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GENERIC COMPETITION AND PHARMACEUTICAL INNOVATION: THE DRUG PRICE COMPETITION AND PATENT TERM RESTORATION ACT OF 1984

*James J. Wheaton**

I.	Genesis of the Act	437
A.	The Movement to Generic Drugs	437
1.	Generics in the Drug Approval Process	439
2.	Generics in the Market	442
a.	Physician Prescribing Habits	442
b.	Pharmacist Dispensing Behavior	446
3.	<i>Roche v. Bolar</i> : Restricting Generic Testing	447
B.	The Case for Patent Term Extension	448
1.	Loss in Effective Patent Life	451
2.	Loss from Generic Competition	454
3.	Legislative Attempts To Restore Incentives for Innovation	456
II.	The Drug Price Competition and Patent Term Restoration Act of 1984	458
A.	Progeneric Provisions of the Act	458
1.	ANDAs	458
2.	Statutory Reversal of <i>Roche v. Bolar</i>	462
B.	Pro-Brand Manufacturer Provisions of the Act	463
1.	Market Exclusivity Periods	463
2.	Patent Term Extension	465
III.	Impact of the Act on the Marketing and Use of Generic Substitutes	467
A.	Barriers to Generic Substitution	468

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1. Brand-Name Product Advertising	468
2. Physician and Pharmacist Behavior	470
3. Erosion of Product Life Due to Patent Term Extension and Market Exclusivity	470
4. Administrative Delay by the Food and Drug Administration	471
B. Incentives to Generic Substitution.....	474
1. Drug Substitution Laws	475
2. Medical Reimbursement Programs	476
IV. Impact of the Act on Pharmaceutical Innovation.....	478
A. Averting Losses from Competition.....	479
B. Lost Improvements in Drug Therapy Due to New Uses ..	481
C. The Disincentive Created by the Statutory Reversal of <i>Roche v. Bolar</i>	484
V. Conclusion.....	486

The Drug Price Competition and Patent Term Restoration Act of 1984¹ (the Act), the first major federal drug legislation enacted by Congress since 1962, has been extolled by some observers as creating many winners but no losers. The Act simplifies the federal drug approval process for generic copies of brand-name pharmaceuticals, and attempts to stimulate pharmaceutical research and development by guaranteeing market exclusivity to innovative drug products. Consumer savings from the greater availability of generic drugs that may be generated by the Act have been predicted at one billion dollars during the next decade,² and the Act's market exclusivity and patent term extension provisions are designed to encourage pharmaceutical innovation.

The Drug Price Competition and Patent Term Restoration Act is an outgrowth of demands for legislative relief by two segments of the pharmaceutical industry: the marketers of brand-name and generic drugs.³ Many

1. Pub. L. No. 98-417, 98 Stat. 1585 (1984).

2. See H.R. REP. NO. 857, pt. 1, 98th Cong., 2d Sess. 17, reprinted in 1984 U.S. CODE CONG. & AD. NEWS 2647, 2650 (\$920 million saved in next 12 years from generic copies of drugs first approved after 1962); Kushner, *More RPh's Choose Generics; Long and Short-Term Data Show Trend Gaining Strength*, AM. DRUGGIST, Oct. 1984, at 23 (one billion dollars in savings from Act); *Prescription for Cheap Drugs*, TIME, Sept. 17, 1984, at 64 (one billion dollar potential savings over next 12 years).

3. For ease of reading, this article labels companies that produce generic drugs as "generic" or "production-intensive" firms, and those responsible for pioneer drugs as "brand-name" or "research-intensive" companies. This terminology is not meant to ignore the trend to production of generic copies of brand-name drugs by traditionally research-intensive firms. These so called "branded generics" will be increasingly important as the market for generic copies of high dollar-volume drug products expands during the next several years.

brand-name drug manufacturers develop pioneer drug products and rely on the market exclusivity guaranteed by patents to assure returns on their investments in innovation. The development and marketing of drugs in the United States are governed by the federal Food, Drug, and Cosmetic Act, which is administered by the Food and Drug Administration (FDA), and drug products sold in the United States often undergo a lengthy process of securing FDA approval prior to marketing. For years, the brand-name pharmaceutical industry lobbied Congress to enact patent extension legislation, claiming that the lengthy drug approval process had eroded the effective patent protection for new drug products far below the seventeen-year grant contemplated by the federal patent statute. Representatives of generic drug producers and consumer groups, however, uniformly opposed patent term restoration.

Similarly, the generic segment of the drug industry asserted that the FDA drug approval process, by forcing generic equivalents of already-approved pioneer drugs to undergo or reproduce the tests conducted for pioneer products, unfairly delayed drug price competition. Generic firms, as well as many consumer groups, sought congressional relief from the FDA's failure to simplify the approval process for generic copies of already-approved drugs. Without patent term restoration, however, brand-name manufacturers were unwilling to endorse changes that would permit generic drugs to compete more readily with their pioneer products.

In 1984, Congress enacted legislation that combined the legislative priorities of the competing industry groups. The Drug Price Competition and Patent Term Restoration Act enables manufacturers of generic drug products to submit their products for approval under an abbreviated New Drug Application (ANDA) procedure. The Act also amends the patent statute to permit the use of a patented drug product in the preparation of tests required by the FDA. The Act addresses the concerns of research-intensive pharmaceutical firms by creating market exclusivity periods for various classes of new drug products and by authorizing patent extensions of up to five years for pharmaceuticals whose remaining exclusive marketing life after FDA approval is less than fourteen years.

Although the Act is likely to affect both the quality and cost of drug therapy, the enthusiasm exhibited by its supporters may not be fully justified.⁴

4. See *supra* note 2. When he signed the Act in September 1984, President Reagan declared that the Act "will save [consumers] more than a billion dollars over the next 10 years . . . and promote medical breakthroughs and drug innovation." President's Remarks on Signing the Drug Price Competition and Patent Term Restoration Act of 1984, 20 WEEKLY COMP. PRES. DOC. 1359, 1359 (Sept. 24, 1984). This glowing outlook has not been adopted by all commentators. See *The Price for More Generic Drugs*, 224 SCI. 369, 369 (1984) (quoting Wil-

The Act's benefits to consumers, generic drug manufacturers, and brand-name drug companies will not accrue simultaneously. As generic manufacturers seek to enter the market, the provisions of the Act that ease the approval of generic drugs will have an immediate effect; the exclusivity and patent extension provisions that are intended to benefit brand-name manufacturers, on the other hand, apply only to products approved by the FDA after January 1, 1982. The Act's market exclusivity periods may stimulate pharmaceutical research and development, but even if this occurs, the benefits of increased innovation will be experienced in the future, and the costs of market exclusivity will be similarly delayed.

The benefits of generic competition, by contrast, will materialize sooner, but will eventually be subject to the offsetting costs of market exclusivity for products for which generic competition will be forestalled. Because even without the changes created by the Act the patents on many new drug products would not have expired for several years, the full effect of patent extension and market exclusivity on the future generic market will not be seen until late in this decade or early in the next. Similarly, the anticipated fruits of the parallel stimuli to research and development in the Act will not reach the market before the end of the 1980's. This lag between the early benefits and later costs of the Act has caused skeptics to allege that the Act exchanges a short-term benefit to competition for a long-term cost to consumers.

This article critiques the Drug Price Competition and Patent Term Restoration Act of 1984. Part I traces the background of the two major sections of the Act by examining the recent trend toward generic competition in the pharmaceutical industry and the need perceived by some industry observers for additional incentives to pharmaceutical research. Part II of the article describes and discusses the sections of the Act designed to benefit the two segments of the pharmaceutical industry. Part III addresses the likely effect of the Act on generic competition, and Part IV provides a parallel analysis for the research-intensive pharmaceutical firms. The article offers several suggestions for legislative and administrative initiatives that would strengthen the Act and further its twin goals of generic price competition and adequate incentives for pharmaceutical innovation.

liam Schultz, Public Litigation Group); National Ass'n of Pharmaceutical Mfrs., *News Bulletin*, Oct. 1984, at 5 (Act "mortgage[s] the future for the consumer for a short-term gain" (analysis of Milton M. Bass, NAPM general counsel)); M. Bass, *Speech at Regulatory Affairs Professional Society Conference, Perspectives on ANDA/PTR Bill* (Sept. 13-14, 1984) (exclusivity provisions of Act will be "dominant factor in drug competition through the beginning of the next century" (quoting Pink Sheet)).

I. GENESIS OF THE ACT

A. *The Movement to Generic Drugs*

During the past half-century, pharmaceutical marketing in the United States evolved from a system in which pharmaceutical companies supplied bulk chemicals to pharmacists who compounded and sold prescription drugs to one in which the pharmaceutical industry produces finished products and some companies invest in development of new drug therapies.⁵ Patent protection and product differentiation became increasingly important to the innovators of new drugs.⁶ The emergence of counterfeit drug products and the willingness of some pharmacists to substitute counterfeit or duplicate drug products for prescribed brand-name drugs led the industry to press for the enactment of state statutes prohibiting pharmacists from substituting for a brand-name product prescribed by a physician.⁷ South Dakota regulators promulgated an antisubstitution rule in 1955, and by 1972 antisubstitution statutes or regulations existed in almost every state.⁸ Most of these state laws required that pharmacists dispense the exact product specified by the prescriber; thus, pharmacists were free to fill prescriptions with generic products only if the prescription was written with the product's generic name, rather than with a brand name.

This restriction on the growth of the generic drug market generated consumer and industry pressure that caused a shift in the legislative attitude toward product substitution by pharmacists. By the late 1970's, antisubstitution laws had been repealed or amended in every jurisdiction,⁹ and by mid-1984, every state had enacted a generic substitution law.¹⁰ The new laws allow pharmacists to substitute equivalent generic products unless the prescribing doctor signs a line on the prescription that indicates his unwillingness to permit substitution, or unless he writes out a phrase such as "Dispense As Written" or "Do Not Substitute." Substitution is limited by state formularies that either designate drug products that are equivalent

5. See BUREAU OF CONSUMER PROTECTION, FED. TRADE COMM'N, DRUG PRODUCT SELECTION 15-17 (1979).

6. *Id.* at 16-17.

7. *Id.* at 143-51. Because of the enactment of antisubstitution legislation, brand-name manufacturers could insulate their market share by creating brand-name recall in physicians and pharmacists, who would tend to prescribe and dispense brand-name drug products.

8. *Id.* at 149-50.

9. See *Prescription for Cheap Drugs*, *supra* note 2, at 65; COMPTROLLER GENERAL OF THE UNITED STATES, PROGRAMS TO CONTROL PRESCRIPTION DRUG COSTS UNDER MEDICAID AND MEDICARE COULD BE STRENGTHENED 40-47, 51-54 (1980).

10. A. MASSON & R. STEINER, GENERIC SUBSTITUTION AND PRESCRIPTION DRUG PRICES: ECONOMIC EFFECTS OF STATE DRUG PRODUCT SELECTION LAWS 1 (1985) (Staff Report of the Bureau of Economics, Federal Trade Comm'n).

(positive formularies) or products that are not interchangeable (negative formularies).¹¹

The generic pharmaceutical market has also been spurred by the ability of competing pharmacies to advertise the availability of generic drugs¹² and by cost-control pressures imposed by private and federal medical reimbursement programs.¹³ The future for generic drugs is bright: by 1988 drug products that accounted in 1984 for over four billion dollars in annual sales will have gone off patent.¹⁴ In its 1979 report on drug product selection, the Federal Trade Commission described the maximum potential savings from substitution of generic copies for brand-name products as \$400 to \$500 million per year.¹⁵ The predicted boom in the generic market has led many

11. The FDA has provided a source for the compilation of state formularies by publishing a list that contains approved drug products and evaluations of therapeutic equivalence. *See* 45 Fed. Reg. 72,582 (1980) (authorizing release of evaluations of equivalence); *see also* 21 C.F.R. § 20.117(a)(3) (1985) (list with therapeutic equivalence evaluations available from FDA).

A recent study concludes, rather suprisingly, that the existence of any formulary, positive or negative, discourages substitution, *see* A. MASSON & R. STEINER, *supra* note 10, at 98-99, and that positive formularies are associated with fewer substitutions than negative formularies. *Id.* at 71-72, 99. *But see* Zeich, *One-line Rx Forms Boost Drug Substitution*, DRUG TOPICS, Jan. 17, 1984, at 37-38 (finding opposite result); *infra* notes 248-49 and accompanying text (advocating a national positive formulary).

12. In *Virginia State Bd. of Pharmacy v. Virginia Citizens Consumer Council, Inc.*, 425 U.S. 748 (1976), the Supreme Court held that the advertising of prescription drug prices is protected commercial speech.

To the extent that consumers will choose between pharmacies on the basis of differences in prescription costs, interpharmacy competition will lead to greater substitution of generic drugs. A. MASSON & R. STEINER, *supra* note 10, at 35-36. In particular, large drug store chains should experience economies of scale in inventory selection and advertising, although one study has shown no significant variations in substitution rates among chain and independent pharmacies. *Id.* at 57-59, 60. Another study found no increase in generic prescribing, despite competition among pharmacies, for prescriptions on which a brand-name product was prescribed. Kralewski, Pitt & Dowd, *The Effects of Competition on Prescription-Drug-Product Substitution*, 309 NEW ENG. J. MED. 213, 215 (1983).

13. *See* BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 44-45; *see also infra* notes 250-61 and accompanying text.

14. *See* Mabon, Nugent & Co., *Generic Drug Industry Monitor No. 6: Summary and Analysis of "The Drug Price Competition and Patent Term Restoration Act of 1984,"* 3 (Oct. 11, 1984) (investment newsletter). One author estimated that the share of the entire market accounted for by patented drugs would be only 55% by the end of 1985. P. TEMIN, *TAKING YOUR MEDICINE* 152 (1980).

15. BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 196. A recently released Federal Trade Commission study provides a more detailed empirical analysis of the potential savings from generic substitution. The study evaluated 1980 data from 48 states and the District of Columbia on prescriptions for 45 multisource drug entities. A. MASSON & R. STEINER, *supra* note 10, at 7-8. The study showed that cost savings from generic substitution were between \$44 and \$80 million in 1980, but more than doubled to \$130-236 million by 1984. *Id.* at 30-31, 178-80. In 1980, the rate of substitution by pharmacists was 5.5%, *id.* at 9, and that statistic escalated to 9.5% in 1984. *Id.* at 19-20. Moreover, the study authors acknowledged

stock analysts to advise investment in generic firms.¹⁶ In spite of the perceived *potential* market for generic pharmaceuticals, however, the actual rate of generic substitution for brand-name products has grown slowly. Recent studies of generic drug usage show that brand-name products continue to control at least eighty percent of the total market for prescription drugs.¹⁷

Three factors constrained sales of generics before the Drug Price Competition and Patent Term Restoration Act. First, the FDA's drug approval process for generic drugs made it expensive to enter the market with generic copies of some already-approved pioneer drugs. Second, physicians and pharmacists remain reluctant to prescribe or dispense generic drugs. Finally, a recent decision of the United States Court of Appeals for the Federal Circuit created a new stumbling block by preventing potential competitors from conducting the tests necessary to secure FDA approval of generic copies of branded products. This section of the article considers each of these three impediments.

1. *Generics in the Drug Approval Process*

In 1962, Congress amended the Federal Food, Drug, and Cosmetic Act to require that new drugs be proved not only safe, as the Act originally required, but also "effective." Drugs approved prior to the 1962 Amendments were reevaluated for efficacy in the Drug Efficacy Study Implementation (DESI) program. As part of its review of the efficacy of pre-1962 drugs, the FDA formulated an abbreviated New Drug Application (ANDA) procedure under which generic copies of effective pre-1962 drugs could gain approval if shown to be pharmacologically equivalent (bioequivalent) to the pioneer.¹⁸

The FDA failed (or refused), however, to implement a similar ANDA procedure for generic copies of drug products first approved after 1962. For

the understated character of their results as predictors of substitution after enactment of the Drug Price Competition and Patent Term Restoration Act of 1984. *Id.* at 9.

It is worth observing here that savings from substitution are not a pure economic gain for society. Most of the cost savings to consumers, and the increased revenues of generic drug producers, represent wealth transfers from brand-name manufacturers. BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 301; A. MASSON & R. STEINER, *supra* note 10, at 15.

16. See, e.g., A. G. Becker Paribas, Inc., Industry Review: Generic Drug Industry (Apr. 6 1984) (investment newsletter).

17. See, e.g., Goldberg, Aldridge, DeVito, Vidis, Moore & Dickson, *Impact of Drug Substitution Legislation: A Report of the First Year's Experience*, 17 J. AM. PHARMACEUTICAL A. (n.s.) 216, 219 (1977) (almost 19% of prescriptions written generically, but some generically written prescriptions filled with brand-name products); Stewart, Grussing & Purohit, *Drug Product Selection in Illinois: The First Year's Experience*, 20 MED. CARE 831, 836 (1982) (12.6% substitution rate in Illinois).

18. See 21 C.F.R. § 314.56 (1985) (ANDAs permitted for drug products covered by Drug Efficacy Study).

some time it insisted that each application for the approval of a generic drug must be supported by test data of the same quantity and scope that a full New Drug Application (NDA) for a pioneer drug would contain. This agency policy was strengthened by the Supreme Court's 1983 holding in *United States v. Generix Drug Corp.*¹⁹ that a generic copy of an already-approved drug is still a "new drug" within the meaning of the Food, Drug, and Cosmetic Act. The FDA could therefore require that each generic product be individually approved on the basis of a full NDA.

Even before *Generix*, however, the FDA had retreated from its position that a full NDA was necessary for generic copies of approved drugs. The agency concluded that its interest in proven safety and efficacy would be met with a "paper NDA" procedure for approval of generic products.²⁰ The Food, Drug, and Cosmetic Act requires that new drug applications contain "full reports of investigations" demonstrating safety and effectiveness,²¹ and according to the FDA, this requirement could be met by an NDA that relied on published reports of studies sufficient to prove safety and efficacy.²²

The paper NDA procedure did not significantly reduce the cost of gaining approval for generic drugs. Many of the essential studies of a pioneer product's safety and efficacy are sponsored or conducted by the company that holds the drug's patent, and the FDA has concurred in the brand-name drug industry's claim that the reports of such studies, even after submission to the FDA, should receive trade secret protection.²³ Without access to these studies, potential marketers of generic copies could not cite published studies sufficient to demonstrate safety and efficacy.

