submitted for FDA approval, and shipment of vials to foreign clinical investigators whose results were not submitted to the FDA.²⁹³

In *Solvay*, the district court stated “[t]here is no question that upon the FDA’s approval of an NDA, a potentially infringing party leaves the safe harbor protection afforded by section 271(e)(1)’s provisions.”²⁹⁴ The court recognized an apparent split of opinion whether filing an NDA removes a potential infringer from the safe harbor provision.²⁹⁵ If a potential infringer leaves the safe harbor provision upon filing an NDA, the question is what effect would this have on the “meaningful preparation” requirement for declaratory judgment.²⁹⁶ *Solvay* argued it met the “meaningful preparation” requirement because they conducted clinical trials at substantial cost for the purpose of filing an NDA.²⁹⁷ Without deciding whether filing an NDA removes a potential infringer from the safe harbor provision, the court held

288. *NeoRx*, 877 F. Supp. at 207.

289. *Id.*

290. *Id.* at 208.

291. *Id.* at 209.

292. *Id.* at 213.

293. *Id.* at 214.

294. *Solvay*, 25 U.S.P.Q.2d at 1350.

295. *Id.* at 1350-51 (citing *Merck*, 874 F.2d at 806 (filing ANDA technically constitutes patent infringement); *Zenith*, 1991 WL 267892, at *7-8 (filing ANDA may constitute patent infringement); *Intermedics*, 775 F. Supp. at 1289-90 (filing for pre-market FDA approval without substantial departure from past activity precludes finding of infringement)).

296. *Id.* at 1350.

297. *Id.*

Solvay's activities were exempt under the safe harbor provision because they were preparing to file an NDA.²⁹⁸

Genentech, Inc. (Genentech) allegedly infringed patents for a protein known as Factor VIII:C which is essential for blood clotting.²⁹⁹ The patent claims a highly purified Factor VIII:C and a process for deriving it from human blood plasma.³⁰⁰ In 1981, Genentech began research into producing human Factor VIII:C through recombinant technology, which would eliminate the risk of transmitting infectious diseases from a tainted blood supply.³⁰¹ By April 1984, Genentech had succeeded in manufacturing recombinant Factor VIII:C using a ground-breaking process.³⁰² In April 1986, Genentech filed a European patent application claiming "human Factor VIII" and recombinant methods for its production.³⁰³ Genentech used a human Factor VIII:C prepared by Speywood Laboratories to determine the protein content, amino acid sequence structure and functional properties.³⁰⁴ The district court found the use of the human Factor VIII:C produced by Speywood Laboratories infringed the patent because it was prepared using the identical process.³⁰⁵ Scripps conceded the Factor VIII:C was produced from human plasma using monoclonal antibodies to Factor VIII:C not Factor VIII:RP.³⁰⁶ Clearly, the Factor VIII:C produced using the ground-breaking recombinant process did not infringe the product-by-process claims because it was produced using a different process.³⁰⁷ However, Genentech's plasma-derived Factor VIII:C infringed the product claims because it was a purified Factor VIII:C having the characteristics of human Factor VIII:C.³⁰⁸ Likewise, the recombinant Factor VIII:C infringed the products claims of

298. *Id.* at 1352.

299. *Scripps*, 666 F. Supp. at 1382.

300. *Id.*

301. *Id.* at 1384. The recombinant technology had not previously produced proteins as large as Factor VIII:C, which consisted of a chain of 2,332 amino acids in the blood stream. *Id.* The gene for Factor VIII:C was too large to transplant using the current technology. *Id.* The coding information for Factor VIII:C was interspersed over less than 5% of the gene. *Id.* A "complete strand of cDNA containing the essential coding information, inserted in a plasmid, was transplanted into a baby hamster kidney cell." *Id.* The gene controlled the synthesis of Factor VIII:C in the hamster kidney cell as it would in a human cell. *Id.*

302. *Id.* at 1384.

303. *Id.* at 1384-85.

304. *Id.* at 1384.

305. *Scripps Clinic*, 666 F. Supp. at 1388.

306. *Id.*

307. *Id.*

308. *Id.* at 1390.

purity and potency.³⁰⁹ The district court decided Genentech's use of the Factor VIII:C was not exempt under the safe harbor provision.³¹⁰ The court reasoned Genentech's activities were not solely related to FDA approval even if they were reasonably related.³¹¹ The sales and uses were clearly beyond the scope of the safe harbor provision because the activities served multiple purposes unrelated to FDA approval.³¹²

D. Manipulating the Hatch-Waxman System

1. FDA Review and Approval

The FDA accepts applications for drug approval, determines the appropriate action based on safety and efficacy studies, and supports the public's interest in approving drugs.³¹³ In an ANDA, the generic manufacturer relies on the studies performed by the pioneer drug company.³¹⁴ In certifying their application, the generic manufacturer must refer to the pioneer's listed patents.³¹⁵ The Paragraph IV Certification must certify the applicable listed patent is invalid, or will not be infringed on a claim-by-claim basis.³¹⁶ The Hatch-Waxman Act requires the pioneer drug company to submit to the FDA a list of all patents which claim an FDA approved drug or a method of using the drug.³¹⁷ After NDA approval or issue of subsequent patents, the NDA holder has thirty days to register their patents.³¹⁸ The failure to comply with FDA registration requirements creates a bar to Paragraph IV ANDA infringement lawsuits.³¹⁹

2. Drug Patent Listing and ANDA Approval

The FDA publishes the registered patents in the APPROVED

309. *Id.* at 1395.

310. *Id.* at 1396.

311. *Scripps Clinic*, 666 F. Supp. 1396. Genentech also submitted a European patent application, formed an agreement with Cutter Laboratories (Cutter) to develop a commercial-scale manufacturing process, and sold proprietary rights to Cutter for a substantial sum. *Id.*

312. *Id.*

313. Sarah M. Yoho, Note, *Reformation of the Hatch-Waxman Act, An Unnecessary Resolution*, 27 NOVA L. REV. 527, 538 (2003) (citing 21 U.S.C. § 355(b) (2000)).

314. *Id.* (citing 21 U.S.C. § 355(c)).