Consumer groups and generic producers continued to lobby both the FDA and Congress for a procedure that would make approval of generic drugs easier. The ANDA provisions contained in the Drug Price Competition and Patent Term Restoration Act purported to answer that demand, but they were not uncontroversial. Under the Act, a manufacturer may secure FDA approval of a generic copy of an approved drug by showing that the generic product contains the identical active ingredients as, and is bioe-

19. 460 U.S. 453 (1983).

20. See 45 Fed. Reg. 85,052 (1980) (FDA notice defending paper NDA procedure). For descriptions of the controversy surrounding implementation of the paper NDA policy, see *Competition in the Drug Industry: Hearing Before the Subcomm. on Oversight and Investigations of the House Comm. on Energy and Commerce*, 97th Cong., 1st Sess. (1981) [hereinafter cited as *1981 House Competition Hearing*].

21. 21 U.S.C.A. § 355(b)(1)(A) (West Supp. 1985).

22. See 45 Fed. Reg. 85,052 (1980) (FDA notice defending paper NDA procedure).

23. See H.R. REP. NO. 857, pt. 1, 98th Cong., 2d Sess. 35-36, reprinted in 1984 U.S. CODE CONG. & AD. NEWS 2647, 2668-69; 21 C.F.R. § 314.430(f) (1985) (safety and effectiveness data only released under certain circumstances).

quivalent to and bioavailable with, the original drug.²⁴ One possible objection to an ANDA process is an argument traditionally made by brand-name manufacturers—that the lower price of generic pharmaceuticals is partly a reflection of quality and reputational differences between brand-name and generic drugs.²⁵ Yet no recent studies have revealed that generic drugs are inferior,²⁶ and the FDA applies the same manufacturing standards to brand-name and generic firms.²⁷

Bioequivalency and bioavailability are also carefully regulated by the FDA. Two drugs are bioequivalent when they contain the same amount of the identical active ingredient and are bioavailable. Drugs are bioavailable when they have the same rate and extent of absorption.²⁸ FDA regulations assure that approved generic products will have been adequately tested for bioequivalency and bioavailability.²⁹ In many states, pharmacists and physicians are informed of bioequivalent drug therapies through formularies.³⁰ In New York, for example, a positive formulary lists 800 drugs deemed by the FDA to have therapeutic equivalents.³¹

24. See *infra* note 125 and accompanying text.

25. See J. EGAN, H. HIGINBOTHAM & J. WESTON, *ECONOMICS OF THE PHARMACEUTICAL INDUSTRY* 51 (1982); M. STATMAN, *COMPETITION IN THE PHARMACEUTICAL INDUSTRY* 53 (1981); see also D. SCHWARTZMAN, *INNOVATION IN THE PHARMACEUTICAL INDUSTRY* 247 (1976) (drug quality is positively correlated to firm size).

26. See D. SCHWARTZMAN, *supra* note 25, at 226-34 (citing several studies demonstrating inferior drug quality, but none after 1971).

27. See 21 C.F.R. §§ 210, 211 (1985) (good manufacturing practices for drugs); id. § 320 (bioequivalence and bioavailability requirements); Hecht, *Generic Drugs: How Good Are They?*, FDA CONS., Feb. 1978, at 17-18; see also BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 250-51 (FDA enforces product quality standards). But see D. SCHWARTZMAN, *supra* note 25, at 234-35, 247 (FDA needs better inspection procedures for generic manufacturers).

28. 21 C.F.R. § 320.1 (1985). Drugs with the same active ingredient will usually contain different non-active ingredients. A product's mix of active and non-active ingredients is protected as a trade secret, but may vary the biological effect of the drug. See id. § 314.430(g) (1985). Bioequivalence and bioavailability regulations therefore require that drugs with the same active ingredient be tested to assure that their mix of inactive ingredients does not alter bioavailability.

29. See id. § 320 (bioequivalence and bioavailability regulations); BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 124-28; Hecht, *supra* note 27, at 18-20; Kushner, *supra* note 2, at 55 (noting increased FDA and HHS involvement in assessing bioequivalency). But see PMA NEWSLETTER, Dec. 23, 1985, at 3-4 (physician group has asked FDA to revamp its bioequivalency regulations).

30. See COMPTROLLER GENERAL OF THE UNITED STATES, *supra* note 9, at 41-44 (table listing types of formularies established by states).

31. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 160; FDA CONS., Feb. 1978, at 19 (FDA has endorsed New York formulary).

The Federal Trade Commission advocates a Model Drug Product Selection Act that would require the FDA to establish a nationwide positive formulary. See Model Drug Product Selection Act, § 5A, reprinted in BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 281-83.

Thus, until the Drug Price Competition and Patent Term Restoration Act, the absence of a simple procedure for the approval by the FDA of generic drugs constituted a major barrier to an increase in the share of the market held by generics. Even without that impediment, however, other obstacles to the widespread acceptance of generics could be found in the prevalent attitudes of pharmacists and physicians.

2. *Generics in the Market*

Prescription drugs are unique among consumer products in that the purchaser of a drug has no practical market power to select among alternative products.³² Authority over prescribing and dispensing decisions rests with the physician and pharmacist, respectively. The incentives that affect the decisions made by these professionals, however, are not necessarily identical to those that would guide a product selection by the consumer.

a. *Physician Prescribing Habits*

Most prescription drugs have three names: a chemical name describing the chemical structure of the drug's active ingredient, a generic name that represents an abbreviated version of the chemical name of the active ingredient, and any brand name given to the finished drug product by its manufacturer.³³ The generic name is the "official"³⁴ name of a product used in scientific and medical literature and by manufacturers that do not give their product a trade name.³⁵ Brand names are established in order to permit manufacturers to distinguish their version of a drug containing a particular active ingredient from other equivalent products. Most physicians still write prescriptions using the brand name of a drug.³⁶ This reliance on brand names has three bases.

First, the pharmaceutical market emphasizes, through print advertising and direct promotion by manufacturer representatives, the brand-name products of various drug producers. Although drug product advertising serves an informational function by generating knowledge about alternative therapies, a primary purpose of most pharmaceutical promotion is the crea-

32. See Jadow, *Competition and "Quality" in the Drug Industry: The 1962 Kefauver-Harris Drug Amendments as Barriers to Entry*, ANTITRUST L. & ECON. REV., Winter 1971-1972, at 103, 105.

33. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 26-27.

34. Generic names are officially assigned by the Secretary of Health and Human Services, who may designate a name assigned to the drug in an official compendium such as the United States Pharmacopoeia. See 21 U.S.C. § 358 (1982).

35. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 27.

36. See A. MASSON & R. STEINER, *supra* note 10, at 6 (physicians specify brand name in 79.9% of prescriptions).

tion of "brand-name recall" in physicians.³⁷ Because generic names are tongue twisters and brand names are deliberately easy to remember,³⁸ physicians exhibit a preference for brand-name products learned about through sales promotion.³⁹ To some extent, then, the use of brand names by physicians is more a result of habit, encouraged by brand-name manufacturers, than an indicated preference for brand-name drugs.⁴⁰

Second, physicians are typically unaware of the differential between retail prices of brand-name and generic drugs.⁴¹ Patients do not choose among equivalent products by price, but are limited to the product selection made by their physician. Few patients will change physicians merely because their doctor prescribes more expensive drugs, and physicians therefore have little incentive to take advantage of available price information.⁴² Nor will advertising of generic drugs force awareness of the comparative cost of equivalent drugs: generic companies often advertise product lines, but have infrequently promoted individual products.⁴³

Third, although FDA's quality controls for drug production apply to all manufacturers, brand-name drug companies use advertising and direct promotion to create and reinforce the perception that generic drugs are qualitatively inferior to their brand-name counterparts. The obvious incentive to suggest inferiority manifests itself in a variety of negative advertising techniques. One brand-name company recently hired a pharmacy professor to preach the hazards of generic drugs at medical meetings.⁴⁴ Print advertising in medical journals often contains slogans that emphasize the superior qual-

37. See Leffler, *Persuasion or Information?: The Economics of Prescription Drug Advertising*, 24 J.L. & ECON. 45, 47 (1981).

38. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 31.

39. *Id.* at 5-6.

40. See *id.* at 63-64.

41. See *id.* at 64-65.

42. *Id.* at 3. Although the Department of Health and Human Services collects and publishes comparative price data for bioequivalent drug products, physicians rarely rely on this sort of market information. See P. TEMIN, *supra* note 14, at 103-05; Zelnio, *Physician's Use of the Guide to Prescription Drug Costs: An Exploration*, 16 DRUG INTELLIGENCE & CLINICAL PHARMACY 874 (1982).

Physician ignorance of price data is not universal, of course. Such information may be relayed to the doctor by patients who receive continuing drug therapy and express their concern over the cost of their prescriptions. See Reekie, *Price and Quality Competition in the United States Drug Industry*, 26 J. INDUS. ECON. 223, 234 (1978). Physicians may also become aware of the costs of their prescription choices when private or public medical reimbursement programs refuse to reimburse the patient for the difference between a low-cost, usually generic product and its more expensive, brand-name competitor. The reaction of the physician may be anger at the reimbursement program or pharmacy, however, rather than a heightened willingness to prescribe generically.

43. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 50.

44. See Waldholz, *Pillbox War*, Wall St. J., Aug. 13, 1984, at 1, col. 6.

ity of the brand-name drug,⁴⁵ the threat of generic drugs to future pharmaceutical research and development,⁴⁶ and the value to the physician of knowing "exactly what his patients are swallowing."⁴⁷ Some of these claims raise the spectre of potential malpractice liability for prescribing an inferior generic product, though many state substitution laws provide that writing a prescription by a generic name cannot be evidence of a physician's negligence.⁴⁸ The concern generated among physicians by brand-name drug advertising might be dispelled if generic drug companies could advertise that their products have undergone FDA bioequivalency and bioavailability tests and are subject to FDA standards of manufacturing, but current law prohibits the representation or suggestion in labeling or advertising that a drug has been approved by the FDA.⁴⁹

Each of the above phenomena—habit, price ignorance, and negative advertising—works to limit the market share of generic products. However, drug substitution laws dampen this effect. These statutes generally provide that a pharmacist can dispense any product deemed by a formulary to be

45. See, e.g., *Patent Term Restoration Act of 1981: Hearings Before the Subcomm. on Courts, Civil Liberties, and the Administration of Justice of the House Comm. on the Judiciary*, 97th Cong., 1st Sess. 223 (1981) ("What's next . . . generic physicians?" (sample advertisement from medical journal)) [hereinafter cited as *1981 House Hearings*]; *id.* at 224 ("Would you fly a plane with no name?" (LSV Laboratories advertisement)).

46. See, e.g., *id.* at 225 ("Is there a generic equivalent for drug research?" (Roche advertisement)); *id.* at 226 ("In 20 years there could be no new drugs to imitate." (Roche advertisement)).

47. See, e.g., *ANNALS INTERNAL MED.*, Feb. 1985, at I-78 to I-80 ("When it comes to cardiovascular medicine, I like to know exactly what my patients are swallowing.' There are doctors who say that generic drugs have a place in their practice—but not necessarily in the treatment of serious or potentially life-threatening disease." (Ayerst advertisement for Inderal)); *id.* at I-179 to I-180 ("When the Ayerst rep told me it costs about 45¢ a day, I said you can stop right there.'" (Ayerst advertisement for Inderal asking physicians to specify "Dispense As Written" or "Do Not Substitute" on their prescriptions)).

48. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 176 (there has been little discussion of the physician liability issue, but at least 14 states provide that the failure to prescribe by brand name is not evidence of negligence).

The argument that the failure to give an ant substitution instruction could lead to physician malpractice liability was advanced in Brennan, *Drug Substitution—Boon to Consumers Versus Legal Trap for the Professional*, *J. LEGAL MED.*, Mar. 1976, at 20, 25. At the time that article was written, Mr. Brennan was vice-president and general counsel of the Pharmaceutical Manufacturers Association.

49. See 21 U.S.C. § 331(l) (1982). One consumer advocate has claimed that this statutory bar is directly responsible for some of the reluctance of physicians and pharmacists to prescribe and dispense generically. See *The Patent Term Restoration Act of 1983: Hearings Before the Subcomm. on Patents, Copyrights, and Trademarks of the Senate Comm. on the Judiciary*, 98th Cong., 1st Sess. 220 (1983) (statement of Ralph Nader) [hereinafter cited as *1983 Senate Hearings*]. Legislation to remove this restriction passed the House during the 98th Congress. PMA NEWSLETTER, Apr. 8, 1985, at 5. A similar bill introduced in 1985 has passed the House and is pending in the Senate. See *infra* note 245.

equivalent to a prescribed drug unless the physician signs the prescription on a line labeled "Do Not Substitute" or "Dispense As Written" (DAW), or, in some states, unless the doctor *writes out* such an instruction.⁵⁰ The rate of drug substitution varies significantly depending on whether the statute requires the doctor to write out the instruction or allows him merely to sign a line on a preprinted form.⁵¹ If the physician needs only to choose between signing two lines, he may inadvertently or subconsciously sign the DAW or "Do Not Substitute" line, and substitution will be unlawful in some cases where the physician does not actually have a strong preference for the brand-name product.⁵² In states where the physician must write out the antisubstitution instruction, however, studies suggest that physicians do so infrequently.⁵³

Drug substitution laws are therefore more effective in giving generic drugs market access when they require the prescriber to write out language designed to prevent substitution. The Federal Trade Commission's Model Drug Product Selection Act requires doctors to handwrite "medically necessary" in order to prevent the pharmacist from dispensing a product equivalent to the one prescribed.⁵⁴ The Model Act attempts to require physicians to make a "conscious decision" that substitution is medically undesirable.⁵⁵ Nevertheless, even if substitution laws increase the proportion of prescriptions for which substitution is permitted, through provisions such as that contained in the Model Act, the choice between drugs is simply shifted to the pharmacist, who may also be reluctant to dispense a generic product.

50. As of 1979, approximately half of the states required that a physician write out the antisubstitution instruction, and 19 states allowed doctors to bar substitution by signing a line on a preprinted form. BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 163-65.

51. See A. MASSON & R. STEINER, *supra* note 10, at 89-97 (regression analysis of 1980 data on 45 drugs in 48 states).

52. *Id.* at 165, 167.

53. See *id.* at 164 (citing several studies); Goldberg, Aldridge, DeVito, Vidis, Moore & Dickson, *supra* note 17, at 220-21 (doctors specified "Dispense As Written" on only 6.4% of prescriptions in Michigan); Goldberg, DeVito, Smith, Stano, Vidis, Moore & Dickson, *Evaluation of Economic Effects of Drug Product Selection Legislation*, 17 MED. CARE 411 (1979) (in another Michigan study, doctors showed little inclination to use "Dispense As Written" instruction); Zeich, *supra* note 11, at 37 (physicians using one-line forms and required to write out antisubstitution instructions did so only 5% of the time, but substitution was prohibited in 60% of instances where prescriber was required merely to sign on a two-line prescription form).

54. Model Drug Product Selection Act, § 2(b), *reprinted in* BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 275-76. The Maximum Allowable Cost (MAC) program of Medicaid and Medicare contains the same requirement. 42 C.F.R. § 447.332(b)(1) (1985).

55. BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 10.

b. Pharmacist Dispensing Behavior

Pharmacists receive two types of prescriptions: those written with a drug's generic name and those written by brand name. Because pharmacists may fill such prescriptions with a brand-name drug, generically written prescriptions are not always filled with a generic product.⁵⁶ Prescriptions for a brand-name drug may be filled with a generic product whenever a state statute permits substitution and the physician does not give a valid antisubstitution instruction, but most state laws that allow selection of the drug by the pharmacist are permissive, not mandatory.⁵⁷

Pharmacists are more likely to fill prescriptions with generic-name drugs if they are given a financial inducement to do so. Increased use of generic drugs decreases inventory costs because a pharmacy will not stock every brand of a particular drug if it will be permitted to fill most prescriptions for the drug with a generic product.⁵⁸ Pharmacies also take a higher markup on lower-cost generic drugs than they do on brand-name drugs.⁵⁹ Most state drug product selection laws also offer financial incentives. Only a few state substitution laws require the pharmacist to pass on the full savings from substituting a generic drug when a brand-name product was prescribed by the physician; requiring full pass-on might discourage generic dispensing.⁶⁰

56. *Id.* at 47. The Masson and Steiner study indicates that 90% of prescriptions written with a generic name are filled with a generic product, but that no more than 15% of those written by brand name are so filled. A. MASSON & R. STEINER, *supra* note 10, at 40. This result overcomes the argument that low rates of substitution among pharmacists can be attributed to limited inventories: if generic prescriptions are filled generically, the inadequacy of inventories will not explain the failure of pharmacists to substitute. *See id.* at 40-41. Overall, more than 70% of all generic drug products dispensed are from prescriptions written by the drug's generic name. *Id.* at 115-17.

Masson and Steiner acknowledge, however, that substitution rates may be understated because one-fourth of prescriptions are ordered by telephone, and the pharmacist may request permission to dispense generically, so that the prescription may be recorded as written generically even though, if written, the physician might have used a brand name. *Id.* at 119-29.

57. *Id.* at 155-57. Of the statutes in effect in 1980, more than three-fourths provided for permissive substitution. *See* A. MASSON & R. STEINER, *supra* note 10, at 67. The Model Drug Product Selection Act also makes substitution permissive. Model Drug Product Selection Act, § 2(a), reprinted in BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 274. The FTC argues that permissive substitution will be effective as long as the pharmacist retains incentives to substitute. *See infra* notes 58-60 and accompanying text. The Masson and Steiner study concluded that mandatory substitution may not lead to higher rates of substitution. A. MASSON & R. STEINER, *supra* note 10, at 99.

58. BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 88-89.

59. *Id.* at 94; J. EGAN, H. HIGINBOTHAM & J. WESTON, *supra* note 25, at 154; A. MASSON & R. STEINER, *supra* note 10, at 36-37.

60. BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 171-73. *But see* A. MASSON & R. STEINER, *supra* note 10, at 99-100 (empirical analysis suggests that mandatory pass-on provisions do not cause a lower rate of substitution).

The Model Act contains no mandatory pass-on provision. The pharmacist is not permitted

In general, pharmacists are well-enough trained to capably choose among drugs,⁶¹ but the fear of liability resulting from their decision to substitute a generic equivalent for a brand-name product deters many pharmacists from filling prescriptions generically.⁶² By substituting their judgment for the physician's, the argument goes, the pharmacist assumes the risk that the patient will be harmed by the generic product.⁶³ This concern is reinforced in advertising by brand-name pharmaceutical manufacturers,⁶⁴ but is unfounded. First, liability insurance for pharmacists is accessible and premiums for pharmacist insurance are low.⁶⁵ Second, many state substitution laws contain provisions stipulating that drug product substitution is not evidence of negligence.⁶⁶ Finally, the one legal action that has been brought against a pharmacist in which liability was based on the pharmacist's product selection involved the substitution of a product that had not received FDA approval.⁶⁷

3. *Roche v. Bolar: Restricting Generic Testing*

A recent federal court decision created a further barrier for generic manufacturers. In *Roche Products, Inc. v. Bolar Pharmaceutical Co.*,⁶⁸ the United States Court of Appeals for the Federal Circuit held that a company's use of another firm's patented active ingredient to perform the tests necessary to

to substitute, however, unless the substituted product is priced below the prescribed drug. Model Drug Product Selection Act, § 2(c), reprinted in BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 278.

61. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 77-80 (describing four studies demonstrating that pharmacists were more capable of judging bioavailability than physicians); *id.* at 80-83 (in hospitals, pharmacists, rather than physicians, are given responsibility for selecting drugs).

62. See *id.* at 11, 174-75 (in a Florida survey, more than 75% of pharmacists thought they were more vulnerable to malpractice actions under drug substitution laws); OFFICE OF TECHNOLOGY ASSESSMENT, PATENT-TERM EXTENSION AND THE PHARMACEUTICAL INDUSTRY 32 (1981); *Large Drug Firms Fight Generic Substitution*, 206 SCI. 1054, 1055 (1979).

63. See Brennan, *supra* note 48, at 23-24.

64. See *Large Drug Firms Fight Generic Substitution*, *supra* note 62, at 1054-55.

65. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 268 n.19.

66. See *id.* at 175. My recent survey of state substitution statutes found such provisions in 21 states. The substitution must generally be made in accordance with the "prudent practice" of pharmacy or from a state formulary. *Id.*

Despite these laws, however, pharmacists in states with liability limitations are usually unaware of their existence. *Id.* at 176 (citing results of several state studies). Moreover, one recent study indicates that such statutory provisions are not associated with higher rates of substitution by pharmacists. A. MASSON & R. STEINER, *supra* note 10, at 100.

67. A. MASSON & R. STEINER, *supra* note 10, at 73. Apparently, there have been no other claims asserting liability of a pharmacist for a drug product selection. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 265.

68. 733 F.2d 858 (Fed. Cir.), *cert. denied*, 105 S. Ct. 183 (1984).

gain approval of a generic version of the patented drug was an infringing "use" under the federal patent law. The court refused to bring testing by a potential competitor within the "experimental use" exception to the statute's protection of patentholders from unauthorized uses of their inventions.⁶⁹

The decision in *Bolar* fueled the controversy over the future of generic competition. If, as seemed to be the case after *Bolar*, a generic company could not do any tests with a patented active ingredient until after the patent expired, generic competition for patented drugs could be delayed for several years after patent expiration while the generic drug company conducted tests and waited for FDA approval. Because the patented active ingredient is the "drug" to which a generic copy must be equivalent, *Bolar* prevented any testing, including testing for bioequivalence and bioavailability, that made use of the active ingredient. This bar applied even if the generic company obtained the compound legally on the market or from a licensee, or manufactured the compound independently.

This new impediment to the approval of generic products, together with the delay built into the FDA drug approval process and the continuing reluctance of physicians and pharmacists to accept generic pharmaceutical products, provided a new impetus for Congress to dismantle the regulatory barriers to generic drugs. A high-dollar volume of generic drugs would go off patent in the few years after 1984,⁷⁰ and the generic industry rallied behind legislative proposals to require the FDA to accept ANDAs for generic versions of pioneer drugs.

Many members of the research-intensive pharmaceutical industry opposed legislation giving generic drugs easier market access. For several years, however, these companies, and their trade association, the Pharmaceutical Manufacturers Association (PMA), had lobbied for extended patent protection on pioneer drugs. By the mid-1970's, FDA approval of new drugs usually occurred long after the patenting of the drug's original compound, and the research-intensive firms argued that this erosion in "effective patent life" should be compensated by some form of patent term extension.

B. The Case for Patent Term Extension

The FDA requires that a new drug undergo animal tests and extensive clinical investigations prior to approval as a new drug.⁷¹ Because of this lengthy testing process, the total time between synthesis of a potential drug

69. *Id.* at 862-65. See generally Hantman, *Experimental Use as an Exception to Patent Infringement*, 67 J. PAT. OFF. SOC'Y 617 (1985).

70. See *supra* note 14 and accompanying text.

71. See generally Pines, *A Primer on New Drug Development*, FDA CONS., Feb. 1974, at 12.

and its eventual marketing may be as long as thirteen years.⁷² Drug research and development is also risky: the high costs of required tests for new products are accompanied by a low rate of success among chemicals initially tested for pharmacological effects. During hearings on one version of the patent term restoration legislation, for example, PMA's president testified that for each 10,000 chemical molecules synthesized, only one chemical entity eventually reaches the market.⁷³

Many potential drugs are abandoned only after considerable testing; only nine percent of drugs sanctioned to be tested in humans as investigational new drugs (INDs), for instance, eventually receive FDA marketing approval.⁷⁴ The costs and time lag implicit in drug innovation make the decision to develop a new drug costly,⁷⁵ and cost and delay confront potential innovators with disproportionate up-front costs. The costs of drug research and development are borne long before the innovating firm begins to market its product; the financial gains that accrue during the marketing life of a drug, however, have a discounted present value that is greatly diminished by even small additional delays in gaining FDA approval.⁷⁶

72. See SUBCOMM. ON SCIENCE, RESEARCH AND TECHNOLOGY OF THE HOUSE COMM. ON SCIENCE AND TECHNOLOGY, 96TH CONG., 2D SESS., THE FOOD AND DRUG ADMINISTRATION'S PROCESS FOR APPROVING NEW DRUGS 13 (Comm. Print 1980) [hereinafter cited as FDA'S DRUG APPROVAL PROCESS]; see also *Pharmaceutical Innovations: Promises and Problems: Hearing Before the Subcomm. on Natural Resources, Agricultural Research and the Environment and the Subcomm. on Investigations and Oversight of the House Comm. on Science and Technology*, 97th Cong., 1st Sess. (1981) (discussing effects of drug approval process on industry innovation) [hereinafter cited as *1981 House Innovations Hearing*].

73. See *The Patent Term Restoration Act of 1981: Hearing on S. 255 Before the Senate Comm. on the Judiciary*, 97th Cong., 1st Sess. 25 (1981) (statement of Lewis A. Engman, President, PMA) [hereinafter cited as *1981 Senate Hearing*].

74. See Clymer, *The Economics of Drug Innovation*, in *THE DEVELOPMENT AND CONTROL OF NEW DRUG PRODUCTS* 107, 127 (M. Pernarowski & M. Darrach eds. 1972) (one-tenth of investigational new drugs eventually approved as new drugs); Hansen, *The Pharmaceutical Development Process: Estimates of Development Costs and Times and the Effects of Proposed Regulatory Changes*, in *ISSUES IN PHARMACEUTICAL ECONOMICS* 151, 155 (R. Chien ed. 1979) (approval rate of 12%); Wardell, May & Trimble, *New Drug Development by United States Pharmaceutical Firms*, in 32 *CLINICAL PHARMACOLOGY THERAPEUTICS* 407, 408 (NDAs approved between 1976 and 1979 represented only 9% of INDs granted).

75. See generally Clymer, *The Changing Costs and Risks of Pharmaceutical Innovation*, in *THE ECONOMICS OF DRUG INNOVATION* 109 (J. Cooper ed. 1970) (discussing the role of time and development costs in innovation). Much of the costs of drug research and development are blamed directly on FDA regulations and the testing requirements imposed by the 1962 amendments to the Food, Drug, and Cosmetic Act. See Peltzman, *The Benefits and Costs of New Drug Regulation*, in *REGULATING NEW DRUGS* 113, 207 (R. Landau ed. 1973) (1962 amendments created costs equivalent to six percent of total drug sales); Sarett, *FDA Regulations and Their Influence on Future R & D*, *RESEARCH MGMT.*, Mar. 1974, at 18, 18-19 (blaming FDA regulation for high development costs and lengthy testing).

76. See Grabowski & Vernon, *A Sensitivity Analysis of Expected Profitability of Pharmaceutical Research and Development*, 3 *MANAGERIAL & DECISION ECON.* 36, 40 (1982) (an 18-

Increasing development costs were evidenced in studies demonstrating a thirteen-fold jump in the costs of a new drug between 1960 and 1973,⁷⁷ and in a study by Ronald Hansen finding a total cost per new drug of \$54 million by 1976.⁷⁸ But when the PMA adjusted the Hansen study result for inflation to arrive at a per drug development cost of \$87 million, consumer representatives and the production-intensive industry criticized the study. Participation in the Hansen study was voluntary, and included neither all companies nor all new drugs.⁷⁹

In spite of these flaws in the studies, however, the research-intensive industry seemed to many observers to be nearing an innovation crisis: the number of new chemical entities (NCEs) approved by the FDA as new drugs fell by eighty-one percent between 1958 and 1979.⁸⁰ Again opponents of patent term restoration argued that these innovation figures, relied upon by PMA, were deceptive. Representative Gore, who originally opposed patent restoration, contended that the drop in NCEs was attributable to the elimination of drugs with little or no therapeutic value.⁸¹ Other critics pointed out that decreased innovation could not be proven by NCE data because the number of NCEs does not reflect innovation: of pending INDs on October 1, 1980, for example, only forty-three percent were NCEs.⁸² Even so, other studies confirmed some decrease in the rate of innovation measured not only by NCEs, but also in new drug compounds and new dosage forms.⁸³

month decrease in approval time is economically equivalent to adding five years of marketing life to the product); H. Grabowski & J. Vernon, *Studies on Drug Substitution, Patent Policy and Innovation in the Pharmaceutical Industry* (May 1983) (unpublished report), reprinted in *1983 Senate Hearings*, *supra* note 49, at 138, 164.

77. See D. SCHWARTZMAN, *supra* note 25, at 65-70.

78. See Hansen, *supra* note 74, at 180.

79. See *1983 Senate Hearings*, *supra* note 49, at 83, 86-87 (statement of the Generic Pharmaceutical Industry Association (GPIA)). The response rate in the Hansen study was only 56%. See Updegraff, *Commentary*, in *ISSUES IN PHARMACEUTICAL ECONOMICS*, *supra* note 74, at 189.

80. See May, Wardell & Lasagna, *New Drug Development During and After a Period of Regulatory Change: Clinical Research Activity of Major United States Pharmaceutical Firms, 1958 to 1979*, 33 *CLINICAL PHARMACOLOGY THERAPEUTICS* 691, 691 (1983).

81. Gore, *Patent Term Extension: An Expensive and Unnecessary Giveaway*, *HEALTH AFF.*, Spring 1982, at 25, 28.

82. See *Patent Term Extension and Pharmaceutical Innovation: Hearing Before the Subcomm. on Investigations and Oversight of the House Comm. on Science and Technology*, 97th Cong., 2d Sess. 3-4 (1982) (statement of Donna Valtri, Office of Technology Assessment) [hereinafter cited as *1982 House Hearing*].

83. See J. EGAN, H. HIGINBOTHAM & J. WESTON, *supra* note 25, at 106 table 7.1 (new drug innovation between 1950 and 1974); see generally Virts & Weston, *Returns to Research and Development in the U.S. Pharmaceutical Industry*, 1 *MANAGERIAL & DECISION ECON.* 103 (1980) (discussing interrelationship between lower rates of return and decreased innovation).

Advocates of patent extension also tried to document the poor health of the pharmaceutical industry in broader economic terms. Although the pharmaceutical industry has long been heavily concentrated—in 1968 twenty companies controlled nearly ninety percent of the drug market and five companies usually occupied at least fifty percent of most therapeutic sub-markets⁸⁴—pharmaceutical innovation has become increasingly concentrated.⁸⁵ The international competitive position of United States firms has also fallen, as measured by the United States share of world pharmaceutical research and development expenditures, the United States-owned share of new drug introductions, and the market share of pharmaceuticals sold by United States firms.⁸⁶

Much of the blame for these trends in the research-intensive industry has been assigned to two factors: decreasing effective patent life for new drugs and losses from generic competition. The following sections evaluate these claims.

1. Loss in Effective Patent Life

In the context of the pharmaceutical industry, the term “effective patent life” describes the period between FDA approval of a patented drug product and the expiration of that product’s patent. Although it is theoretically possible for effective patent life to exceed the nominal seventeen-year patent grant of the federal patent statute when the FDA approves a drug before the Patent and Trademark Office issues the patent, the effective patent life for drug products is normally less than seventeen years. Much of the loss in effective patent life, if lost patent life is defined as the difference between effective patent life and seventeen years, is accounted for by the time during which innovating firms conduct the tests required to gain FDA approval.

During the 1970’s and early 1980’s, numerous published studies estimated a sharp decline in effective patent life for new drugs. The PMA and research-intensive drug firms asserted that this data justified their call for patent restoration legislation. The results of the different studies varied, but they documented a clear trend: effective patent life prior to the 1962 amendments was near the full seventeen years specified by the patent laws, but for

84. See Jadow, *supra* note 32, at 104-05.

85. See Grabowski & Vernon, *Innovation and Invention: Consumer Protection Regulation in Ethical Drugs*, 67 AM. ECON. REV. 359, 360-61 (1977). One writer argues to the contrary, however, that the pharmaceutical industry is very stable even though the large companies in the industry have continued their dominance. See Cocks, *Product Innovation and the Dynamic Elements of Competition in the Ethical Pharmaceutical Industry*, in *DRUG DEVELOPMENT & MARKETING* 225, 240-45 (R. Helms ed. 1975).

86. See *THE COMPETITIVE STATUS OF THE U.S. PHARMACEUTICAL INDUSTRY* 21-53 (Nat’l Academy Press 1983).

drugs approved in 1981, effective patent life had fallen to less than seven years.⁸⁷

Opponents of patent extension developed several arguments that uncovered flaws in the effective patent life studies. They concluded that many of the studies were biased because they measured effective patent life only for new chemical entities, and not for all drugs.⁸⁸ The studies also calculated effective patent life using the earliest patent applicable to each drug, even though many drugs have multiple patents that can extend the product's practical monopoly beyond the period covered by the earliest patent.⁸⁹ The Generic Pharmaceutical Industry Association countered PMA's estimates of effective patent life with its own calculation that, for the highest selling drug products, effective patent life might be as high as 18.5 years.⁹⁰

Estimates of effective patent life have limited usefulness as tools for justi-

87. See *Drug Legislation: Hearings Before the Subcomm. on Health and the Environment of the House Comm. on Energy and Commerce*, 98th Cong., 1st Sess. 13 (1983) (average effective patent life (EPL) from 1962 to 1970 was 12.5 years, but by the late 1970's had declined to between 9 and 10 years) (FDA staff report submitted by Dr. Mark A. Novitch, Deputy Comm'r, FDA) [hereinafter cited as *1983 House Drug Legislation Hearings*]; *1983 Senate Hearings*, *supra* note 49, at 34-35 (EPL for new chemical entities approved during 1980 and 1981 was 7.06 years in 1980 and 6.72 years in 1981) (statement of Gerald J. Mossinghoff, Acting Deputy Secretary of Commerce and Comm'r of Patents and Trademarks); *1982 House Hearing*, *supra* note 82, at 77 (EPL declined to 6.8 years in 1981) (testimony of Dr. William M. Wardell, Director, Center for the Study of Drug Development); H. GRABOWSKI & J. VERNON, *THE REGULATION OF PHARMACEUTICALS: BALANCING BENEFITS AND RISKS* 50 (1983) (EPL in 1979 was 9.5 years); D. SCHWARTZMAN, *supra* note 25, at 167-73 (mean EPL between 1966 and 1973 was 13.1 years); Eisman & Wardell, *The Decline in Effective Patent Life of New Drugs*, *RESEARCH MGMT.*, Jan. 1981, at 18, 19 (EPL decreased from 13.6 years in 1966 to 9.5 years in 1979); Grabowski & Vernon, *Substitution Laws and Innovation in the Pharmaceutical Industry*, *LAW & CONTEMP. PROBS.*, Winter-Spring 1979, at 43, 59 (EPL in 1977 was 8.9 years); Hutt, *The Importance of Patent Term Restoration to Pharmaceutical Innovation*, *HEALTH AFF.*, Spring 1982, at 6, 16-17 (EPL of 18.2 years in 1950 declined to 8.8 years by 1977) (study by Pracon, Inc.); *id.* at 17 (PMA data for 1980 showed EPL for drugs approved that year was 7.4 years); Statman, *The Effect of Patent Expiration on the Market Position of Drugs*, in *DRUGS & HEALTH: ECONOMIC ISSUES AND POLICY OBJECTIVES* 140, 142 (R. Helms ed. 1981) (EPL was 16.5 years in 1960 but only 9.7 years in 1978).

88. See *supra* note 82 and accompanying text (NCEs account for less than half of drug innovation).

89. See *1982 House Hearing*, *supra* note 82, at 281 (testimony of William F. Haddad, President, GPIA) (specifically criticizing the article by Eisman & Wardell, *supra* note 87).