315. *Id.*

316. S. 812, 107th Cong., § 103 (2002), available at <http://thomas.loc.gov/home/c107query.html>.

317. Yoho, *supra* note 313, at 538 (citing 21 U.S.C. § 355(b), (c) (2000)).

318. S. 812, § 103.

319. *Id.*

DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, known as the Orange Book.³²⁰ The Orange Book elevates each patent listed as a potential source of delay for generic competition.³²¹ As pioneer drug companies and generic manufacturers have learned,

the Orange Book can be a strategic weapon, providing an advanced warning mechanism to the marketing department for possible tactical response, and giving the patent/NDA holder almost automatic injunctive relief for even marginal infringement claims. Adding to a patentee/NDA holder's advantage is FDA's long-standing policy of avoiding patent disputes, as evidenced by its willingness to list in the Orange Book virtually any patent submitted by an NDA holder and its refusal to hear any challenge to the adequacy or completeness of a generic applicant's Paragraph IV certification.³²²

The FDA rules encourage NDA holder's to "evergreen their drug patents" by filing and refiling improvement patents for the same basic drugs.³²³ Under FDA rules, the Orange Book is supposed to list only drug patents.³²⁴ If a generic applicant disputes the relevancy of a listed patent, the generic manufacturer could notify the FDA and state its grounds for the dispute.³²⁵ Unless the NDA holder voluntarily agrees to amend

320. FOOD AND DRUG ADMIN., CTR. FOR DRUG EVAL. & RES., APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, available at <http://www.fda.gov/cder/ob/default.htm> (last updated Dec. 22, 2003).

321. Mahn, *supra* note 135, at 250.

322. *Id.* (citing 59 Fed. Reg. 50,345 (Oct. 3, 1994)).

323. *Id.* The generic manufacturer's cite as examples of such evergreening "claims for disectable tablets and special coatings, new formulations, crystalline forms of the same drug, and variations on drug delivery technologies." *Id.*

324. *Id.* at 250 (citing 21 C.F.R. § 314.53(b) (1998)). The FDA defines "drug patents" as including drug ingredients, drug formulations and compositions, and methods of use. *Id.* at 250-51. (citing 21 C.F.R. § 314.53(b)). Although methods of manufacturing are not eligible for Orange Book listing, some intermediate patents may be eligible if they satisfy the FDA's definition of "active ingredient." *Id.* at 251 (citing 21 C.F.R. § 210.3(b)(7) (1998)). The definition of active ingredient includes components that may undergo chemical change in the manufacture of the drug and be present in the final product in a modified form intended to furnish the specific activity or effect. *Id.* at n.50. A "component does not have to be present in the final drug product." *Id.* (citing Ben Venue Labs. v. Novartis Pharm. Corp., 10 F Supp. 2d 446, 456-57 (D.N.J. 1998)).

325. *Id.* at 251.

the information, the FDA will not modify the Orange Book.³²⁶ The FDA regulations expressly require a generic applicant to submit an appropriate certification for each patent listed even when there is a valid dispute.³²⁷ Neither the FDA nor the courts have addressed whether a false patent declaration is sanctionable under the FDA rules because a “trip-wire” listing can give rise to counterclaims by generic applicants, or possible sanctions from a court under Rule 11 of the Federal Rules of Civil Procedure.³²⁸

Prior to 2003, generic manufacturers challenged the propriety of Orange Book listings without success because they lacked a viable mechanism to challenge listings.³²⁹ In one case, Bristol-Meyers Squibb (Bristol-Meyers) listed a patent claiming “a method of using BuSpar for all its approved [uses].”³³⁰ Danbury Pharmacal, Inc. (Danbury) challenged the listing because the patent claimed the metabolic product of BuSpar, not the drug itself.³³¹ Bristol-Meyer responded by saying the patent claimed a method of using BuSpar and the metabolic product.³³² The court stated:

“it is paramount to keep in mind that the FDA, in deciding to make an Orange Book listing, is not acting as a patent tribunal. It has no expertise—much less any statutory franchise—to determine matters of substantive patent law. In making its decision to list a patent, it is entirely appropriate and reasonable for the FDA to rely on the patentee’s declaration as to coverage. . . .”³³³

326. *Id.* (citing 21 C.F.R. §§ 314.53(b), 314.94(a)(12)(vii)).

327. *Id.* (citing 21 C.F.R. § 314.94(a)(12)).

328. *Id.* (citing FED. R. CIV. P. 11). The pioneer company will submit to the FDA a new method of use, new labeling or a new patent, which covers a generic copy of the original patent. Powell-Bullock, *supra* note 101, at 29-30 (citing Chris Adams & Gardiner Harris, *Drug Makers Face Battle to Preserve Patent Extensions—Governors Join Businesses, Labor Unions in Effort to Hasten Generics to Market*, WALL ST. J., Mar. 19, 2002, at 24). The pioneer company submits the patent listing immediately before the generic manufacturer planned to introduce the generic drug into the market and files an infringement lawsuit to trigger the thirty-month stay on competition. *Id.* at 30. This strategy guarantees the brand-name drug additional years of market exclusivity and millions of dollars of profits. *Id.*

329. *See, e.g.* Mylan Pharms., Inc. v. Thompson, 139 F. Supp. 2d 1, 19-21 (D.D.C. 2001), *rev’d on other grounds*, 268 F.3d 1323 (Fed. Cir. 2002); Watson Pharm., Inc. Henney, 194 F. Supp. 2d 442 (D. Md. 2001).

330. Watson Pharm., Inc. Henney, 194 F. Supp. 2d 442, 444 (D. Md. 2001).

331. *Id.*

332. *Id.*

333. *Id.* at 445.

In a related case, Mylan Pharmaceutical, Inc. (Mylan) challenged Bristol-Meyer's BuSpar metabolite patent listing in another court.³³⁴ The district court granted injunctive relief because the metabolite patent did not "claim the approved product" as required by FDA listing regulations.³³⁵ The injunction directed Bristol-Meyers to de-list the patent from the "Orange Book," and directed the FDA to grant final approval of Mylan's ANDA for a generic version of buspirone.³³⁶ The Federal Circuit reversed because they found the declaratory relief was not available under patent laws and was not created under the Hatch-Waxman Act.³³⁷ In response, the Medicare, Prescription Drug, Improvement, and Modernization Act of 2003 (MPDIMA) created a mechanism for challenging improper Orange Book listings.³³⁸

As an interesting twist to the problem, a generic manufacturer attempted to compel the FDA to list its patent in the Orange Book.³³⁹ Although only the NDA holder can submit patents for listing, AaiPharma, Inc. sought to have its patent listed in the Orange Book along with the NDAs patents.³⁴⁰ The Fourth Circuit concluded the FDA does not violate the Administrative Procedure Act because they have a "purely ministerial role regarding Orange Books listings."³⁴¹ The MPDIMA does not create a mechanism for a non-NDA holder to list a patent in the Orange Book.³⁴²

3. Paragraph IV ANDA Infringement Lawsuits

Several pioneer companies have taken advantage of the ability to trigger the thirty-month stay of generic competition.³⁴³

334. Mylan Pharms., Inc. v. Thompson, 139 F. Supp. 2d 1, 4 (D.D.C. 2001), *rev'd on other grounds*, 268 F.3d 1323 (Fed. Cir. 2002).

335. Mylan Pharms., Inc. v. Thompson, 268 F.3d 1323, 1328 (Fed. Cir. 2002).

336. *Id.* at 1325.

337. *Id.*

338. Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066, 2450-2451 (2003)(codified in 21 U.S.C. § 355); *see infra* part VII.

339. AaiPharma, Inc. v. Thompson, 296 F.3d 227, 233 (4th Cir. 2002). Because only the NDA holder can submit patents for listing in the Orange Book, AaiPharma asked Eli Lilly & Co. (Eli Lilly) to submit their patent. *Id.* Eli Lilly refused to avoid conferring Orange Book benefits to a competitor. *Id.* If a patent is not listed in the Orange Book, ANDA applicants are not required to file a Paragraph IV Certification, and the patent holder is not eligible for the thirty-month stay on competition. *Id.* at 232.

340. *Id.* at 233.

341. *Id.* at 230.

342. 21 U.S.C. § 355(a)(1)(2003).

343. Susan R. Miller, *Protecting Patents, Some Giant Brand-Name Drug Makers Using Delay Tactics to Keep Generic Competitors at Bay*, MIAMI DAILY BUS. REV., May 20,

In many cases, the subsequent listed patent is essentially the same as the original patent.³⁴⁴ Eli Lilly & Company (Eli Lilly) had essentially two patents for Prozac — one for the compound fluoxetine hydrochloride and one for the administration of fluoxetine hydrochloride.³⁴⁵ Similarly, AstraZeneca had one patent for Prilosec and another for Nexium, which is merely half of the Prilosec molecule.³⁴⁶ Bristol-Meyers Squibb Company (Bristol-Meyers) listed two patents for BuSpar—one for the compound buspirone and one for the composition of buspirone in the human stomach.³⁴⁷

Eli Lilly & Company submitted additional patent listings to protect its popular brand-name drug, Prozac.³⁴⁸ In December 1995, Barr Laboratories, Inc. (Barr) filed an ANDA for a generic antidepressant consisting of fluoxetine hydrochloride, which is the active ingredient in Prozac.³⁴⁹ In April 1996, Eli Lilly filed a Paragraph IV ANDA infringement lawsuit against Barr.³⁵⁰ The FDA could not approve Barr's ANDA until the end of the thirty-month stay or the date the court decided the patent is invalid or not infringed.³⁵¹ The Federal Circuit found Eli Lilly had two

2002, at A10.

344. NAT'L INST. FOR HEALTH CARE MGMT. RESEARCH AND EDUC. FOUND., CHANGING PATTERNS OF PHARMACEUTICAL INNOVATION 19 (2002), available at <http://www.nihcm.org/innovations.pdf>. From 1989 and 2000, 35% of new drugs approved used new active ingredients (NMEs) and rest used active ingredients already available on the market. *Id.* at 7. "Over half (54%) were incrementally modified drugs (IMDs) or new versions of medicines whose active ingredients were already available in an approved product." *Id.* The rest (11%) were new drugs, "which contained the same active ingredient as identical marketed products." *Id.* The FDA rated 58% of NMEs and 85% of IMDs as standard drugs, which provided no significant clinical improvement over existing products. *Id.* at 7-8.

345. *Eli Lilly & Co. v. Barr Labs.*, 251 F.3d 955, 959 (Fed. Cir. 2001)(concluding that Eli Lilly staggered the timing of its patents to extend its monopoly beyond the usual seventeen-years).

346. Gardiner Harris, *Drug Prices—Why They Keep Soaring—Fast Relief: As a Patent Expires, Drug Firm Lines Up Pricy Alternative—Prilosec's Maker Is Switching Users to a Lookalike Pill While It Thwarts Generics—Mr. Young Scrapes to Afford It*, WALL ST. J., June 6, 2002, at A1 (stating that AstraZeneca used the thirty-month stay on generic competition to launch its successor heartburn drug, Nexium). In March 2001, Astra introduced a successor heartburn drug, Nexium. *Id.* It spent \$487 million on a promotional campaign to switch Prilosec users to Nexium, known as the "new purple pill" in their advertising campaigns. *Id.* By April 2002, Prilosec's market share decreased from 49 to 25 percent and Nexium's increased to 19 percent. *Id.*

347. *In re Buspirone Patent Litig.*, 185 F. Supp. 2d 363, 365-66 & n.1 (S.D.N.Y. 2002). Buspirone hydrochloride is the acid salt of buspirone. *Id.* at 365 n.1.

348. *Eli Lilly*, 251 F.3d at 959.

349. *Id.* at 958.