90. See *1982 House Hearing*, *supra* note 82, at 210-11 (statement of Kenneth N. Larsen, Chairman, GPIA). Peter Hutt, representing the PMA, responded to this study with three criticisms. First, the GPIA study includes only high dollar-volume drugs. Second, many of the drugs on the GPIA list were approved prior to 1968, so the GPIA data does not really conflict with studies estimating effective patent life for drugs first approved in the 1970's. Finally, most of the drugs on the GPIA list would not have been eligible for patent restoration even under the liberal (compared to the 1984 Act) standards for patent extension included in the legislation pending at the time of the GPIA testimony. *Id.* at 171-72 (statement of Peter B. Hutt, on behalf of PMA).

ying patent extension, moreover, because they ignore the reality that many inventions are not ready for marketing at the moment a patent is issued. Even without FDA approval requirements, for example, drug manufacturers would perform tests to measure the safety and efficacy of their new products. All of the effective patent life studies included the time gap between the issuance of a patent and the patentholder's application to have the new product classified as an IND,⁹¹ but the animal tests that take place during the pre-IND period would probably be conducted absent federal regulation. The Drug Price Competition and Patent Term Restoration Act accounts for this bias in effective patent life studies by restoring none of the time that elapses before the IND is filed and only half of the IND pendency period.⁹²

Critics of patent restoration also contended that pharmaceutical innovators abuse the patent process by dilatory techniques like patent application continuances and the substitution of new patent applications for pending applications.⁹³ One study concluded, however, that much of the recent decline in effective patent life is attributable to a decrease in the patent pendency period,⁹⁴ a phenomenon that belies the suggestion that many drug patents are subject to delaying tactics.⁹⁵ Patents for drug compounds are issued an average of twenty-eight months after the patent application is filed,⁹⁶ and for pioneer compounds patents usually issue within two years.⁹⁷

Finally, the practice of obtaining multiple patents on a single pharmaceutical product has been criticized because multiple patents will sometimes extend exclusive marketing rights. Some drugs will be protected not only by a patent that describes the compound (compound patent), but will also be described in patents issued for a drug manufacturing process (process patents) and for methods of use for the drugs (use patents). If process and use patents exclude potential competitors from marketing a drug on which the compound patent has expired, studies based on compound patents will fail to reflect the true length of protection afforded by patents to innovative phar-

91. Gore, *supra* note 81, at 29.

92. See *infra* note 173 and accompanying text.

93. See, e.g., Engelberg, *Patent Term Extension: An Overreaching Solution to a Nonexistent Problem*, HEALTH AFF., Spring 1982, at 34, 38.

94. When drug patents are issued more quickly, the 17-year patent grant begins to run at an earlier stage in the drug development process, and the effective life of the patent is lessened.

95. See 1982 House Hearing, *supra* note 82, at 72 (statement of Dr. William M. Wardell, Director, Center for the Study of Drug Development) (27% of decline in EPL resulted from lessened patent pendency period).

96. See 1983 Senate Hearings, *supra* note 49, at 25 (testimony of Gerald J. Mossinghoff, Acting Deputy Secretary of Commerce and Comm'r of Patents and Trademarks).

97. See 1981 Senate Hearing, *supra* note 73, at 22 (statement of Lewis A. Engman, President, PMA).

maceutical products.⁹⁸ Nevertheless, product and use patents are probably ineffective in extending exclusive rights to drug products. As for any invention, a basic drug compound patent will disclose the original methods of use and manufacture for a patented drug, and a subsequent use or product patent could not bar a generic drug manufacturer from making the drug for its unprotected uses once the patent expires.⁹⁹ Even if continuing use patents theoretically forestall marketing of a generic drug for its still-protected uses, moreover, it will be impossible for the patentholder to police the uses to which pharmacists, physicians, and patients put the generic copy.¹⁰⁰

Even accepting the criticisms that the decline in effective patent life over the last several years was not as dramatic as the research-intensive industry claimed, some real decline in patent protection is evident in the lengthening gap between submission of an IND and eventual FDA approval of new drugs. Patent protection is an important variable in the research and development decision: adequate protection provides the economic incentive that justifies high expenditures during the period of drug development, when the innovating firm makes outlays that can only be recovered, if at all, by long-term sales revenue.¹⁰¹

2. *Loss from Generic Competition*

Patents are valuable to patentholders precisely because they forestall competition. For a limited period of time society tells innovators: "Charge what the market will bear until your patent expires, but at the end of that period the market may limit you to competitive returns." The innovator relies on the exclusive marketing grant, the patent, to guarantee him the opportunity to recover research and development costs plus a real rate of return on that investment. Whether the patentholder's period of exclusive marketing is adequate to capture these economic opportunities depends on two factors: the product life of the drug and the total time necessary to recover the research and development investment. Product life for new drugs is usually long enough. One recent study estimated that the average prescription drug

98. See 1982 House Hearing, *supra* note 82, at 5 (statement of Donna Valtri, Office of Technology Assessment).

99. See *id.* at 169-70 (statement of Peter B. Hutt, on behalf of PMA); 1981 House Hearings, *supra* note 45, at 410 (statement of Gerald J. Mossinghoff, Comm'r of Patents and Trademarks); Hutt, *supra* note 87, at 19.

100. See 1981 House Hearings, *supra* note 45, at 410 (statement of Gerald J. Mossinghoff, Comm'r of Patents and Trademarks).

101. See generally Kiley, *The Importance of Patent Term Restoration to Small, High Technology Companies*, HEALTH AFF., Spring 1982, at 46 (patent protection especially important for small firms); Yorke, *Pharmaceutical Patent Protection*, 4 MEDICINAL RESEARCH REVS. 25 (1984) (defending value of drug patents).

product has a useful life of more than thirty years.¹⁰² Another study calculated that, depending on the various rates of return assumed by the studies' authors, between twelve and nineteen years of exclusive marketing life would be needed by the patentholder to recover his initial cost plus a normal rate of return.¹⁰³

Patents are relatively unimportant, however, unless the patentholder faces a threat of competition once the patent expires. Greater use of generic drugs magnifies the effect of shortened effective patent life on an innovating firm's ability to recover its research and development expenditures. When market competition begins sooner because the patentholder has a shorter period of market exclusivity, the expected losses to competitive products have a greater present value than they would if substitution occurred several years later. Simply stated, the time value of a \$100 loss five years from now will, at every discount rate, be greater than the present value of the same loss in ten years.¹⁰⁴

The extent of post-patent generic competition thus has a crucial impact on the value of patent term extension. If generic competition is insignificant, patent term restoration does not restore much revenue to the brand-name manufacturer.¹⁰⁵ In the past, expiration of patents did not bring an onslaught of generic competitors, and brand-name products suffered only insignificant losses to competition.¹⁰⁶ As the generic market grew, however, the value of patent extension legislation to the research-intensive pharmaceutical industry increased. By delaying the future economic loss from competition, patent extension can make the present value of that loss insignificant. In other words, longer patent life might almost completely offset, for the brand-name manufacturer, the monetary disincentive to innovation posed by the threat of generic competition.¹⁰⁷

102. See M. STATMAN, *supra* note 25, at 34.

103. See Grabowski & Vernon, *supra* note 76, at 36 (at 10% real rate of return recovery would take 19 years, but at 8% discount rate recovery takes only 12 years). The theories of optimum patent life described in the economic literature correspond to the model set out by Grabowski and Vernon. See W. NORDHAUS, *INVENTION, GROWTH, AND WELFARE* 76-86 (1969); Grabowski & Vernon, *supra* note 87, at 63-66; Nordhaus, *The Optimum Life of a Patent: Reply*, 62 AM. ECON. REV. 428 (1972); Scherer, *Nordhaus' Theory of Optimal Patent Life: A Geometric Reinterpretation*, 62 AM. ECON. REV. 422 (1972).

104. Cf. H. GRABOWSKI & J. VERNON, *supra* note 87, at 57-58; Grabowski & Vernon, *supra* note 87, at 48.

105. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 43.

106. See M. STATMAN, *supra* note 25, at 63; Grabowski & Vernon, *supra* note 87, at 60.

107. See Grabowski & Vernon, *supra* note 87, at 61; see also OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 42-43 (patent term restoration has significant effect in competitive market); Statman, *supra* note 87, at 225 (statement of William Comanor) (there is a market tradeoff between low pharmaceutical prices and drug research and development).

3. Legislative Attempts To Restore Incentives for Innovation

Most of these arguments were reiterated during congressional consideration of the several patent term restoration bills introduced since 1981. Advocates of such legislation pointed to the real declines in drug innovation and patent protection experienced by their industry, while opponents of patent extension insisted that these problems were being overstated. The opponents argued that additional patent protection would not decrease research and development costs, increase the number of innovative breakthroughs, or ensure the commercial success of new drug products.¹⁰⁸ Most consumer groups opposed any form of patent term restoration, recognizing that the potential benefits of longer patent protection to drug research and development could be matched by costs imposed on consumers as a result of delayed competition.¹⁰⁹

While patent legislation stalled in Congress,¹¹⁰ two other initiatives designed to encourage pharmaceutical innovation took effect. The first, a general tax credit of twenty-five percent for all research and development expenditures, expired at the end of 1985.¹¹¹ The other, the Orphan Drug Act, authorizes tax credits¹¹² and market exclusivity periods to encourage research into drug therapies for what are defined in the Act as "orphan" diseases.¹¹³ Research and development expenditures for orphan drugs re-

108. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 39.

109. See H.R. REP. NO. 696, 97th Cong., 2d Sess. 21-23 (dissenting remarks of Rep. Frank); see also BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 225 (study by Schiffrin showing that consumer gains from substitution outweigh substitution's effect on research and development); *id.* at 226-27 (study by Jadlow demonstrates that drug product substitution has only a negligible effect on research and development).

110. See *The Push to Protect Patents on New Drugs*, 222 SCI. 593, 594 (1983).

111. See I.R.C. § 30 (West Supp. 1985) (provision expired on Dec. 31, 1985). Proposed legislation to renew this provision was introduced in this Congress. See, e.g., S. 58, 99th Cong., 1st Sess., 131 CONG. REC. S180 (daily ed. Jan. 3, 1985). However, the credit provision lapsed at the end of last year. Some of the various tax reform proposals pending in Congress reinstate the credit in some form, although at least one proposal would weaken it. See PMA NEWSLETTER, Oct. 14, 1985, at 1. The tax reform package presently before the Senate Finance Committee restores the 25% credit. *Id.*, March 17, 1986, at 1.

112. The Internal Revenue Service did not publish proposed regulations for the use of the orphan drug tax credit until last year. See 50 Fed. Reg. 15,930 (1985). It appears that no firm has yet received or filed for the credit. See PMA NEWSLETTER, Apr. 22, 1985, at 1.

113. See Orphan Drug Act, Pub. L. No. 97-414, 96 Stat. 2049, 2050-51 (1982), amended by Pub. L. No. 98-551, § 4, 98 Stat. 2815, 2817. An "orphan drug" is a drug for a "rare disease or condition," defined in the statute as a disease or condition affecting fewer than 200,000 persons in the United States or affecting more than 200,000 persons but for which there is no reasonable expectation that the cost of developing and marketing a drug for the disease or condition will be recovered from sales of the drug in the United States. 21 U.S.C.A. § 360bb(a)(2) (West Supp. 1985).

The Act also authorizes protocol assistance and grants. See generally Finkel, *The Orphan*

ceive a fifty percent tax credit,¹¹⁴ and orphan drugs are guaranteed a seven-year exclusive marketing license for their orphan disease applications.¹¹⁵

Patent term legislation was introduced again in the first session of the 98th Congress,¹¹⁶ but the proposal faced strong opposition. During the same year Congressman Waxman, who had been one of the major critics of patent restoration proposals, introduced a bill to authorize the FDA to approve generic copies of approved drugs through ANDAs.¹¹⁷ When it became clear that neither proposal could muster sufficient support to pass through Congress alone,¹¹⁸ spokesmen for each bill agreed to combine the two pieces of legislation. After lengthy negotiations, the bill was reported out of House and Senate committees in early summer 1984.¹¹⁹ Floor efforts to make further changes in the bill were defeated, and on September 6 and 12 respectively, the House and Senate passed the Drug Price Competition and Patent Term Restoration Act of 1984.¹²⁰ The new Act was signed into law by President Reagan on September 24, 1984.¹²¹

Drug Act and the Federal Government's Orphan Products Development Program, 99 PUB. HEALTH REP. 313 (1984) (describing the Act).

114. Orphan Drug Act, Pub. L. No. 97-414, § 4, 96 Stat. 2049, 2053-56 (1982) (codified as amended at I.R.C. § 28 (West Supp. 1985)).

115. *Id.* § 2, 96 Stat. 2049, 2050-51 (codified at 21 U.S.C. § 360cc (1982)).

The provisions of the Orphan Drug Act were extended by Congress in 1985. Orphan Drug Amendments of 1985, Pub. L. No. 99-91, 99 Stat. 387. The original act offered market exclusivity periods only to drugs that were ineligible for patents. The newly amended law recognizes that a seven-year exclusivity period will often exceed postapproval patent life. *See* H.R. REP. NO. 153, 99th Cong., 1st Sess. 2-5, *reprinted in* 1985 U.S. CODE CONG. & AD. NEWS 301, 302-05. The amendments authorize market exclusivity even for patentable orphan drugs. Orphan Drug Amendments of 1985, § 2, 99 Stat. at 387.

116. *See* S. 1306, 98th Cong., 1st Sess., 129 CONG. REC. S6383-84 (daily ed. May 17, 1983); H.R. 3502, 98th Cong., 1st Sess., 129 CONG. REC. H4895 (daily ed. June 30, 1983).

117. *See* H.R. 3605, 98th Cong., 1st Sess., 129 CONG. REC. H5273 (daily ed. July 19, 1983).

118. *See The Price for More Generic Drugs*, 224 SCI. 369 (1984).

119. *See* S. REP. NO. 547, 98th Cong., 2d Sess. (1984); H.R. REP. NO. 857, pt. 1, 98th Cong., 2d Sess., *reprinted in* 1984 U.S. CODE CONG. & AD. NEWS 2647; H.R. REP. NO. 857, pt. 2, 98th Cong., 2d Sess., *reprinted in* 1984 U.S. CODE CONG. & AD. NEWS 2686.

A group of dissident PMA-member companies insisted on further concessions and assurances before the bill reached its final form in September, 1984. *See* H.R. REP. NO. 857, pt. 1, 98th Cong., 2d Sess. 71-76, *reprinted in* 1984 U.S. CODE CONG. & AD. NEWS 2647, 2681-86; PMA NEWSLETTER, July 2, 1984, at 3-4 (discussing split among PMA members over the Act).

120. *See* H.R. 3605, 98th Cong., 2d Sess., 130 CONG. REC. H9145 (daily ed. Sept. 6, 1984); S. 1538, 98th Cong., 2d Sess., 130 CONG. REC. S10,989-90 (daily ed. Sept. 12, 1984).

121. Pub. L. No. 98-417, 98 Stat. 1585, 1585 (1984).

II. THE DRUG PRICE COMPETITION AND PATENT TERM RESTORATION ACT OF 1984

The Act consists of three titles, of which only two concern us here. Title I addresses abbreviated New Drug Applications; title II authorizes patent term extension and makes other changes in the patent law. Title III, which is irrelevant to this article, is an amendment to the Act that originated in the Senate that requires textile product labels to identify the country in which the textile product was manufactured.¹²²

A. Progeneric Provisions of the Act

1. ANDAs

The Act amends section 505 of the Food, Drug, and Cosmetic Act to permit the filing and approval of abbreviated New Drug Applications for generic copies of pioneer drugs.¹²³ ANDAs must contain information showing: that the approval is sought only for uses already approved for the pioneer drug; that the active ingredients and the route of administration, dosage form, and strength of the new drug are the same as those of the pioneer drug;¹²⁴ that the generic is bioequivalent to, and bioavailable to the same extent as, the pioneer; that the labeling of the generic will be the same as that for the pioneer; the details of the ingredients and manufacturing process of the generic; and a certification that approval of the ANDA will not violate a patent held by the maker of the pioneer.¹²⁵

The Act enumerates the circumstances that will justify FDA disapproval of an ANDA.¹²⁶ If the ANDA is disapproved, the applicant must be given

122. See Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, § 301, 98 Stat. 1585, 1603-05 (1984).

123. See *id.* § 101, 98 Stat. at 1586 (to be codified at 21 U.S.C. § 355(j)(1)). The provision, which merely speaks of a drug that contains an active ingredient that has been "previously approved," applies to drugs approved in NDAs both before and after 1962.

124. If an applicant desires to file an ANDA for a drug whose active ingredient or route of administration, dosage form, or strength differ from that of the pioneer drug, a petition for permission to file an ANDA must be submitted to the Secretary of Health and Human Services. The Secretary is required to approve the petition unless he makes a finding that additional investigations must be conducted to show the safety and efficacy of the new drug or that on the basis of an ANDA the new drug could not be adequately evaluated for safety and effectiveness. Approval or disapproval of the petition must take place within 90 days. *Id.* § 101, 98 Stat. at 1587 (to be codified at 21 U.S.C. § 355(j)(2)(C)).

125. *Id.* § 101, 98 Stat. at 1585-86 (to be codified at 21 U.S.C. § 355(j)(2)(A)).

126. The Secretary "shall approve" an ANDA unless the Secretary finds: that the methods used in the manufacture, processing, and packing of the generic product are inadequate to assure the drug's strength, identity, quality, and purity; that the ANDA contains insufficient information to show that the proposed conditions of use have been previously approved for the pioneer; that the application contains insufficient information to show that the active ingredi-

notice of an opportunity for a hearing.¹²⁷ The FDA must act on an abbreviated New Drug Application within 180 days of the *initial receipt* of the application, unless the applicant and the Secretary of Health and Human Services agree to an additional period for FDA consideration of the ANDA.¹²⁸ This provision should be distinguished from the statute governing FDA approval of full NDAs. Under that statute, the FDA must approve or disapprove an NDA within 180 days of its *filing*.¹²⁹ The FDA has construed an NDA to be "filed" within the meaning of the statute only when the NDA is substantially ready for final evaluation.¹³⁰

New Drug Applications for pioneer drugs must, after the Act, identify all product and use patents for the drug.¹³¹ Consequently, an ANDA must certify that the generic drug will not infringe any patents held by the maker of the pioneer drug, that any patents on the pioneer drug have expired or the date on which relevant patents will expire, or that the patent on the pioneer drug is invalid.¹³² If the ANDA applicant certifies a future date or dates on which the patent or patents will expire, but does not assert that the product for which the ANDA seeks approval will not infringe the patents or that the patents are invalid, the effective date of an approved ANDA will be the date of patent expiration certified by the ANDA applicant.¹³³ If the ANDA applicant certifies only that the relevant patents have expired or that the pioneer drug's NDA contained no patent information, the ANDA will be made

ent of the generic is the same as that of the pioneer; that, unless a petition was granted, the route of administration, dosage form, or strength of the generic drug are not the same as the pioneer; that it does not contain the information required by the petition submitted under the proper procedure (described *supra* note 124); that the application fails to show bioequivalence or bioavailability; that the approved labeling for the generic is not the same as that for the pioneer; that the ANDA shows that the generic drug is unsafe under the conditions of use intended for the drug; that the pioneer drug of which the generic is a copy has been withdrawn or suspended from the market under § 505(e) for reasons of safety or effectiveness; that the ANDA fails to contain any of the information required by § 355(j)(2)(A); or that the ANDA contains any untrue statement of material fact. *Id.* § 101, 98 Stat. at 1587-88 (to be codified at 21 U.S.C. § 355(j)(3)).