350. *Id.* Several actions were consolidated because Eli Lilly had also filed infringement lawsuits against the other ANDA applicants including Geneva Pharmaceuticals, Inc., Apotex, Inc., and Bernard C. Sherman. *Id.*

351. 21 U.S.C § 355(c)(3)(C)(i)(2003).

patents for the same drug—one for the compound fluoxetine hydrochloride and one for the administration of fluoxetine hydrochloride.³⁵² The court concluded Eli Lilly's patents were not patentably distinct and thus invalid.³⁵³ Even though the patent was invalid, the infringement lawsuit triggered an automatic thirty-month stay on generic competition, which provided a significant marketing and profit advantage for the pioneer company.³⁵⁴

Similarly, AstraZeneca (Astra) submitted additional patent listings to protect its blockbuster heartburn drug, Prilosec, commonly known as the "purple pill" in their advertising campaigns.³⁵⁵ In June 2000, Mutual Pharmaceutical Company (Mutual) filed an ANDA for a generic ten milligram felodipine tablet, and an amendment for a 1.5 milligram tablet and a five milligram tablet.³⁵⁶ The ANDA contained three Paragraph IV certifications, one for each tablet.³⁵⁷ In September 2000, Astra filed a Paragraph IV ANDA infringement lawsuit arguing Mutual's notice letters failed to explain how the generic product would not infringe its patent.³⁵⁸ Even though Eli Lilly admitted neither precedent nor statute established a legal remedy for an incomplete ANDA notice,³⁵⁹ the infringement lawsuit triggered the thirty-month stay on competition, which enabled Astra to generate huge additional profits.³⁶⁰ As in the previous example, the FDA could not approve Mutual's ANDA until the end of the

352. *Eli Lilly*, 251 F.3d at 959, 971.

353. *Id.* at 972. In 2000, Eli Lilly generated \$2.7 billion in Prozac domestic sales. Rafeal Gerena-Morales, *Substitute Will Push Up Co-Payments for Prozac*, TAMPA TRIB., July 31, 2001, at 1.

354. Joseph Brown, *Prozac for the Long Term: Eli Lilly & Co. Introduces Prozac Weekly*, MED. AD. NEWS, May 1, 2001, at 1. In August 2000, Eli Lilly introduced Sarafem, a new brand-name for fluoxetine, which is the active ingredient in Prozac. *Id.* In March 2001, Eli Lilly also introduced a successor depression drug, Prozac Weekly, the first and only prescription medication that is administered weekly for depression. *Id.* With patent protection until 2017, Eli Lilly anticipates that Prozac Weekly will dominate the market. *Id.*

355. Harris, *supra* note 346, at A1.

356. *AstraZeneca v. Mut. Pharm. Co.*, 221 F. Supp. 2d 528, 531-32 (E.D.Pa. 2002).

357. *Id.*

358. *Id.* at 531-32. Although the district court acknowledged the notice was "far from exemplary," it concluded Astra failed to show the "defective notice has prejudiced them" or "inadequate notice constitutes an actionable violation under the Hatch-Waxman Act." *Id.* at 534.

359. *Id.* at 534.

360. Ronald D. White, *Key Drug Patent Ruling Nears; Courts: Effort to Block Generic Versions of Prilosec Could Set Trend in the Industry*, L.A. TIMES, May 28, 2002, at B1; Harris, *supra* note 346, at A1. In 2001, Astra generated \$3.7 billion in Prilosec domestic sales. Ronald D. White, *Key Drug Patent Ruling Nears; Courts: Effort to Block Generic Versions of Prilosec Could Set Trend in the Industry*, L.A. TIMES, May 28, 2002, at B1.

thirty-month stay or the date the court decided the patent is invalid or not infringed.³⁶¹

Bristol-Meyers Squibb Company (Bristol-Meyers) submitted an additional patent listing to protect its blockbuster anxiety drug, Buspar.³⁶² In 1980, Bristol-Meyers obtained a patent for buspirone for the treatment of anxiety.³⁶³ Within one day of the patent's expiration, Bristol-Meyers listed a second patent in the Orange Book covering the uses of buspirone when they knew the uses would be in the public domain after the original patent expired.³⁶⁴ On the same day, Bristol-Meyers filed Paragraph IV ANDA infringement lawsuits against generic manufacturers, which triggered the automatic thirty-month stay on FDA approval of the generic products.³⁶⁵ In response, the end-payor plaintiffs, Mylan, Watson and thirty States raised state law causes of action for anti-trust, unfair competition, deceptive trade practices, and unjust enrichment arising out of Bristol-Meyer's patent listing activities.³⁶⁶ The plaintiffs alleged the Schein settlement agreement, which included a confidentiality provision, was a cover-up for an illicit payment of \$72.5 million to delay generic competition and create the illusion of patent validity for the other generic manufacturers.³⁶⁷ The district court held Bristol-Meyer was not entitled to *Noerr-Pennington* immunity against claims arising out of its allegedly fraudulent listing of a patent in the Orange Book of approved products, and the antitrust claims arising out of the Schein settlement agreement was time-barred because more than four-years had elapsed.³⁶⁸ The court explained:

361. 21 U.S.C § 355(c)(3)(C)(i)(2003).

362. *In re Buspirone Patent Litig.*, 185 F. Supp. 2d 363, 366 (S.D.N.Y. 2002).

363. *Id.* at 365.

364. *Id.* at 366.

365. *Id.* (citing 21 U.S.C. § 355(j)(5)(B)(iii) (2001)).

366. *Id.* at 366-67.

367. *Id.* at 377-78.

368. *In re Buspirone Patent Litig.*, 185 F. Supp. 2d at 380-81. "Neither the Supreme Court nor the Federal Circuit has addressed whether the *Walker Process* exception applies to fraudulent patent listing in the Orange Book along with subsequent infringement lawsuits to exploit the listing for anticompetitive advantage." *Id.* at 373 (citing *Walker Process Equip., Inc. v. Food Mach. & Chem. Corp.*, 382 U.S. 172, 177-78 (1965)). In creating the *Walker Process* doctrine, the Supreme Court explained a claim alleging an initial fraud on the Patent & Trademark Office would avoid *Noerr-Pennington* immunity because "[t]he far-reaching social and economic consequences of a patent. . . give the public a paramount interest in seeing that patent monopolies spring from backgrounds free from fraud or other inequitable conduct and that such monopolies are kept within their legitimate scope." *Id.* The district court stated the same considerations apply to fraudulent patent listings because a company can effectively extend a patent monopoly by listing in the Orange Book and then subsequently filing a Paragraph IV ANDA infringement lawsuit. *Id.*

Bristol-Meyers could have listed the [second patent] in the Orange Book without subsequently bringing infringement lawsuits against Mylan and Watson, and Bristol-Meyers could Bristol-Meyers have brought these suits without relying on its Orange Book listing. What listing does is simply provide the owner of a Patent with a number of additional and automatic benefits under the Hatch-Waxman [Act]. For example by listing a patent that allegedly covers a listed drug or method of using a listed drug, a pioneer drug company obtains (1) the right to receive notice of any ANDA from applicants seeking FDA approval of a generic form of the drug who have filed a Paragraph IV certification with regard to the patent in question; (2) a grace period of forty-five days in which to bring a patent infringement suit against any such applicant before the applicant can file a declaratory judgment action; and (3) if the pioneer drug company brings such lawsuit, a stay of up to thirty-months of the FDA' approval of the ANDA.³⁶⁹

Although they would lose these benefits by not listing the second patent, Bristol-Meyer could still file an infringement lawsuit against the generic manufacturers for a declaration of its rights.³⁷⁰ The Paragraph IV ANDA infringement lawsuit is one of many approaches to delaying generic competition in the market.