127. *Id.* § 101, 98 Stat. at 1589-90 (to be codified at 21 U.S.C. § 355(j)(4)(C)). This requirement parallels the existing statute for approval of drugs in an NDA. *See* 21 U.S.C. § 355(c)(2) (1982). If the applicant chooses to accept the opportunity for hearing by written request within 30 days after the notice, the hearing must commence within 90 days after the expiration of the 30-day period unless the Secretary and the applicant agree otherwise. The hearing is to be expedited, and the Secretary's order on the hearing must be issued within 90 days after the date fixed by the Secretary for filing final briefs. *Id.*

128. Pub. L. No. 98-417, § 101, 98 Stat. at 1588 (to be codified at 21 U.S.C. § 355(j)(4)(A)).

129. 21 U.S.C. § 355(c) (1982).

130. *See* 21 C.F.R. § 314.101 (1985).

131. Pub. L. No. 98-417, § 102, 98 Stat. 1585, 1592 (to be codified at 21 U.S.C. § 355(b)).

132. *Id.* § 101, 98 Stat. at 1586 (to be codified at 21 U.S.C. § 355(j)(2)(A)(vii)).

133. *Id.* § 101, 98 Stat. at 1588-89 (to be codified at 21 U.S.C. § 355(j)(4)(B)(ii)).

effective immediately upon approval.¹³⁴

If the ANDA contains a certification that the generic drug will not infringe existing patents or that existing patents are invalid, however, the ANDA applicant must give notice to the patentholder (and the holder of the approved pioneer NDA, if different) that the ANDA has been submitted. The notice must include a detailed explanation of the applicant's factual and legal basis for the claim that the original patent is invalid or not infringed.¹³⁵ If the patentholder fails to bring an action for infringement within forty-five days of the receipt of the notice,¹³⁶ an ANDA shall be made effective immediately if otherwise approvable.¹³⁷ If an infringement suit is brought, however, the FDA cannot make the ANDA approval effective for thirty months from the date of the notice from the applicant to the patentholder, unless the trial court decides prior to that time that the patent is invalid or not infringed.¹³⁸ If the infringement action is still pending after thirty months, the FDA has no authority to refuse to make an approvable ANDA effective.

This patent challenge provision has been criticized on two grounds. First, ANDA applicants are given an incentive to challenge potentially valid patents.¹³⁹ The first ANDA applicant who challenges the patent is given a 180-day head start over any future ANDAs,¹⁴⁰ and if the patentholder fails to file his suit within forty-five days—an extraordinarily short period for initiating such complex litigation—an approved ANDA will be made effective immediately. Second, just as the giving of notice by an ANDA applicant involves little cost and encourages patent litigation,¹⁴¹ the thirty-month delay in generic competition assured when a patent infringement suit is filed

134. *Id.* § 101, 98 Stat. at 1588-89 (to be codified at 21 U.S.C. § 355(j)(4)(B)(i)).

135. *Id.* § 101, 98 Stat. at 1586 (to be codified at 21 U.S.C. § 355(j)(2)(B)).

136. The Act makes the filing of an ANDA, the approval of which would infringe a valid patent, an act of infringement itself, so the ANDA filing and notice triggers the patentholder's right to bring an infringement suit. *See id.* § 202, 98 Stat. at 1603 (to be codified at 35 U.S.C. § 271(e)(2)).

137. *Id.* § 101, 98 Stat. at 1588-89 (to be codified at 21 U.S.C. § 355(j)(4)(B)(iii)).

138. *Id.* The Act does not extend the period to the full 30 months if the trial court decision is appealed. Unless the trial court stays its judgment, once the ANDA applicant secures a favorable trial judgment the FDA must make an approved ANDA effective.

139. *See* Johnstone, *Impact of the Drug Price Competition and Patent Term Restoration Act of 1984 on the Generic Industry—Business Considerations and Potential Legal Issues*, 40 FOOD DRUG COSM. L.J. 339, 341 (1985).

140. Pub. L. No. 98-417, § 101, 98 Stat. 1585, 1589 (to be codified at 21 U.S.C. § 355(j)(4)(B)(iv)).

141. *See Drug Price Competition and Patent Term Restoration Act of 1984: Hearing on S. 2748 Before the Senate Comm. on Labor and Human Resources*, 98th Cong., 2d Sess. 206-07 (1984) (statement of William E. Schuyler, Jr., Esq.) [hereinafter cited as *1984 Senate Hearing*]; Ryan, *Impact of the Act on Research-Based Industry*, 40 FOOD DRUG COSM. L.J. 345, 348 (1985).

provides an incentive for patentholders to defend weak and even invalid patents. Unless the patent litigation terminates in less than thirty months, an unlikely result in most federal courts, the holder of even an invalid patent is permitted to extend his exclusive market power, without facing damages, merely by filing an infringement suit.¹⁴²

The Act also codifies the paper NDA procedure for copies of drugs originally approved under section 505 of the Food, Drug, and Cosmetic Act.¹⁴³ Yet because the ANDA procedure does not require an applicant to submit the reports of published studies required for paper NDAs,¹⁴⁴ the paper NDA procedure is unlikely to be used by many applicants.¹⁴⁵

Finally, the Act authorizes ANDAs only for drugs originally approved under section 505. Because many drugs are approved under other sections, ANDAs seem not to be available for several classes of drugs. The FDA has already concluded that batch-certified antibiotics, which are approved under section 507,¹⁴⁶ are not eligible for ANDAs.¹⁴⁷ The Act also makes no provision for permitting licensees of a patentholder to submit an ANDA, and because the FDA cannot make an ANDA effective before the pioneer's patents have expired, a full NDA would appear to be required.¹⁴⁸ Veterinary drugs are also excluded from the ANDA provisions in the Act.¹⁴⁹

142. See 130 CONG. REC. H9115 (daily ed. Sept. 6, 1984) (statement of Rep. Shaw).

143. See Pub. L. No. 98-417, § 103, 98 Stat. 1585, 1593-97 (to be codified at 21 U.S.C. § 355(b)(2)).

144. See *supra* notes 20-22 and accompanying text.

145. See J. Hoffman, Drug Price Competition and Patent Term Restoration Act of 1984: An Overview (Nov. 13, 1984) (paper delivered to the Food and Drug Law Institute); Hutt, *Drug Bill Balances Patent Protection, Competition*, LEGAL TIMES, Sept. 24, 1984, at 8, 8.

146. 21 U.S.C. § 357 (1982).

147. See PMA NEWSLETTER, Nov. 19, 1984, at 1; J. Hoffman, *supra* note 145. Antibiotics that are not batch certified are approved under § 505, and are therefore within the Act's ANDA provisions. PMA NEWSLETTER, Jan. 7, 1985, at 7. PMA has complained that because the *Bolar* reversal provisions of the Act apply to all drugs, including antibiotics, patentholders should be afforded the protection that the notice provisions of Title I of the Act guarantee. See *infra* notes 151-53 and accompanying text.

Insulin and biologics are also excluded from the Act's ANDA and market exclusivity provisions. See Pape, *Market Exclusivity Under the Drug Price Competition and Patent Term Restoration Act of 1984—The Five Clauses*, 40 FOOD DRUG COSM. L.J. 310, 315-16 (1985) (insulin approved under 21 U.S.C. § 356 (1982) and biologics approved under 42 U.S.C. § 262 (1982)).

148. See Johnstone, *supra* note 139, at 341. Of course, a license holder might bargain with the patentholder and agree that the ANDA would not infringe a patent (and with a valid license it probably would not). The license holder could then certify noninfringement, and when the 45-day waiting period expired FDA could make an approved ANDA effective.

149. See 1984 Senate Hearing, *supra* note 141, at 17-18 (statement of Dr. Mark A. Novitch, Acting Comm'r, FDA). Veterinary drugs are approved under § 512 of the Food, Drug, and Cosmetic Act, 21 U.S.C. § 360b (1982).

2. Statutory Reversal of *Roche v. Bolar*

The Act reverses the result of *Roche Products, Inc. v. Bolar Pharmaceutical Co.*¹⁵⁰ In *Bolar*, the United States Court of Appeals for the Federal Circuit held that a generic manufacturer could not "use" a patented pioneer drug product to conduct the tests necessary for FDA approval of a generic drug.¹⁵¹ The Act overrules *Bolar* by providing that it is not an act of patent infringement "to make, use, or sell a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs."¹⁵²

The *Bolar* provision does not specify that the information "submitted" under a federal drug law be required to be submitted by that law. Nor is the provision limited to the compilation of information necessary to submit an ANDA, instead, the statute refers to "any Federal law" regulating the manufacture, use, or sale of drugs. Thus, as the provision is written, it would not be an act of infringement for a manufacturer to conduct tests needed to submit a paper NDA for a generic copy of the new drug, or a full NDA for a use or dosage form not already approved in the pioneer drug's NDA.¹⁵³

During congressional hearings it was suggested that the retroactive reversal of *Bolar* would work an unconstitutional deprivation of property rights on some patentholders. This issue will be litigated. The *Bolar* provision applies to patents issued before the enactment of the 1984 Act as well as to future patents. Because the *Bolar* decision found that the use of a patented product for testing in anticipation of drug approval was an infringing use, it is possible to argue that holders of patents issued before the effective date of the Act possessed a property right to be shielded from infringing uses of the type adjudicated in *Bolar*. If so, the retroactive reversal of *Bolar* may be a "taking" of that property right without compensation. As critics of the provision testified during the Senate hearings on the Act, if the health interest in reversing *Bolar* is insufficient to justify an exercise of police power that would allow an uncompensated taking, then this provision in the Act would be unconstitutional when applied retroactively.¹⁵⁴

150. 733 F.2d 858 (Fed. Cir.), *cert. denied*, 105 S. Ct. 183 (1984).

151. See *supra* notes 68-69 and accompanying text.

152. Pub. L. No. 98-417, § 202, 98 Stat. 1585, 1603 (to be codified at 35 U.S.C. § 271(e)(1)).

153. See *infra* notes 291-94 and accompanying text.

154. This analysis traces the argument made by Professor Dorsen in the 1984 hearings on the Act. See 1984 Senate Hearing, *supra* note 141, at 179-203 (statement of Prof. Norman Dorsen, New York University School of Law); see also Krulwich, *Statutory Reversal of Roche v. Bolar: What You See Is Only the Beginning of What You Get*, 40 FOOD DRUG COSM. L.J. 519 (1985) (suggesting similar arguments). During congressional consideration of the Act, others expressed similar doubts regarding the constitutionality of the *Bolar* provision. See

Supporters of the Act's *Bolar* reversal responded to each of these arguments. *Bolar*, they claimed, was merely a statutory interpretation by a single court,¹⁵⁵ and Congress remained free to provide a legislative definition for the term "use." The *Bolar* reversal does this. *Bolar* was also a unique case because its interpretation of the patent statute had never before been reached in a judicial decision. Therefore, the exercise of police power does not deprive patentholders of any investment-based reliance interest.¹⁵⁶ Moreover, Congress' interest in public health is served by the *Bolar* reversal if less expensive drugs are thereby made available to some who could not otherwise afford them. This justification for the provision, according to its proponents, validates use of the police power in these circumstances.¹⁵⁷

B. Pro-Brand Manufacturer Provisions of the Act

1. Market Exclusivity Periods

The Act creates five different exclusivity periods for drugs approved by the FDA after 1981 in full or supplemental NDAs (See Table). There is no magic to the distinctions made by these various periods; rather, they reflect the legislative compromises implicit throughout the Act. Some new drugs or drug uses will receive exclusivity protection that will run simultaneously with patent protection, but products that are not protected by patents, or that are ineligible for patents, can also be given exclusive marketing life.¹⁵⁸ This sort of incentive for innovation is not new with this Act—market exclusivity is also granted in the 1982 Orphan Drug Act.¹⁵⁹ Postmarketing exclusivity does more than guarantee some return of drug innovation costs: it also provides the pioneer manufacturer with an exclusive market within which the drug can be studied for further safety and effectiveness data and possible adverse drug reaction problems.¹⁶⁰

Each of the Act's five exclusivity provisions is contained in the sections governing the submission or earliest effective date of ANDAs and paper NDAs. None of the exclusivity provisions prevents a competitor from mar-

Innovation and Patent Law Reform: Hearings Before the Subcomm. on Courts, Civil Liberties, and the Administration of Justice of the House Comm. on the Judiciary, 98th Cong., 2d Sess. 677-87 (1984) (letter of James F. Fitzpatrick, Esq., Arnold & Porter); *id.* at 741-58 (memorandum of Laurence H. Tribe, Tyler Professor of Constitutional Law, Harvard Law School).

155. See *Bolar*, 733 F.2d at 861.

156. See H.R. REP. NO. 857, pt. 2, 98th Cong., 2d Sess. 28-29, reprinted in 1984 U.S. CODE CONG. & AD. NEWS 2686, 2712-13.

157. See *id.* at 28, reprinted in 1984 U.S. CODE CONG. & AD. NEWS 2712.

158. See Ryan, *supra* note 141, at 347.

159. See *supra* notes 113-15 and accompanying text.

160. See 1983 House Drug Legislation Hearings, *supra* note 87, at 6-9 (testimony of Dr. Mark A. Novitch, Deputy Comm'r, FDA); *id.* at 133 (statement of PMA).

keting, or the FDA from approving, a generic copy during the exclusivity period for the pioneer drug if FDA approval is obtained through a full NDA.

Two of the provisions apply only to drugs approved between January 1, 1982, and September 24, 1984 (the date of enactment). For any NCE approved in an NDA during that period, an approved ANDA or paper NDA may not be *made effective* for ten years after the date of approval of the pioneer's NDA.¹⁶¹

MARKET EXCLUSIVITY GRANTS UNDER THE ACT

approval date	before Jan. 1, 1982	Jan. 1, 1982, to Sept. 24, 1982	after Sept. 24, 1982
type of pioneer			
NCE	none	cannot make ANDA or paper NDA effective for 10 years after NDA approval	ANDA or paper NDA cannot be submitted prior to 5 years after NDA approval, but 4 year limitation applies if patent challenged
NON-NCEs			
NDA	none	cannot make ANDA or paper NDA effective before Sept. 24, 1986	cannot make ANDA or paper NDA effective for 3 years after date of NDA approval
Supplement	none	cannot make ANDA or paper NDA effective before Sept. 24, 1986	cannot make ANDA or paper NDA effective for change reported in supplement for 3 years after approval, supplement must contain reports of essential new clinical investigations

For non-NCEs approved in an NDA or supplemental NDA between 1982

161. Pub. L. No. 98-417, § 101, 98 Stat. 1585, 1590 (to be codified at 21 U.S.C. § 355(j)(4)(D)(i)); *id.* § 103, 98 Stat. at 1595 (to be codified at 21 U.S.C. § 355(b)(2)(D)(i)).

and the date of enactment, an approved ANDA or paper NDA may not be made effective before September 24, 1986.¹⁶²

The other three exclusivity periods apply to drugs approved by FDA after September 24, 1984. For post-enactment NCEs, an ANDA or paper NDA cannot be *submitted* to the FDA prior to five years after the date of approval of the pioneer NDA.¹⁶³ If it contains a certificate of patent invalidity or noninfringement, however, an ANDA or a paper NDA may be submitted four years after the date of approval.¹⁶⁴ Thus, even if the patent that protects an NCE is invalid, the original drug is guaranteed at least four years of market exclusivity. If the patentholder files an infringement suit, the thirty-month delay in the effective date of the ANDA or the paper NDA is added to the usual five-year exclusivity term, so that an approved ANDA or paper NDA would not take effect until 7.5 years after the pioneer NDA is approved.¹⁶⁵

Generic versions of non-NCE drugs approved in an NDA cannot be *made effective* for three years after the approval date.¹⁶⁶ If a supplemental NDA contains reports of new clinical investigations "essential"¹⁶⁷ to the approval of the supplement and conducted or sponsored by the applicant, an ANDA or paper NDA for the change reflected in the supplemental NDA cannot be made effective for three years after the date of approval.¹⁶⁸

2. Patent Term Extension

Title II of the Act adds a patent extension provision to the federal patent statutes. Patent extension is permitted for any "product" whose patent has not expired, if a patent extension application has been submitted, if the product was subject to regulatory review by a federal authority before the prod-

162. *Id.* § 101, 98 Stat. at 1591 (to be codified at 21 U.S.C. § 355(j)(4)(D)(v)); *id.* § 103, 98 Stat. at 1596-97 (to be codified at 21 U.S.C. § 355(b)(2)(D)(v)).

163. *Id.* § 101, 98 Stat. at 1590 (to be codified at 21 U.S.C. § 355(j)(4)(D)(ii)); *id.* § 103, 98 Stat. at 1595-96 (to be codified at 21 U.S.C. § 355(b)(2)(D)(ii)).

164. *Id.* § 101, 98 Stat. at 1590 (to be codified at 21 U.S.C. § 355(j)(4)(D)(ii)); *id.* § 103, 98 Stat. at 1595-96 (to be codified at 21 U.S.C. § 355(b)(2)(D)(ii)).

165. *Id.* § 101, 98 Stat. at 1590 (to be codified at 21 U.S.C. § 355(j)(4)(D)(ii)); *id.* § 103, 98 Stat. at 1595-96 (to be codified at 21 U.S.C. § 355(b)(2)(D)(ii)).

166. *Id.* § 101, 98 Stat. at 1590 (to be codified at 21 U.S.C. § 355(j)(4)(D)(iii)); *id.* § 103, 98 Stat. at 1596 (to be codified at 21 U.S.C. § 355(b)(2)(D)(iii)).

167. The Act does not define "essential studies." See Pape, *supra* note 147, at 314-15. The FDA has taken the position that the Act intends that such studies be human studies, and that animal studies do not qualify a supplement for exclusivity. The Act's sponsors, Representative Waxman and Senator Hatch, have stated publicly that FDA's conclusion is correct. See PMA NEWSLETTER, Aug. 28, 1985, at 4-5.

168. Pub. L. No. 98-417, § 101, 98 Stat. 1585, 1590-91 (to be codified at 21 U.S.C. § 355(j)(4)(D)(iv)); *id.* § 103, 98 Stat. at 1596 (to be codified at 21 U.S.C. § 355(b)(2)(D)(iv)).

uct's commercial marketing or use, and if the commercial marketing or use after the regulatory review period was the first marketing or use under the law under which the regulatory review occurred.¹⁶⁹ A "product" is defined by the Act as a "human drug product" or a "medical device, food additive, or color additive subject to regulation under the Federal Food, Drug, and Cosmetic Act."¹⁷⁰

An application for patent extension must be filed within sixty days after the product is approved,¹⁷¹ so the Act applies to products whose regulatory review period ended on or after July 26, 1984. Patent extension applications are submitted to the Commissioner of Patents and Trademarks, who forwards the application to the Secretary of Health and Human Services for determination of the regulatory review period applicable to the product.¹⁷² The regulatory review period for drug products is equal to half the IND period plus the full period during which the NDA is pending.¹⁷³ The sum of the patent extension and the amount of the patent remaining after the product finishes the regulatory review cannot exceed fourteen years.¹⁷⁴ Furthermore, the maximum extension is five years,¹⁷⁵ and only one patent per drug may be extended.¹⁷⁶ A patent extension applies only to the uses claimed in the patent extended,¹⁷⁷ and thus would not apply to any nondrug uses for a drug product, nor to any new drug uses devised and approved that were not claimed in the extended patent.

A finding of the regulatory review period must be published in the Federal Register within thirty days after the receipt by the Secretary of Health and Human Services of the patent extension application.¹⁷⁸ Within 180 days after publication of that determination, anyone may submit a petition to the

169. Pub. L. No. 98-417, § 201(a), 98 Stat. at 1598 (to be codified at 35 U.S.C. § 156(a)). For a patent that claims a method of manufacture that primarily uses recombinant DNA technology, the permission for the commercial marketing or use must be the first period of review under the process claimed in the patent.

170. *Id.* § 201(a), 98 Stat. at 1600 (to be codified at 35 U.S.C. § 156(f)(1)).

171. *Id.* § 201(a), 98 Stat. at 1599 (to be codified at 35 U.S.C. § 156(d)(1)).

172. *Id.* § 201(a), 98 Stat. at 1599 (to be codified at 35 U.S.C. §§ 156(d)(1), 156(d)(2)(A)).

173. *Id.* § 201(a), 98 Stat. at 1601 (to be codified at 35 U.S.C. §§ 156(g)(1)). See PMA NEWSLETTER, Feb. 18, 1985, at 2-3; Hutt, *supra* note 145, at 12. The statute refers to the date on which an NDA is initially submitted, distinguishing that date from the date on which the FDA will consider the FDA filed. See *supra* text accompanying notes 129-30; H.R. REP. NO. 857, pt. 1, 98th Cong., 2d Sess. 44, reprinted in 1984 U.S. CODE CONG. & AD. NEWS 2647, 2677.

174. Pub. L. No. 98-417, § 201(a), 98 Stat. 1585, 1599 (to be codified at 35 U.S.C. § 156(c)(3)).

175. *Id.* § 201(a), 98 Stat. at 1602 (to be codified at 35 U.S.C. § 156(g)(4)).

176. *Id.* § 201(a), 98 Stat. at 1599 (to be codified at 35 U.S.C. § 156(c)(4)).

177. *Id.* § 201(a), 98 Stat. at 1598 (to be codified at 35 U.S.C. § 156(b)).

178. *Id.* § 201(a), 98 Stat. at 1599 (to be codified at 35 U.S.C. § 156(d)(2)(A)).

Secretary asserting that the patentholder did not act with "due diligence" during the regulatory review period.¹⁷⁹ The Secretary must make a determination on the due diligence petition within ninety days, and may delegate the authority to make the due diligence determination to the Commissioner of the FDA.¹⁸⁰

The Act provides that the regulatory review period set by the Secretary will be reduced by the amount of time during which the extension applicant did not act with due diligence,¹⁸¹ but the due diligence procedure will probably be wasted. For most drugs, the regulatory review period will significantly exceed the maximum five-year patent extension,¹⁸² so a finding that the applicant was not diligent will rarely deprive the patentholder of any part of the five-year extension. Even reduced by the lack of due diligence, the review period usually will exceed five years, unless the FDA speeds its drug approval process. The FDA criticized the due diligence concept for precisely the reason that it will bear the burden of reviewing due diligence and providing hearings on the due diligence determination,¹⁸³ but rarely to any purpose.¹⁸⁴ Furthermore, both the FDA and pharmaceutical companies will endeavor to "build a record" throughout the drug approval process, generating useless work merely to protect each side in the event that a due diligence petition is filed.¹⁸⁵

III. IMPACT OF THE ACT ON THE MARKETING AND USE OF GENERIC SUBSTITUTES

As discussed earlier in this paper,¹⁸⁶ the potential for growth in the generic pharmaceutical industry is tremendous. The next several years will see the market share held by patented drugs fall, and many of the drugs on which patents have recently or will shortly expire are the market's biggest

179. *Id.* § 201(a), 98 Stat. at 1599-1600 (to be codified at 35 U.S.C. § 156(d)(2)(B)); *see also* Lawton, *What Is Due Diligence?*, 40 FOOD DRUG COSM. L.J. 371 (1985) (Act does not define "due diligence").

180. Pub. L. No. 98-417, § 201(a), 98 Stat. 1585, 1599-1600 (to be codified at 35 U.S.C. § 156(d)(2)(B)).

181. *Id.* § 201(a), 98 Stat. at 1598 (to be codified at 35 U.S.C. § 156(c)(1)).

182. *See supra* note 87 and accompanying text (discussing effect of FDA review on effective patent life).

183. Pub. L. No. 98-417, § 201(a), 98 Stat. 1585, 1600 (to be codified at 35 U.S.C. § 156(d)(2)(B)(ii)).

184. *See 1984 Senate Hearing, supra* note 141, at 21 (statement of Dr. Mark A. Novitch, Acting Comm'r, FDA).

185. *See* P. Miller, *Impact on Innovation: Drug Price Competition and Patent Term Restoration Act 1984*, at 6-7 (Nov. 13, 1984) (outline of comments delivered to the Food and Drug Law Institute).

186. *See supra* note 14 and accompanying text.

selling products. One extremely enthusiastic prediction soon after the Act was passed foresaw consumer savings of one billion dollars in the next decade, a halving of the average price of many prescription drugs, and a doubling of the generic market.¹⁸⁷ This prediction seems overstated, for despite the advances in the generic drug industry made possible by the Drug Price Competition and Patent Term Restoration Act, substantial barriers to widespread drug substitution remain.

A. Barriers to Generic Substitution

1. Brand-Name Product Advertising

As already noted, the advertising of brand-name products plays a significant role in the maintenance of large market shares by brand-name pharmaceutical companies.¹⁸⁸ Efforts by firms to achieve brand-name recognition cater not only to physician preferences for the best possible treatment, but also solidify the position of brand-name drugs after patent expiration removes the legal barrier to generic substitution.¹⁸⁹ Advertising can therefore retard entry into the market by low-priced generic substitutes because the brand-name drug will be the product already preferred by physicians and pharmacists, and the high cost of drug promotion will prevent generic firms from competing in that "market for information."¹⁹⁰

Some studies have shown that brand-name drugs lose little of their market share in the years following patent expiration. Schwartzman, for example, found only limited competition among equivalent antibiotic drugs, but did not study market share erosion in other therapeutic areas.¹⁹¹ A more extensive study by Statman concluded that in the market as a whole, brand-name drugs retained 96.1% of the drugstore market and 89% percent of the hospital market.¹⁹² Most commentators seem to agree, however, that the Statman study severely understates the impact of generic competition. The study

187. See Kushner, *supra* note 2, at 22.

188. See *supra* notes 37-40, 45-48, 64 and accompanying text.

189. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 34; Leffler, *supra* note 37, at 47; J. Wheaton, Optimal Research Patterns: The Pharmaceutical Firm 2 (Dec. 1981) (paper submitted to the Department of Economics, Wake Forest University); see also Statman & Tyebjee, *Trademarks, Patents, and Innovation in the Ethical Drug Industry*, J. MARKETING, Summer 1981, at 71 (brand loyalty causes continued market dominance following patent expiration).

190. See F. SCHERER, INDUSTRIAL MARKET STRUCTURE AND ECONOMIC PERFORMANCE 329 (1970) (rate of promotional expenditures to total drug industry sales is 29%); Comanor, *Research and Competitive Product Differentiation in the Pharmaceutical Industry in the United States*, 31 ECONOMICA (n.s.) 372, 380 (1964) (selling expenditures are a barrier to entry); Leffler, *supra* note 37, at 47-48 (advertising speeds entry of new products).

191. See D. SCHWARTZMAN, *supra* note 25, at 251-99.

192. See Statman, *supra* note 87, at 145.

used data that predated most of the state generic substitution laws enacted during the 1970's.¹⁹³ Thus, the proliferation of generic drugs in the market during the next several years, when combined with state drug substitution statutes, will encourage brand-name companies to find new or more aggressive promotion techniques.

The increased generic competition contemplated by the Drug Price Competition and Patent Term Restoration Act will spur manufacturers to intensify their promotional efforts. To the extent that advertising allows higher-price brand-name drugs to retain most of their market share after patent expiration, brand promotion will be more aggressive during the period immediately prior to patent expiration.¹⁹⁴ The longer exclusivity period guaranteed to brand name drug products by the Act will also provide a longer term during which the drug product can generate brand loyalty.¹⁹⁵

Antigeneric advertising is another method for maintaining brand-name market share.¹⁹⁶ At present, generic companies still are unable to counter such advertising by pointing out that their products are approved by the FDA.¹⁹⁷ FDA permission for preapproval promotion may also be sought by brand-name manufacturers as a means to lay a market foundation for new drugs.¹⁹⁸ Although such promotion is opposed by many industry and professional groups,¹⁹⁹ the FDA recently lifted its moratorium on direct-to-consumer advertising,²⁰⁰ which could engender patient pressure on physicians and pharmacists to prescribe and dispense "high quality" brand-name drugs.²⁰¹

193. See *1983 Senate Hearings*, *supra* note 49, at 45 (testimony of Lewis A. Engman, President, PMA); OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 33; Statman, *supra* note 87, at 166-68 (commentary of Leonard Schiffrin, Professor of Economics, College of William and Mary).

194. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 35.

195. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 44.

196. See *supra* notes 45-48, 64 and accompanying text.

197. See *supra* note 49 and accompanying text. Pending legislation would remove this statutory restriction. See *infra* note 245.

198. See PMA NEWSLETTER, Feb. 4, 1985, at 2 (commentary of Jonah Shacknai from Pink Sheet).

199. See STAFF OF SENATE COMM. ON OVERSIGHT AND INVESTIGATIONS OF THE HOUSE COMM. ON ENERGY AND COMMERCE, 98TH CONG., 2D SESS., *PRESCRIPTION DRUG ADVERTISING TO CONSUMERS* (Comm. Print 1984).

200. See FDA CONS., Dec. 1985-Jan. 1986, at 3. Direct-to-consumer advertisements must include brief summaries of a drug's potential side effects. *Id.* Congressional opponents of this form of promotion have expressed displeasure with the FDA decision to lift a moratorium in place since 1983, and have warned the industry to proceed carefully. See PMA NEWSLETTER, Jan. 13, 1986, at 5-6.

201. See PMA NEWSLETTER, Feb. 4, 1985, at 2 (commentary of Jonah Shacknai from Pink Sheet). But see Masson & Rubin, *Matching Prescription Drugs and Consumers: The Benefits of Direct Advertising*, 313 NEW ENG. J. MED. 513 (1985). Masson and Rubin assert

Finally, brand-name manufacturers will turn to trademark and trade dress protection to insulate their market shares. The size, shape, and color of drug products can be virtually as effective as patents as barriers to entry.²⁰² Patients identify drugs they have taken before by such characteristics, and will be uncomfortable with receiving a "different" drug.²⁰³ The legal protection of the Lanham Act will continue to permit brand-name firms to distinguish their products by unique trade dress,²⁰⁴ and could help retard the trend to generic substitution.

2. *Physician and Pharmacist Behavior*

All of the factors that historically have discouraged physicians and pharmacists from generic substitution, such as product advertising, the perception that generic products often are inferior, price ignorance, and fear of liability,²⁰⁵ will continue even after adoption of the Act. Proposals such as the Model Drug Product Selection Act offer some opportunity to minimize the reluctance of physicians not to substitute by, for example, requiring prescriptions to indicate that a brand-name product is medically necessary in order to preclude substitution.²⁰⁶ To some extent, however, the attitudes of pharmacists and physicians always will be a limiting factor for the potential of the generic drug industry.

3. *Erosion of Product Life Due to Patent Term Extension and Market Exclusivity*

Just as brand-name manufacturers calculate the potential commercial benefits of a new project when they make decisions to expend funds on drug research and development, after a patent or market exclusivity period for a pioneer drug expires, a potential generic manufacturer will weigh the cost of market entry against the potential commercial gain during the remaining market life of the pioneer drug. For many pioneer drugs that receive patent extension or market exclusivity, generic competition may be so delayed that

that direct-to-consumer advertising might create positive health effects by, for example, providing information about disease symptoms, treatment, and drug side effects, as well as economic benefits such as shifts to lower-priced brands, retail competition, and overall price level decreases.

202. See generally BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 35-36; M. STATMAN, *supra* note 25, at 63-64; Statman, *supra* note 87, at 143.

203. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 32; Ryan, *supra* note 141, at 349.

204. See Lanham Act, 15 U.S.C. §§ 1051-1127 (1982 & Supp. II 1984); Inwood Laboratories, Inc. v. Ives Laboratories, Inc., 456 U.S. 844 (1982).

205. See *supra* notes 37-48, 62-67, and accompanying text.

206. See *supra* note 54 and accompanying text.

the potential sales revenue of a generic product will be less than the cost of securing FDA approval of and marketing the generic drug.²⁰⁷ This problem can be anticipated, but its real effect on the generic market cannot be measured until the generation of products that will receive patent extensions and market exclusivity reach the market. For some drugs there might be little or no useful market life remaining after the exclusivity period or extension ends.²⁰⁸ In this manner, patent extension and market exclusivity periods will act as disincentives to generic drug manufacturers.

The Act also permits brand-name manufacturers to use market exclusivity to foreclose to generic competitors part of the market for a drug. If a drug has multiple uses, each new use (or other improvement to the drug) is eligible for market exclusivity if approved by the FDA in a full or supplemental NDA.²⁰⁹ The FDA is only permitted to approve ANDAs for uses that are not protected by a patent or market exclusivity period. Thus, by delaying improvements or the approval of new uses, the manufacturer of a pioneer drug can prevent new market entrants from gaining approval in an ANDA of a generic drug that can be prescribed for every approved use of the product.²¹⁰ Despite its "equivalence" to the pioneer, proven in an ANDA, the generic drug would not legally be available for all its potential uses.²¹¹ The generic product will be approved for the nonpatented uses of the pioneer, but legally could not be prescribed for the full range of uses for which the drug is indicated.²¹² To the extent that doctors and pharmacists find it inconvenient to remember when the use of a generic drug is "legal," the generic product will find limited acceptance in the market, and the pioneer's market share will be effectively insulated.

4. *Administrative Delay by the Food and Drug Administration*

The effectiveness of the Act's progenetic provisions also depends on the FDA's ability to make approval of a generic copy of a pioneer drug effective as soon as the patent or market exclusivity protection for the pioneer expires. In theory, the Act makes it difficult for agency delay to act as a barrier to timely market entry: the Act's ANDA provisions, with one exception, merely prohibit the FDA from making approved ANDAs *effective* before

207. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 44, 45.

208. See 1982 House Hearing, *supra* note 82, at 7 (statement of Donna Valtri, Office of Technology Assessment).

209. See *supra* notes 166-68 and accompanying text.

210. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 40, 44-45.

211. See *infra* notes 281-83 and accompanying text.

212. But see *supra* note 100 and accompanying text (it will be impossible to police actual use for which generic drug is prescribed).

the patent or exclusivity period expires. Only in the case of post-enactment new chemical entities approved in an NDA does the Act prevent the *submission* of an ANDA during the period of exclusivity (in that case for five years). For many pioneer drugs, therefore, a generic competitor may submit an ANDA as soon as the NDA on which it relies has been approved. The Act's reversal of *Bolar* permits potential competitors to conduct the bioavailability and bioequivalency testing needed for the ANDA, and even if these studies take eighteen months to two years to complete,²¹³ the FDA should be able to act on the ANDA before generic competition becomes legally permissible.

The Act requires the FDA to approve or disapprove an ANDA within 180 days of its receipt. This requirement departs from the current FDA practice of not considering an NDA "filed" until it is virtually ready for approval.²¹⁴ The FDA can only disapprove an ANDA for one of the eleven reasons enumerated in the statute.²¹⁵ The Act's nominal deadline may be avoided, however, because the Act allows the FDA and the applicant to agree on a deadline extension, and Congress recognized that extensions would be necessary.²¹⁶

Prior to enactment of the new law, the FDA warned that its resources would be insufficient to process timely the volume of ANDAs it expected. Then-Acting FDA Commissioner Novitch originally estimated that the agency would need \$2.5 million in additional funds and fifty-five to sixty new drug reviewers²¹⁷ to cope with a backlog of ANDAs he estimated would total 900 within six months of enactment.²¹⁸ He argued for a phase-in of the ANDA procedure, stated plainly that the FDA would be unable to act on ANDAs within 180 days,²¹⁹ and noted that even with adequate funding and additional staff it would be impossible to hire enough qualified reviewers to process ANDAs.²²⁰

Dr. Novitch later revised his funding and staff estimates upward to \$3

213. See 1981 Senate Hearing, *supra* note 73, at 129 (testimony of Kenneth N. Larsen, Chairman, GPIA) (estimating such a period for biostudies).