4. Pioneer-Generic Anti-Competitive Agreements

In response to settlement agreements, the Federal Trade Commission (FTC) has challenged the legality of paying generic manufacturers millions of dollars to delay generic competition.³⁷¹ The generic manufacturers gain substantially less profits than the pioneer companies lose because the generic competition dramatically reduces the market price.³⁷² As a result, both parties

369. *Id.* at 372 (citing *Eli Lilly*, 496 U.S. at 677-78).

370. *Id.*

371. Powell-Bullock, *supra* note 101, at 36.

372. *Hearing on Genetic Pharm.: Marketplace Access and Consumer Issues Before the Senate Commerce, Sci., and Energy Comm.*, (2002) (statement of Timothy Muris, Chairman, Fed. Trade Comm'n) at 6-7, available at <http://commerce.senate.gov/hearings/042302muris.pdf> [hereinafter Muris Testimony].

have economic incentives to delay generic competition through collusion.³⁷³ The FTC's first-generation litigation focused on agreements to delay generic competition.³⁷⁴ The FTC has intervened successfully in two settlement agreement cases, which were resolved by consent order.³⁷⁵

The first case involved the Abbot-Geneva settlement agreement relating to Hytrin.³⁷⁶ The Commission alleged Abbott Laboratories (Abbot) paid Geneva Pharmaceuticals, Inc. (Geneva) \$4.5 million per month to delay the introduction of its generic product.³⁷⁷ Geneva had allegedly agreed to delay the introduction of any product until final resolution of the patent infringement litigation or market introduction by another generic manufacturer.³⁷⁸

The second case involved the Hoechst-Andrx agreement relating to Cardizem CD.³⁷⁹ The Commission alleged Hoechst Marion Roussel (Hoechst) paid Andrx Corporation (Andrx) over \$80 million to refrain from introducing its generic product.³⁸⁰ As the first ANDA filer, Andrx allegedly used its 180-day market exclusivity rights to delay other generic competition.³⁸¹

The consent "orders prohibited the respondent companies from entering into brand/generic agreements pursuant to which a generic company that is the first ANDA filer with respect to a particular drug agrees not to: (1) enter the market with a non-infringing product, or (2) transfers its 180-day marketing exclusivity rights."³⁸² The companies were required to obtain court approval with advance notice to the Commission for any settlement agreements providing payment to delay generic competition.³⁸³ Advance notice to the Commission was also required for such agreements in non-litigation contexts.³⁸⁴

The FTC's second-generation litigation focused on eliminating improper Orange Book listings.³⁸⁵ Unlike the settlement cases, an improper Orange Book listing involves an

373. *Id.*

374. *Id.* at 7-8.

375. *Id.*

376. *Id.* at 7.

377. *Id.*

378. Muris Testimony, *supra* note 373, at 7.

379. *Id.*

380. *Id.*

381. *Id.*

382. *Id.* at 8.

383. *Id.*

384. Muris Testimony, *supra* note 373, at 8.

385. *Id.* at 9.

abuse of the Hatch-Waxman system to restrain trade.³⁸⁶ Such improper conduct has raised *Noerr-Pennington* issues — an area of longstanding Commission interest.³⁸⁷ The *Noerr-Pennington* doctrine was never intended to protect the “misuse of government processes.”³⁸⁸

In re Buspirone, the Commission had an opportunity to clarify the *Noerr-Pennington* doctrine.³⁸⁹ Bristol-Meyer Squibb Company (Bristol-Meyer) allegedly filed an improper Orange Book listing to delay generic competition with its BuSpar product, in violation of the Sherman Act.³⁹⁰ Bristol-Meyers responded by filing a motion to dismiss and raising a claim of *Noerr-Pennington* immunity.³⁹¹ The Commission filed an *amicus* brief, opposing the motion to dismiss.³⁹² The district court accepted most of the Commission’s arguments and denied Bristol-Meyer’s immunity claim.³⁹³ The court reasoned two exceptions to the *Noerr-Pennington* doctrine — the *Walker Process* and “sham” exceptions — would preclude a finding of antitrust immunity even if Orange Book filings constituted petitioning the government.³⁹⁴ After the *Buspirone* decision, an improper Orange Book listing may be remedied without substantial interference from the *Noerr-Pennington* doctrine.³⁹⁵

5. Direct-to-Consumer Advertising Campaigns

Pioneer companies are also using direct to consumer (DTC) advertising campaigns to enhance their blockbuster drug profits.³⁹⁶ Under the Federal Food, Drug, and Cosmetic Act (FFDCA) the FDA requires manufacturers, and distributors who

386. *Id.*

387. *Id.* The *Noerr-Pennington* doctrine provides antitrust immunity for individuals who are petitioning the government. *Id.* (citing *United Mine Workers of Am. v. Pennington*, 381 U.S. 657, 670 (1965); *E.R.R. Presidents Conference v. Noerr Motor Freight, Inc.*, 365 U.S. 127, 136 (1961)).

388. *Id.* (citing ROBERT H. BORK, *THE ANTITRUST PARADOX: A POLICY AT WAR WITH ITSELF* 364 (Free Press 1993)).

389. *Id.* at 10 (citing *In re Buspirone Patent Litig.*, 185 F. Supp. 2d at 370-71).

390. *Id.* at 10-11.

391. *Id.* at 11.