214. See J. Hoffman, *supra* note 145; *supra* notes 127-28 and accompanying text.

215. See *supra* note 126 and accompanying text.

216. See H.R. REP. NO. 857, pt. 1, 98th Cong., 2d Sess. 27, reprinted in 1984 U.S. CODE CONG. & AD. NEWS 2647, 2660.

217. See PMA NEWSLETTER, Sept. 10, 1984, at 2 (attributing statement to Senate testimony by Dr. Novitch).

218. See 1984 Senate Hearing, *supra* note 141, at 15-16 (statement of Dr. Mark A. Novitch, Acting Comm'r, FDA).

219. *Id.*

220. *Id.* at 30 (testimony of Dr. Mark A. Novitch, Acting Comm'r, FDA).

million and from ninety to one hundred new reviewers.²²¹ His backlog prediction was borne out. Within a week of the first permissible date for ANDA submission, 370 ANDAs had been filed, and pending paper NDAs, which the agency planned to convert to ANDAs,²²² added 140 applications to that total.²²³

The influx of ANDAs seemed likely to exacerbate the already serious workload problems in FDA's Center for Drugs and Biologics. Previous studies have concluded that the FDA drug review process is inefficient because of uneven workloads among reviewers, high turnover, poor-quality personnel, and the inordinate time reviewers must devote to tasks other than reviewing drug applications.²²⁴ Moreover, the FDA drug approval process for new drugs already consumes several years on average, and a high volume of ANDAs might not only delay the approval of generic drugs, but may divert resources allocated to review of NDAs for pioneer drugs.²²⁵ Together with the FDA manpower shortage predicted by Dr. Novitch, the workload created by the Act will add further delay to the new drug approval process, and could conceivably prevent the agency from complying with the statutory deadline for ANDAs.

In spite of initial pessimism about ANDA processing, the FDA has thus far complied with the 180-day deadline. By December 1985, the average ANDA processing time was only 140 days,²²⁶ an apparent result of their consideration in a separate and fully staffed division of FDA.²²⁷ Nevertheless, there has been no comparable improvement in the time required for new drug approval.²²⁸

Finally, two federal budget issues cloud the future of the ANDA and NDA approval processes. First, President Reagan's 1986 budget proposed that "user fees" be assessed against those who seek approval from the FDA. The industry opposes such fees, but Gerald Mossinghoff, the new president of PMA and until recently the Commissioner of Patents and Trademarks, has argued that these revenues, if collected, should be channeled back into

221. See PMA NEWSLETTER, Oct. 1, 1984, at 4 ("worst case" backlog scenario was 900 ANDAs during first six months after enactment and 1200 in first year).

222. See Letter from Dr. Harry M. Meyer, Jr., Director, Center for Drugs and Biologics, FDA (Oct. 11, 1984).

223. See PMA NEWSLETTER, Dec. 3, 1984, at 1.

224. See FDA's DRUG APPROVAL PROCESS, *supra* note 72, at 61-62; COMPTROLLER GENERAL OF THE UNITED STATES, FDA DRUG APPROVAL—A LENGTHY PROCESS THAT DELAYS THE AVAILABILITY OF IMPORTANT NEW DRUGS 17-20 (1980).

225. See 1984 Senate Hearing, *supra* note 141, at 125-26 (statement of PMA dissident companies) (ANDAs will receive priority because of 180-day deadline).

226. See PMA NEWSLETTER, Jan. 13, 1986, at 2-3.

227. See *id.*, Nov. 5, 1984, at 2; *id.*, Sept. 9, 1985, at 2-3.

228. See *id.*, Sept. 9, 1985, at 3.

the drug approval process to provide funds for a more effective drug approval system.²²⁹ Although user fees would increase the cost of gaining FDA approval,²³⁰ the increased financial resources available to the agency if the fees were earmarked might provide resources sufficient to minimize FDA delay. When they were proposed last year, the agency had no plans to channel user fees into the drug approval process. Instead, two-thirds of the funds collected would have reverted to the general federal treasury, and the remaining percentage would have been used by FDA for capital expenditures.²³¹

User fees attracted considerable congressional opposition in 1985,²³² and did not appear as a feature of the Senate-approved budget.²³³ However, one FDA official recently endorsed user fees as a means of expediting new drug approval,²³⁴ an apparent shift from the agency's position last year, and the user fee issue will again arise during consideration of the agency's 1987 budget.²³⁵

Second, the restraints of Gramm-Rudman-Hollings may hamper the ability of FDA to continue to meet its time burden under the Act or to improve its record in NDA approval. The agency must trim its budget during the current fiscal year,²³⁶ and is likely to suffer further restrictions as Congress continues its attempt to achieve lower budget deficits.

B. Incentives to Generic Substitution

In spite of the various disincentives to generic drug use described in the previous section, the new Act blends well with other trends in the pharmaceutical market to encourage the use of generic products. For high dollar-volume drugs the incentive to enter the generic market is very high. By mid-1985, for example, a dozen ANDAs had been filed for generic equivalents of Valium,²³⁷ a drug whose sales volume in 1983 was \$225 million and whose

229. *See id.*, Mar. 11, 1985, at 5.

230. The user fees proposed by FDA in 1985 were \$126,000 for NDAs and \$9900 for ANDAs. *See id.*, July 22, 1985, at 5.

231. *See id.*, Apr. 8, 1985, at 1. The PMA strongly opposes this allocation of user fees. *See id.*, Apr. 15, 1985, at 5.

232. *See id.*, Oct. 14, 1985, at 6.

233. *See id.*, Oct. 21, 1985, at 5.

234. *See id.*, Jan. 13, 1986, at 1.

235. The administration's proposed 1987 budget includes more than \$25 million in user fees. OFFICE OF MANAGEMENT & BUDGET, BUDGET OF THE UNITED STATES GOVERNMENT, FISCAL YEAR 1987, app. 1-K1. FDA has indicated that it would like to plough collected user fees into the drug approval process. *See PMA NEWSLETTER*, Feb. 10, 1986, at 1.

236. *See PMA NEWSLETTER*, Jan. 20, 1986, at 1.

237. *See id.*, July 8, 1985, at 5.

compound patent expired in February 1985.²³⁸ By the end of 1985, the FDA approved, through ANDAs, three generic versions of Valium,²³⁹ as well as two generic equivalents of Inderal, a drug with an annual retail sales volume of \$400 million.²⁴⁰ The potential market for generic drugs, according to one FDA official, could escalate from a twenty percent share of a \$20 billion market in 1984 to a thirty-five percent share of \$8.5 billion in projected 1990 pharmaceutical sales.²⁴¹ The Act certainly makes it easier for generic drug companies to bring generic drug products to market, and the continuing impact of state drug substitution laws and the pressures of medical reimbursement programs will make generic drugs more available and give them increased market acceptance.

1. *Drug Substitution Laws*

Drug substitution statutes help nullify the importance of brand-name promotion. As observed above, both pharmacists and physicians are reluctant to dispense or prescribe generic drugs,²⁴² but these barriers are not insurmountable. By increasing the volume of generic products, the Act will enhance the acceptability of generic drugs, and the financial incentive of pharmacists to promote generic drugs²⁴³ will underscore the value of consumer savings. The FDA's testing and manufacturing standards should serve as assurances that the quality of generic drugs is equivalent to that of pioneer pharmaceutical products.²⁴⁴

Nevertheless, several legislative changes would enhance the impact of drug substitution laws. First, drug manufacturers should be permitted to state in advertising or labeling that a product has received FDA approval. With proper disclaimers to avoid the appearance that the FDA is acting as a guarantor of quality, repealing the federal statute prohibiting such labeling or advertising²⁴⁵ would make generic drugs more acceptable to consumers,

238. Hollie, *Generic Drugs in Bigger Role*, N.Y. Times, July 23, 1984, at D1, col. 2.

239. See FDA CONS., Nov. 1985, at 3. With the approval of generic copies of Valium, nine of the ten drugs with the highest 1984 sales volumes are now available in the form of generic equivalents. *Id.*

240. See FDA CONS., Oct. 1985, at 2.

241. See Rados, *Generic Drugs: Cutting Costs, Not Corners*, FDA CONS., Oct. 1985, at 27.

242. See *supra* text accompanying notes 33-67.

243. See *supra* notes 58-60 and accompanying text.

244. See *supra* notes 27-31 and accompanying text.

245. See *supra* note 49 and accompanying text. A bill is pending before the current Congress that would remove the statutory bar to such labeling established by 21 U.S.C. § 331(l) (1982) and instead *require* labels to indicate that a drug has received FDA approval. See H.R. 2244, 99th Cong., 1st Sess., 131 CONG. REC. H2570 (daily ed. Apr. 25, 1985). The bill passed the House last year, see 131 CONG. REC. H4760 (daily ed. June 24, 1985), and has been referred to the Senate Committee on Labor and Human Resources. See 131 CONG. REC. S8722

physicians, and pharmacists.

Second, state substitution laws should be rewritten to require physicians to write a phrase such as "medically necessary" on their prescriptions if they desire to forbid substitution. The FTC's Model Act advocates such a provision,²⁴⁶ which would mandate that the prescriber consciously decide against substitution and could increase the rate of generic substitution by pharmacists.²⁴⁷

Third, federal legislation should authorize a national drug formulary that would list drug products for which substitution is permitted.²⁴⁸ A national formulary would bring drug substitution into conformance with the judgments of drug equivalency made by the FDA, the federal agency that determines bioavailability and bioequivalence. If created, a national formulary should also accommodate the concern of some brand-name drug manufacturers that drug formularies will not account for multiple-use products that have approved uses for which patents or market exclusivity periods are still in effect.²⁴⁹

2. Medical Reimbursement Programs

Medical reimbursement programs, both public and private, can affect the incidence of generic drug use by tailoring their maximum reimbursements for drug costs to the prices of generic products. In state Medicaid and Medicare programs this form of cost control is imposed by the Maximum Allowable Cost (MAC) program, which is in place in twenty-six states.²⁵⁰ Under the MAC program, the government establishes maximum allowable cost levels for multisource equivalent drugs at the lowest price at which the drug is "widely and consistently available."²⁵¹ Unless a physician certifies, in his own handwriting, that a higher-priced product is "medically necessary," the maximum reimbursement for a prescribed drug product will be the MAC

(daily ed. June 25, 1985). The PMA opposes this legislation, claiming that such labeling would encourage promotional excesses. PMA NEWSLETTER, July 1, 1985, at 2-3.

246. See *supra* note 54 and accompanying text.

247. See *supra* notes 54-55 and accompanying text.

248. But see *supra* note 11 (formularies may discourage substitution). Nevertheless, even if substitution is higher when a pharmacist is free from the formal constraint of a formulary, formularies serve an equivalency screening function that is not accounted for by substitution rates. See A. MASSON & R. STEINER, *supra* note 10, at 98-99. Moreover, some of the disincentive effect associated with state positive formularies might result from delay in incorporating FDA determinations of equivalency. *Id.* at 71-72. If so, a national formulary coordinated with FDA equivalency findings could function without such delay.

249. See *infra* note 286 and accompanying text.

250. See *Prescription for Cheap Drugs*, *supra* note 2, at 65.

251. 42 C.F.R. § 447.332 (1985); 45 C.F.R. § 19.5(c) (1985).

price,²⁵² regardless of whether the prescription is actually filled with a brand name or generic drug. In some cases a state substitution statute may prevent the pharmacist from substituting a generic product on a prescription written by brand name, but the MAC regulations will still forbid full reimbursement because the physician has failed to certify that the more expensive product is medically necessary. The pharmacist has several options in this situation: he can fill the prescription with the brand-name drug and lose the price differential between the brand name price and the MAC price; refuse to fill the prescription; call the prescribing doctor and ask for permission to substitute; or request that the doctor make the "medically necessary" certification.²⁵³

The potential savings from MAC to federal and state government medical entitlement programs have been estimated at twenty-four percent of the total anticipated expenditures on multisource drug products that are potentially subject to MAC levels.²⁵⁴ Most of this benefit has not yet been realized: the current MAC regulations do not allow pharmacists to override state substitution laws, and cost savings depend on the willingness of physicians to allow substitution.²⁵⁵ Moreover, the MAC program has been stalled since 1983. A task force of the Department of Health and Human Services has been studying the program and alternative cost-control measures, and no new MAC levels have been established.²⁵⁶

The benefits of programs such as MAC extend, however, beyond the savings gained in the treatment of Medicaid and Medicare recipients. Because a MAC level is established at the "widely available" price, the price of competing drugs should fall for all consumers, and not just for Medicaid and Medicare beneficiaries. Drug companies supply pharmacists and, as such, are incapable of practicing price discrimination among the ultimate consumers of their drugs.²⁵⁷ A MAC limit for a drug also encourages pharmacists to stock low-priced drugs, usually generics, with which Medicaid and Medi-

252. 42 C.F.R. § 447.332(a), (b) (1985).

253. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 135. The pharmacist might also charge the patient the difference between the higher and lower price. See D. SCHWARTZMAN, *supra* note 25, at 328. Medicaid rules may forbid this result, however. Providers of Medicaid services are required to accept Medicaid reimbursement as full payment for their services. 42 U.S.C. § 1396o(c) (1982); 42 C.F.R. § 447.15 (1985).

254. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 213.

255. See COMPTROLLER GENERAL OF THE UNITED STATES, *supra* note 9. The Comptroller General's report, issued in 1980, also noted the failure of some states to fully comply with federal Maximum Allowable Cost (MAC) regulations.

256. See PMA NEWSLETTER, Nov. 11, 1985, at 2 (discussing possible alternatives to MAC levels); *id.*, July 29, 1985, at 3-4 (Department of Health and Human Services searching for less cumbersome method of establishing reimbursement levels).

257. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 139; D. SCHWARTZMAN, *supra* note 25, at 299, 329.

care prescriptions can be filled. With these products already on their shelves, pharmacists will become more likely to use generic products in filling non-Medicaid prescriptions.²⁵⁸ The MAC program thus adds to the acceptability of generic drugs by creating a financial incentive for pharmacists and consumers to use them and to relay price information to physicians, and by forcing pharmacists to acclimate themselves to dispensing generic drugs.

Private medical insurance also has potential for enlarging the market share held by generic pharmaceuticals. Some insurance companies will now reimburse 100% of the cost of generic drugs but only 80% of the cost of brand-name products.²⁵⁹ Private insurance reimbursement limits (such as those relating to "diagnostic related groups," or DRGs) that establish maximum insurance reimbursement levels for particular illnesses may also encourage consumers to prefer generic drugs. This preference may be translated into pressure on physicians and pharmacists to prescribe and dispense generically, a consumer preference that may not be fully expressed now. As part of the total package of health care services purchased by a patient, prescription drug costs will represent a small proportion of total expenditures,²⁶⁰ and patients who are publicly or privately insured have little incentive, absent effective cost-control measures, to prefer generic drugs.²⁶¹

IV. IMPACT OF THE ACT ON PHARMACEUTICAL INNOVATION

One critic has asserted that the research-intensive segment of the pharmaceutical industry is the "big gainer [from the Drug Price Competition and Patent Term Restoration Act] because of the additional monopoly periods"

258. See BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 139; OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 33.

259. See *Prescription for Cheap Drugs*, *supra* note 2, at 65.

260. See A. MASSON & R. STEINER, *supra* note 10, at 6. Patients are typically ignorant of the price differential between brand-name and generic drugs, *id.* at 6-7, and often the pharmacist's decision not to substitute may reflect a consumer preference to accept the brand prescribed by their physician. *Id.* at 46-47. This tendency is amplified by insurance for drug costs, *id.* at 42, but may be overcome by cost-control programs and by statutory requirements that pharmacists who substitute inform patients that they have done so. Such notification provisions in state statutes serve a function similar to advertising in that they convey both price information and the confidence of the pharmacist that generic drugs are therapeutically equivalent to their brand-name competitors. A notification requirement will therefore increase substitution rates. *Id.* at 97-98. The FTC Model Act incorporates such a provision. Model Drug Product Selection Act, § 2(c), reprinted in BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 279.

261. See A. MASSON & R. STEINER, *supra* note 10, at 56 (substitution rate highest for prescriptions filled under MAC program, and lowest for patients whose drug costs were reimbursed by private insurance).

created by the Act's patent extension and market exclusivity provisions.²⁶² The Act certainly assumes that greater returns to pharmaceutical innovation will result from longer effective patent life and the financial incentives of market exclusivity, but it is not clear that the Act's effects are one-sided. Enhanced generic competition will erode market gains now realized by the research-intensive industry, and in some areas, such as innovation in the form of new uses for and improvements to existing drugs, the Act may so dissipate anticipated returns that this source of therapeutic improvements will dry up.

A. Averting Losses from Competition

The thesis underlying the compromise wedding between provisions that stimulate generic drugs and those guaranteeing market protection to innovative manufacturers was that increased generic competition without added market exclusivity for brand-name products would further dampen pharmaceutical research and development. The danger of generic competition, as encouraged by the Act, is that any disincentives to innovation that result from short-term falling revenues will not be manifested in decreased drug development until the point in the future where research decisions made now would begin to yield therapeutic gains.²⁶³ The important question that a long-term view of the Act will answer, then, is whether the incentives it provides to innovation will at least balance out the disincentives implicit in increased price competition.

Although the expectations of long-term gains are the immediate incentives to innovation furthered by the Act,²⁶⁴ any stimulus to research caused by these future returns should not be delayed until those gains are realized and used to finance future innovation expenditures. The *expectation* is immediate, and could affect current decisions that reflect expected returns.²⁶⁵ Even if the actual future profits are not themselves earmarked for future innovation projects, but are dispersed to stockholders,²⁶⁶ a firm's decision to pursue a particular research project necessarily will consider future monetary returns, and research will be more likely to be pursued under a regulatory regime that guarantees innovators extended periods of exclusive marketing

262. See M. Bass, *supra* note 4.

263. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 36.

264. See *id.* at 37.

265. See S. REP. NO. 138, 97th Cong., 1st Sess. 12 (1981) (letter of June 5, 1981 from Morton A. Myers, Director, General Accounting Office).

266. See *The Push To Protect Patents on Drugs*, 222 SCI. 593, 593 (1983) (attributing this argument to critics of patent term extension).

power.²⁶⁷

Increased drug substitution will offset some of the research and development gains. Substitution will be decreased somewhat when longer effective patent life discourages market entry by generic competitors,²⁶⁸ but, on the other hand, programs such as MAC may drive drug prices (and through low prices returns to investment) so low on some multiple-source products that some innovation will be stymied.²⁶⁹ Increased price competition will also force brand-name manufacturers to cut their variable production costs; price competition will, in some cases, create disincentives to manufacturing high-quality drugs and, in others, discourage brand-name manufacturers from making expenditures to develop improvements on existing drug products.²⁷⁰

A cost of the Act's market exclusivity provisions, in comparison, is the loss experienced by consumers from the higher prices charged by brand-name manufacturers during the longer periods of market exclusivity. Although some argued that these consumer losses would be smaller than the innovation benefits created by patent extension,²⁷¹ this conclusion is not obvious. Despite the economic thesis that anticipated competition will, near patent expiration, drive a drug's price to near its marginal variable cost,²⁷² the opposite effect may occur: as patent expiration nears, the manufacturer of a pioneer drug may raise the drug's price in order to capture the full gains available in the remaining period of monopoly.²⁷³

Proponents of patent restoration contended, however, that longer periods of market exclusivity would actually lower the price of a pioneer drug over

267. In fact, comparative static results indicate that an increase in effective patent life will not only increase the absolute amount of research and development expenditures, but also accelerate the research and development spending pattern so that innovative drugs reach the market more quickly. See J. Wheaton, *supra* note 189, at 18. This result follows easily from the inference that although compressing total research costs into a shorter time increases the present value of those expenditures, the gains from marketing a new drug are also greater if the drug enters the market sooner, rather than later.