392. *Id.*

393. *Id.* (citing *In re Buspirone Patent Litig.*, 185 F. Supp. 2d at 380-81).

394. *Id.* (citing *Walker Process Equip., Inc. v. Food Mach. & Chem. Corp.*, 382 U.S. 172, 177 (1965)).

395. Muris Testimony, *supra* note 373, at 12.

396. *Recent Developments Which May Impact Consumer Access to, and Demand for, Pharm. Before the Subcomm on Health of the House Comm. on Energy Commerce* (2001) (statement of Janet Woodcock, Director, Food and Drug Admin., *Statutory and Regulatory Authority*, available at <http://energycommerce.house.gov/107/hearings/6132001Hearing276/Woodcock412.htm> (last visited Jan 18, 2004) [hereinafter Woodcock Testimony].

advertise prescription drugs to disclose in advertisements “information in brief summary relating to side effects, contraindications, and effectiveness. . .”³⁹⁷ For forty-years, the FDA has required “prescription drug advertisements cannot be false or misleading, cannot omit material facts, and must present a fair balance between effectiveness and risk information.”³⁹⁸ There are three categories of prescription drug ads.³⁹⁹ The product-claim advertisements, which make representations about a prescription drug, must include a fair balance of risks and benefits.⁴⁰⁰ A help-seeking advertisement informs the customer about a specific disease and advises him to discuss possible treatments with his physician.⁴⁰¹ The FDA does not regulate help-seeking ads because the drug is not mentioned or implied.⁴⁰² The FDA regulations exempt the reminder advertisement from risk disclosure requirements because the ad is directed towards healthcare professionals and not the patient.⁴⁰³ By the mid-1990s, reminder advertisements were on television.⁴⁰⁴ The ads were extremely confusing to consumer because they did not mention the drug.⁴⁰⁵

In August 1997, the FDA announced a draft guidance that clarified the Agency’s interpretation of the existing regulations.⁴⁰⁶ By August 1999, the FDA issued the guidance in final form following a detailed review period.⁴⁰⁷ The regulations required broadcast advertisements to include a toll-free telephone number, referral to print ads in a concurrent publication, access to product brochures, or referral to a healthcare provider.⁴⁰⁸ As a result, Pioneer drug companies could produce product-claim advertisements without including a fair balance of risks and benefits in the ad.

After this change, the promotional spending on direct-to-

397. Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified, as amended, at 21 U.S.C. § 352 (n)).

398. Woodcock Testimony, *supra* note 397, *Statutory and Regulatory Authority* (citing 21 C.F.R. § 202.1).

399. *Id.*

400. *Id.*

401. *Id.*

402. *Id.*

403. *Id.*

404. Woodcock Testimony, *supra* note 397, *Evolution of DTC Promotion*.

405. *Id.*

406. *Id.*

407. *Id.* (citing Guidance for Industry: Consumer-Directed Broadcast Advertisements, 21 C.F.R. § 202.1 (1999), 64 Fed. Reg. 43,197, available at <http://www.fda.gov/cder/guidance/1804fnl.html>).

408. *Id.* at 6.

consumer advertising has grown from \$1.1 billion in 1997 to \$2.5 billion in 2000.⁴⁰⁹ As a result, physicians prescribed 146 drugs for every 100 office visits in 1999 compared to 109 drugs for every 100 office visits in 1985.⁴¹⁰ A recent study revealed direct-to-consumer advertising has a profound effect on the drugs most frequently prescribed.⁴¹¹ The study found 80% of the heavily marketed drugs, which were approved within the past few years, were among the top 20% of drugs physicians prescribed.⁴¹² In contrast, a mere 10% of drugs not heavily marketed were in the top 20%.⁴¹³

V. FTC RECOMMENDATIONS

In response to the anti-trust litigation, the FTC designed a study to access the practices of pioneer drug companies and generic manufacturers.⁴¹⁴ The purpose of the study was to examine whether the Hatch-Waxman 180-day market exclusivity and thirty-month stay provisions have encouraged generic competition or facilitated anti-competitive behavior.⁴¹⁵ Based on the collected data, the FTC released its report in July 2002 and recommended two modifications to the Hatch-Waxman Act.⁴¹⁶ First, the FTC recommended the Hatch-Waxman Act be amended to allow only one thirty-month stay per ANDA application.⁴¹⁷ Second, the FTC supported the Drug Competition

409. NAT'L INST. FOR HEALTH CARE MGMT., PRESCRIPTION DRUGS AND MASS MEDIA ADVERTISING 3 (2001), available at <http://www.nihcm.org/pharm.html>.

410. *Id.* at 4.

411. *Id.* at 6 (citing Donald K. Cherry et al., NAT'L CTR. FOR HEALTH STATISTICS, NATIONAL AMBULATORY MEDICAL CARE SURVEY: 1999 SUMMARY, Advance Data Report No. 322 (2001), available at <http://www.cdc.gov/nchs/products/pubs/pubd/ad/ad.html>).

412. *Id.* In 1999, the FDA sponsored a telephone survey that focused on the national probability sample of patients who had visited their doctor within three months prior to the survey. Woodcock Testimony, *supra* note 397, *Research on DTC Promotion*. Of the patients who discussed a drug with their doctor: 81% said that the doctor welcomed the question; 50% said that the doctor prescribed the drug discussed; and 32% said that the doctor recommended a different drug. *Id.* An alarming 24% indicated that the direct-to-consumer ads reduce the need for a doctor to decide which drug is appropriate for the patient. *Id.*

413. NAT'L INST. FOR HEALTH CARE MGMT., PRESCRIPTION DRUGS AND MASS MEDIA ADVERTISING 6 (2001), available at <http://www.nihcm.org/pharm.html>.

414. FED. TRADE COMM'N, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY i, (2002), available at <http://www.ftc.gov/os/2002/07/genericdrugsstudy.pdf> [hereinafter FTC Study 2002].

415. Fed. Trade Comm'n, Agency Information Collection Activities; Submission of OMB Review; Comment Request, available at <http://www.ftc.gov/os/2001/02/v000014.htm>.

416. FTC STUDY 2002, *supra* note 415, at ii. The study discovered the pioneer drug company may receive multiple thirty-month stays if it listed additional patents after the generic manufacturer filed its first ANDA application. *Id.* at iii.

417. *Id.* at ii. The study revealed generic market entry is delayed when the pioneer

Act, which requires pioneer drug companies to provide agreements relating to the manufacture, marketing or sale of a generic drug, or the 180-day market exclusivity to the Department of Justice (DOJ) and the FTC.⁴¹⁸

After release of FTC's recommendations, President George W. Bush proposed a new FDA regulation to expedite generic drug approvals.⁴¹⁹ The FDA approved this regulation in its entirety.

VI. NEW FDA REGULATION

Effective August 19, 2003, a new FDA regulation clarifies the types of patents which may be listed in the Orange Book.⁴²⁰ Any patents claiming metabolites, intermediate, or packaging features may not be submitted for listing.⁴²¹ Polymorph patents may be submitted for listing if they contain the same active ingredient as the approved product.⁴²² For polymorph patents, the applicant shall certify he has test data establishing the polymorph performs as well as the original drug product, including demonstration of bioequivalence and comparative in vitro dissolution testing.⁴²³ The new declaration forms require the applicant to certify the patent being submitted is a product-by-process patent, which the product is novel rather than the process.⁴²⁴ This certification is intended to eliminate the submittal of process patents, which cannot be submitted for Orange Book listing.⁴²⁵ Any patent information claiming approved methods of use must identify each individual claim and the corresponding indication in the approved drug labeling.⁴²⁶

If a patent holder lists a patent after the filing of a generic ANDA, the new regulations specify no additional notice needs to be provided by the applicant following re-certification to the

drug company and the generic manufacturer enter a private agreement to prevent triggering the 180-day generic exclusivity period. *Id.* at vii-viii.

418. *Id.* at viii.

419. President George W. Bush, *Remarks by the President on Prescription Drugs* (Oct. 21, 2002), available at <http://whitehouse.gov/news/releases/2002/10/print/20021021-2.html>.

420. 21 C.F.R. § 314.53(b)(1) (2003).

421. *Id.* A metabolite is a chemical compound created when the body metabolizes the active ingredient of a drug product. FTC STUDY 2002, *supra* note 415, at A-40.

422. FTC STUDY 2002, *supra* note 415, at A-41. Polymorph patents claim a chemical compound differing from the active ingredient that has FDA approval. *Id.* at A-40-41.

423. 21 C.F.R. § 314.53(b)(2).

424. Application for FDA Approval to Market a New Drug, 68 Fed. Reg. 36,676, 36,680 (June 18, 2003) (codified at 21 C.F.R. § 314.53 (c)(2)(i)(L)).

425. *Id.* at 36,676.

426. *Id.* at 36,682. The applicant must also publish this information under the "use code description" in the Orange Book. *Id.*

later-listed patent.⁴²⁷ The patent holder will not have the opportunity to file a subsequent infringement suit to invoke an additional thirty-month stay on generic competition.⁴²⁸ The regulations effectively limit the patent holder to one thirty-month stay per ANDA application.⁴²⁹

VII. RECENTLY ENACTED AND PROPOSED LEGISLATION

A. *Medicare, Prescription Drug, Improvement, and Modernization Act of 2003*

In December 2003, Congress passed the Medicare, Prescription Drug, Improvement, and Modernization Act of 2003 (MPDIMA).⁴³⁰ The MPDIMA includes provisions from the Greater Access to Affordable Pharmaceuticals Act of 2002 (GAAP).⁴³¹ The GAAP amendments are intended to tighten loopholes in the Hatch-Waxman Act and expedite generic market entry.⁴³²

B. *Greater Access to Affordable Pharmaceuticals Act of 2002*

In early 2002, Senator John McCain introduced the Greater Access to Affordable Pharmaceuticals Act of 2002 (GAAP), which proposed reform to the Hatch-Waxman Act.⁴³³ Although the GAAP passed the Senate with an overwhelming margin, the House failed to act on the bill.⁴³⁴ In 2003, a bipartisan compromise passed the Senate (94-1) on June 19, 2003.⁴³⁵ The

427. Food and Drug Admin., *FDA generic drugs final rule: questions and answers*, available at <http://www.fda.gov/oc/initiatives/generics/qna.html>.

428. *Id.*

429. *Id.* The FDA estimates the elimination of multiple thirty-month stays per ANDA application and expedited generic market entry will reduce consumer expenditures for pharmaceutical drugs by \$2.040 billion per year. Application for FDA Approval to Market a New Drug, 68 Fed. Reg. 36,676, 36,700 (June 18, 2003). The savings to generic manufacturers will also be substantial because litigation will be limited to one patent infringement suit per ANDA application. *Id.* at 36,701.

430. Medicare, Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003).

431. *Id.*

432. S. 1225, 108th Cong. (2003), available at <http://thomas.loc.gov/home/c108query.html>.

433. Testimony of Senator Howard M. Metzenbaum (Ret.), Chairman of the Consumer Federation of America, before the Senate Judiciary Committee, regarding Legislative and Regulatory Responses to the FTC Study on Barriers to Entry in the Pharmaceutical Marketplace (June 17, 2003), available at http://www.ama-assn.org/sci-pubs/amnews/pick_03/gvsc0630.htm.

434. *Id.*

435. USA TODAY, available at <http://capwiz.com/usatoday/issueaction/votelist> (last

Medicare, Prescription Drug Improvement, and Modernization Act of 2003 includes provisions from the bipartisan compromise.⁴³⁶

1. Eliminating Multiple Thirty-Month Stays

As with the new FDA regulation, the GAAP amendments would only allow one thirty-month stay per ANDA application.⁴³⁷ The thirty-month stay would be triggered by an infringement lawsuit for a patent listed in the Orange Book prior to the ANDA application.⁴³⁸ As a result, the thirty-month stay would not cause significant delay of generic market entry because the stay would run concurrent to FDA approval, which usually takes 18-25-months.⁴³⁹

2. Challenging Improper Orange Book Listings

Unlike the new FDA regulation, the GAAP amendments do not specify which patent may be listed in the Orange Book.⁴⁴⁰ Instead, the Act creates a mechanism for challenging improper Orange Book listings.⁴⁴¹ If a pioneer drug company lists an improper patent, a court may order the patent holder to delete the patent information from the Orange Book.⁴⁴²

3. Facilitating 180-Day Market Exclusivity

The 180-day market exclusivity provision has been criticized because it creates an incentive for pioneer drug companies and generic manufacturers to enter anti-competitive agreements.⁴⁴³ If the 180-day exclusivity period does not begin to run, the FDA is prohibited from approving any subsequent generic applicants indefinitely.⁴⁴⁴ The GAAP amendments would forfeit the generic manufacturer's rights to market exclusivity if the generic entered

visited Aug. 22, 2004).