268. See H. Grabowski & J. Vernon, *supra* note 76, at 150-51; *supra* notes 207-08 and accompanying text.

269. See C. BEZOLD, *THE FUTURE OF PHARMACEUTICALS* 88 (1981); D. SCHWARTZMAN, *supra* note 25, at 329.

270. See D. SCHWARTZMAN, *supra* note 25, at 331; Leffler, *supra* note 37, at 66 n.57.

271. See 1981 *House Hearings*, *supra* note 45, at 190-91 (statement of Dr. Lewis H. Sarett, Senior Vice President, Merck & Co.) (research and development benefit to consumers exceeds increased drug costs); OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 41 (generic competition hurts manufacturers of pioneer drugs more than it helps consumers).

272. See J. EGAN, H. HIGINBOTHAM & J. WESTON, *supra* note 25, at 48.

273. See Waldholz, *supra* note 44, at 8, col. 4. Of course, this tactic would have little success if consumers of drug products chose to forgo treatment, but the demand for patented prescription drugs is likely to be inelastic. Not only is a patient unlikely to refuse treatment because of marginal price increases, but the availability of private and public medical reimbursement programs will leave patients with little incentive to economize in drug expenditures.

the period of its exclusive marketing life. First, they argued, patent extension allows manufacturers a longer time during which the costs of research and development may be recouped, and permits them to establish lower price levels during the period of the patent.²⁷⁴ Second, assuming patent restoration stimulates innovation, many of the newly innovated drugs will compete with drug therapies already on the market. Competition among therapeutic alternatives will exert downward pressure on drug prices, resulting in a lower overall price level in the pharmaceutical market.²⁷⁵

Both of these suggested benefits have been disputed by opponents of patent extension. If brand-name companies retain a monopoly in a product, they have no incentive to lower prices merely because they are capable of spreading prior costs over a longer period.²⁷⁶ Moreover, even if future competition might lower overall drug prices, that effect will appear only in the long run and might not outweigh the consumer losses occasioned by patent extension.²⁷⁷

Thus, patent extension and market exclusivity may be costly to consumers, but real increases in future drug innovation may not follow. New market monopoly periods create general incentives to research and development, but as the following sections indicate, the Act may actually discourage particularly valuable forms of research.

B. Lost Improvements in Drug Therapy Due to New Uses

Not all drug innovation takes the form of the discovery of new chemical entities; many therapeutic advances result from new uses of already-approved drug compounds or new dosage forms for existing drugs. As long as a pioneer drug manufacturer retains an incentive to improve its product by developing new uses and methods of delivery, patent term extension may encourage research into such improvements.²⁷⁸ The three-year market exclusivity period guaranteed for new uses and dosage forms approved in full or supplemental NDAs provides an incentive to innovation in cases where the improvement is unpatentable;²⁷⁹ use and process patents can give even

274. See 1981 Senate Hearing, *supra* note 73, at 40-41 (testimony of Dr. Edwin H. Clark, II, Acting Assistant Administrator, EPA); OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 40.

275. See 1983 Senate Hearings, *supra* note 49, at 40 (testimony of Lewis A. Engman, President, PMA); OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 44.

276. See 1981 House Hearings, *supra* note 45, at 58-59 (colloquy between Rep. Kas-tenmeier and Dr. John Andelin, Assistant Director, Office of Technology Assessment).

277. See 1981 Senate Hearing, *supra* note 73, at 125-26 (testimony of William F. Haddad, GPJA).

278. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 41.

279. See *supra* notes 166-68 and accompanying text.

greater market exclusivity to drug improvements.²⁸⁰

To some extent, the Act continues to protect innovative improvements on old drugs. Even when an ANDA is made effective by the FDA for uses of the pioneer drug that are no longer protected by a patent or market exclusivity period, an ANDA can never be made effective for protected uses of the drug; the manufacturer that holds the use patent or grant of exclusivity will have legal claim to an exclusive market for some uses of the drug compound.²⁸¹ The generic drug would be approved only for some indications, but could not legally be promoted for the still-protected uses of the pioneer drug.²⁸²

Nevertheless, if a generic equivalent is available for a pioneer drug that retains legally protected uses, the pioneer's exclusive right to be the sole product prescribed and dispensed for some uses will be eroded. First, enforcement of use patents, and by analogy, enforcement of the new market exclusivity periods provided for in the Act, is virtually impossible. The generic manufacturer does not infringe the use patent unless it *induces* the prescriber or consumer, who are the actual infringers, to violate the use patent.²⁸³ Because the generic manufacturer has the right to make the generic drug for some uses, the brand-name firm cannot restrict market access to the substitute product.²⁸⁴ Yet a suit against each infringing pharmacist or consumer²⁸⁵ is impractical: both the information costs and the expense involved in litigating against single violators would outweigh potential recoveries for infringement.

Medical reimbursement programs and state formularies might also work to disadvantage pioneer drugs with protected uses. Drug formularies are unlikely to specify the *uses* for which a generic product is equivalent to the brand-name pioneer,²⁸⁶ and pharmacists and physicians possess no incen-

280. See 1982 House Hearing, *supra* note 82, at 163-64 (statement of Peter B. Hutt, on behalf of PMA).

281. See Hutt, *supra* note 145, at 8; see also 1983 House Drug Legislation Hearings, *supra* note 87, at 116 (statement of PMA) (this difference between the pioneer and generic drugs is an incentive to research and development for product improvements).

282. See 1983 House Drug Legislation Hearings, *supra* note 87, at 141-42 (statement of PMA); P. Miller, *supra* note 185, at 9-10.

283. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 52.

284. The inability of a drug manufacturer to restrict the use to which its product is put has non-innovation implications as well. In one case involving DES, for example, a DES producer that never sought approval or marketed its product for the prevention of miscarriages was held to have nevertheless received financial benefits from the use of DES in problem pregnancies, and was held liable under a concert of action/enterprise liability theory. See *Miles Laboratories, Inc. v. Superior Court*, 133 Cal. App. 3d 587, 184 Cal. Rptr. 98 (1982).

285. This would appear to be the only remedy available to the pioneer manufacturer. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 8.

286. See P. Miller, *supra* note 185, at 9-10. Formularies are, in general, either positive

tive, absent a real threat of liability for infringement, to educate themselves on the legal substitutability of equivalent products.²⁸⁷ Hospital DRGs will not account for the higher cost of a superior, but newly innovated, dosage form.²⁸⁸ The Medicaid MAC program sets price levels for multisource products, but presently does not make clear that a product could be multisource for one use but single source for another use or dosage form.²⁸⁹ In any event, it would be impossible for a manufacturer subject to price competition to practice price discrimination among those who consume its product for distinct uses.

The ability of a generic manufacturer to secure an ANDA for some subset of a drug's uses thus discourages innovation into potential new uses. However, the availability of multiple uses provides other, sometimes perverse, incentives. Generic products provide price competition, but to the extent that a new use or dosage form allows the innovator to price its product at a higher than competitive level, new uses and dosage forms act as therapeutic competition²⁹⁰ that could allow the pioneer manufacturer to keep its market share.

The structure of the exclusivity provisions in the Act, as well as the potential extension of a product patent, encourage innovating firms to delay improvements on pioneer drugs until shortly before the compound patent expires. The extension of the compound patent will already have lengthened the exclusive marketing time for the pioneer drug, and by introducing an improvement that will itself receive exclusivity, the innovating firm protects its market position. These firms, in contrast to generic competitors, will be able to advertise to physicians and pharmacists that their product is the only

(listing drugs that are interchangeable), or negative (listing those that are not equivalent). See *supra* note 10 and accompanying text; see also BUREAU OF CONSUMER PROTECTION, *supra* note 5, at 157-58; Goldberg, Aldridge, DeVito, Vidis, Moore & Dickson, *supra* note 17, at 216.

An FDA official has indicated that it will indeed be difficult to control the manner in which the equivalent products are dispensed, but that the design of formularies to accommodate this concern will have to be resolved at the state level. F-D-C REPORTS, Jan. 28, 1985, at 6.

287. But as may be the case for physicians, the prescription (or dispensing) of a product for a nonapproved use might be the basis for a malpractice claim. See Wardell, *The Impact of Regulation on New Drug Development*, in ISSUES IN PHARMACEUTICAL ECONOMICS, *supra* note 74, at 145-147. This concern has already been expressed by California pharmacists, who inquired of Rep. Waxman whether they might be subject to malpractice liability if they substituted a generic equivalent of a brand name drug for an indication protected by an exclusivity period. Waxman expressed his opinion that the matter should be clarified, but that a malpractice claim could not arise out of such a substitution as long as the substituted product was equivalent to the brand-name product. See PMA NEWSLETTER, Dec. 23, 1985, at 5-6.

288. See P. Miller, *supra* note 185, at 10.

289. *Id.* at 11-12.

290. Cf. 1983 Senate Hearings, *supra* note 49, at 56 (statement of Lewis A. Engman, President, PMA).

one available for a full range of uses. If state formularies and medical reimbursement programs are reworked, as suggested above, to protect exclusive marketing rights for new uses, the pharmacist and physician will be disinclined to remember whether a particular generic product can be prescribed or dispensed for a particular use, and will tend to prescribe and dispense the pioneer brand-name product.

C. The Disincentive Created by the Statutory Reversal of Roche v. Bolar

Finally, the statutory reversal of *Roche Products, Inc. v. Bolar Pharmaceutical Co.*²⁹¹ is so broad that research-intensive firms will lose much of their incentive to test for new uses of existing drug products. The Act permits the use of a patented product to conduct any tests required for the submission of information under any federal law that regulates the manufacture, sale, or use of drugs.²⁹² By the statute's terms, any person can use a patented drug to conduct *any* of the tests required for FDA approval of a drug product. The *Bolar* reversal applies not only to ANDAs, then, but also to any uses related to the submission of a full or supplemental NDA on a new drug use, new dosage form, or combination drug product that could not be formulated without the pioneer compound.

Traditionally, only the holder of a patent on a pioneer drug could develop and gain approval of improvements upon the pioneer drug during the life of the patent, and under the result of *Bolar*, a use of the patented drug to exploit a commercial gain would have infringed the original patent. After the reversal of *Bolar*, however, any potential competitor can secure approval of an ANDA or NDA without infringing the compound patent. Because even basic testing of a drug is required for FDA approval,²⁹³ competition for the discovery of drug improvements is now open to all potential competitors.

Although the *Bolar* reversal provision permits testing and submission of test data, it will not allow the competitor to *market* a drug that contains the patented product during the legal exclusivity period. The competitor would therefore be allowed to submit to FDA testing, but would probably infringe the patent if it allowed an NDA to become effective during the life of the patent. This scenario, which is plausible under the statute, presents an interesting problem for drug innovators. The pioneer manufacturer's previously exclusive right to file NDAs for improvements on the pioneer drug may be

291. 733 F.2d 858 (Fed. Cir.), *cert. denied*, 105 S. Ct. 183 (1984).

292. Pub. L. No. 98-417, § 202, 98 Stat. 1585, 1603 (to be codified at 35 U.S.C. § 261(j)(4)(D)(i)); *id.* § 103, 98 Stat. at 1595 (to be codified at 21 U.S.C. § 156(d)(1)).

293. See OFFICE OF TECHNOLOGY ASSESSMENT, *supra* note 62, at 14-15 (preclinical animal tests, IND and NDA safety and efficacy studies, and long-term animal toxicity testing all required); 21 C.F.R. §§ 310, 312, 314 (1985) (FDA drug approval requirements).

usurped, but it is possible for the first-filed NDA not to be the first NDA approved because the competitor cannot market an NDA-approved product until the pioneer's patent expires. Nevertheless, the competitor, by filing its NDA, can foreclose the pioneer's manufacturer from receiving any patent protection for the drug improvement. The submission of the improvement idea to clinical testing will make that use of the product public, and should suffice to prevent another party, in this example, the original patentholder, from being granted a patent on the improvement.²⁹⁴

Nor could the competitor file for a patent: the *Bolar* reversal provision does not avoid the act of infringement that would result from the use of a patented product for the purpose of completing a patent application. Nevertheless, the competitor will face no barrier to market entry once the original compound patent on the drug expires. The market exclusivity periods granted by the Act, which begin to run on the date the *first* NDA for a new drug or drug improvement is approved, provide no protection in this case to the holder of the compound patent. Even if the patent owner is the first to obtain an approved NDA for a drug improvement, a competing firm may file an NDA on the same improvement (and may even have filed first) without infringing the compound patent. The original patent will be infringed only if the NDA is made effective prior to the patent's expiration. As soon as the patent expires, the competitor is free to market its version of the drug. Thus, the patentholder may win the race to start the exclusivity period, but cannot prevent a competitor who files an NDA for the same improvement from competing during the post-patent exclusivity period.

The patentholder, and its competitors who file NDAs, will retain market exclusivity as against other competitors who do not receive approval for their product in a new or supplemental NDA, but the incentive to pursue pharmaceutical innovations obtainable by testing existing drugs will be greatly diminished. In effect, the Act's reversal of *Bolar* introduces a risk that the holder of a compound patent will be prevented from receiving additional patents for otherwise patentable improvements.

Even worse for the patentholder, however, is the prospect that a competitor might obtain an exclusive marketing period based on an improvement to

294. See 35 U.S.C. § 102(a) (1982) (applicant not entitled to patent if invention known or used by others in the United States before its invention by applicant); *id.* § 102(b) (applicant not entitled to patent if invention described in published material or subjected to public use more than one year before application filed); Kitch, *The Patent System and the New Drug Application: An Evaluation of the Incentives for Private Investment in New Drug Research and Marketing*, in *REGULATING NEW DRUGS*, *supra* note 75, at 81, 85 (submission for clinical testing will activate public use within meaning of 35 U.S.C. § 102(b) (1982)).

the patentholder's product.²⁹⁵ Because the FDA accords trade secret status to the *existence* of an NDA file unless the existence of the file has been acknowledged or disclosed by the applicant,²⁹⁶ a potential competitor can file an NDA for an improvement without the patentholder's knowledge. The Act gives notice to patentholders when ANDAs are filed, but makes no such provision for NDAs, and thereby avoid alerting the patentholder that a therapeutic improvement of its product is nearing approval. Once the compound patent expires, the competitor can allow an NDA to be approved, and will be entitled to the market exclusivity periods authorized for drug innovations by the Act. Any other competitor, including the original patentholder, might avoid exclusion from the market by securing approval of the same improvement through an NDA, but would probably not complete required testing until after the new product has enjoyed significant exclusive marketing for the new use or product.

This application of the *Bolar* reversal provision inverts the incentive to innovate that now exists. Before the Act, the holder of a drug's compound patent could gain a post-patent marketing advantage by making its product more attractive than generic equivalents. If its improved drug product were therapeutically superior to generic alternatives, or if generic drugs could not be prescribed for the full range of uses of the drug, the brand-name product could expect to retain much of its market share even if it priced its product above a "competitive" level.²⁹⁷ After the Act, however, both patentholders and potential competitors are free to work on improvements to patented products. Each will also suffer the uncertainty that it has not been the first to discover an improvement, or that it will not be the first to bring the new product to market. Neither patentholders nor their competitors, therefore, possess a clear incentive under the Act to invest in research to discover improvements on old drugs.

V. CONCLUSION

In spite of the broad claims made for the Drug Price Competition and Patent Term Restoration Act by its supporters, the new law is not an obvious cure-all for the separate problems faced by patients, generic drug compa-

295. NAPM general counsel Milton Bass theorized that the Act's exclusivity periods could encourage a new class of pharmaceutical firms—"brandgen companies"—that will develop the ability to research and market new dosage forms and delivery systems. F-D-C REPORTS, Jan. 28, 1985, at 7-8.

296. See 21 C.F.R. § 314.430 (1985) ("FDA will not publicly disclose application before an approvable letter is sent to the applicant under § 314.110, unless the existence of the application has been previously publicly disclosed or acknowledged.").

297. See *supra* note 290 and accompanying text.

nies, and brand-name drug firms. A simplified approval process for generic drugs may make entry into the "generic market" more attractive, but barriers to generic drug substitution remain. Brand-name drug companies will continue to protect their market share through advertising, and pharmacists and physicians, who are the targets of such promotion, choose whether a brand-name or generic drug will be dispensed to fill a prescription. Extended market exclusivity for brand-name products will also make entry into some markets less attractive if the brand-name drug's market share is reinforced or if the product has a limited useful commercial life after the expiration of the brand-name drug's market exclusivity period. Moreover, even if the ANDA provisions of the Act cause an explosion in the generic drug market, the FDA may not possess resources adequate to process generic drug applications as quickly as the Act contemplates.

Likewise, the patent extensions and market exclusivity periods provided for by the Act are designed to give financial incentives to pharmaceutical research and development, but heightened generic competition may offset the monetary gains that accrue from exclusive marketing rights. Some provisions of the Act actually contradict the goal of increased research and development by creating disincentives to the discovery of new uses and dosage forms for already-approved drugs.

This article has suggested several initiatives that seem necessary to allow the Act to realize the results promised for it. Generic drug substitution will have greater impact in the pharmaceutical market if physicians are required to handwrite antisubstitution instructions and thus decide consciously whether substitution is truly inappropriate. A national drug formulary and enactment of a pending statutory amendment permitting manufacturers of approved drugs to advertise that their products have received FDA approval would make generic drugs more acceptable to pharmacists and physicians. Formularies should distinguish, however, products for which some uses have exclusive marketing life from those that have only limited application.

Finally, the new Act should be amended to limit the impact of the *Bolar* reversal provision. When enacted, its sponsors intended merely to permit potential generic competitors to conduct the bioequivalency and bioavailability tests required for approval of an ANDA. As written however, the statute discourages innovation into new uses and variations of already-approved drug products.