436. Medicare, Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003).

437. *Id.*; see also 21 C.F.R. § 314.53(b)(1).

438. Press Release, Sen. Judd Gregg, *Breakthrough, Bipartisan Legislation to Make More Prescription Drugs Affordable, Available Gets Boost* (Jun. 11, 2003).

439. *Id.*

440. S. 1225, § 2(a)(2)(C)(iii)(II).

441. *Id.*

442. *Id.*

443. Robin J. Stongin, *Hatch-Waxman, Generics, and Patents: Balancing Prescription Drug Innovation, Competition, and Affordability*, Nat'l Health Pol'y Forum Background Paper, June 21, 2002, available at <http://www.tufts.edu/communications/stories/120401BallooningCosts.htm>.

444. FTC STUDY 2002, *supra* note 415, at vii.

into an anti-competitive agreement with the pioneer drug company.⁴⁴⁵ The 180-day market exclusivity would be awarded to the next generic applicant.⁴⁴⁶

4. Requiring Bioequivalence Testing

The FDA will not approve a generic drug without bioequivalence testing.⁴⁴⁷ Typically, bioequivalence is determined by measuring absorption rate of the drug into the bloodstream.⁴⁴⁸ For topical drugs, the FDA requires different test to determine bioequivalence.⁴⁴⁹ In some instances, pioneer drug companies have challenged the tests and have delayed FDA approval of the generic drug.⁴⁵⁰ The GAAP amendments clarify the FDA's authority to establish special tests provided the tests are scientifically valid.⁴⁵¹

C. Drug Competition Act of 2001

Several legislators have introduced the Drug Competition Act, which target the pioneer-generic anti-competitive agreements.⁴⁵² The Act is designed to 1) provide timely notice to the DOJ and the FTC regarding pioneer-generic agreements, which could delay generic market entry; and 2) to enhance the enforcement of anti-trust laws and competition laws.⁴⁵³ A pioneer drug company and generic manufacturer, which enter into an agreement regarding either 1) the manufacture, marketing or sale of a generic drug would compete with the brand-name drug; or the 180-day market exclusivity period, must file the agreement with the Attorney General and the FTC.⁴⁵⁴ The parties must file within ten-days after executing the agreement

445. Press Release, Sen. Judd Gregg, *Breakthrough, Bipartisan Legislation to Make More Prescription Drugs Affordable, Available Gets Boost* (Jun. 11, 2003).

446. *Id.*

447. *Id.*

448. *Id.*

449. *Id.*

450. *Id.*

451. S. 1225, § 4(a).

452. Press Release, Sen. Charles Schumer, *Gregg-Schumer Generic Drug Amendment Passes Full Senate* (June 19, 2003), available at http://www.senate.gov/~schumer/SchumerWebsite/pressroom/press_releases/PR01804.pf.html. The Senate bill, S. 754, was sponsored by Senator Patrick Leahy and co-sponsored by Senators Herb Kohl, Charles Schumer, Richard Durbin, and Russell Feingold. *Id.* The House bill, H.R. 1530, was sponsored by Representative Henry Waxman and co-sponsored by Representatives Marion Berry, Peter Deutch, Fortney "Pete" Stark, and Sherrod Brown. *Id.*

453. S. 754, 107th Cong. § 3 (2001), available at <http://thomas.loc.gov/home/c107query.html>.

454. *Id.* § 5.

an explanation the purpose of the agreement and discuss the impact on the production, manufacture, or sale of the generic drug product.⁴⁵⁵ If the parties fail to comply, they may be subject to a civil penalty of \$10,000 per day for non-compliance.⁴⁵⁶

On October 18, 2001, the Senate Judiciary Committee approved the Drug Competition Act by a voice vote.⁴⁵⁷ In July 2002, the FTC recommended passage of the bill when it released the report on the generic pharmaceutical marketplace.⁴⁵⁸ The Senate passed the Act on November 18, 2002, and referred it to the House Committee on the Judiciary.⁴⁵⁹ The House failed to vote on the bill before Congress closed session.

VIII. CONCLUSIONS

In 1984, the Hatch-Waxman Act sought to induce pioneer drug companies to invest in the research, development and approval of new prescription drugs; and to encourage generic manufacturers to market cheaper, generic copies of those drugs. Initially, the Hatch-Waxman Act was effective in promoting an unprecedented increase in generic drugs.⁴⁶⁰ As development costs have risen, the pharmaceutical industry has aggressively manipulated the Hatch-Waxman system to increase drug profits.

Although the new FDA regulation and recently enacted MPDIMA should relieve some of the abuses, they do not define the activities protected by the safe-harbor provision, address generic manufacturer's filing of multiple non-final ANDAs or prohibit the pioneer-generic anti-competitive agreements.⁴⁶¹ More legislation will be required to restore the balance of the Hatch-Waxman system. Until such legislation is enacted, the consumer is at the mercy of the pharmaceutical industry and will ultimately bear the cost of litigation.

Teresa J. Lechner-Fish

455. *Id.* §§ 5, 6.

456. *Id.* § 7.

457. *Senate Panel Approves Bill on Generic Drug Availability*, NAT'L J. CONG. DAILY, Oct 18, 2001, available at LEXIS, News & Business Library, News File, <http://www.lexisnexis.com>.

458. FTC STUDY 2002, *supra* note 415, at viii.

459. Press Release, Sen. Patrick Leahy, *Senate Passes Leahy Bill Targeting Sweetheart Deals That Delay Low-Cost Generic Drugs* (No. 19, 2002), available at <http://www.senate.gov/~leahy/press/200211/111902.html>.

460. PhRMA INDUSTRY PROFILE 2003, *supra* note 11, at 61-62.

461. Medicare, Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003); see also S. 1225, 108th Cong. (2003).