



# Baby Steps Toward Better Pharmaceutical Care: Market Exclusivity Incentives to Research Pediatric Drug Uses Under the FDA Modernization and Accountability Act of 1997

## Citation

Baby Steps Toward Better Pharmaceutical Care: Market Exclusivity Incentives to Research Pediatric Drug Uses Under the FDA Modernization and Accountability Act of 1997 (1998 Third Year Paper)

## Permanent link

<http://nrs.harvard.edu/urn-3:HUL.InstRepos:8852147>

## Terms of Use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at <http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA>

## Share Your Story

The Harvard community has made this article openly available.  
Please share how this access benefits you. [Submit a story](#).

[Accessibility](#)

BABY STEPS TOWARD BETTER PHARMACEUTICAL CARE:  
MARKET EXCLUSIVITY  
INCENTIVES TO RESEARCH PEDIATRIC DRUG USES UNDER THE  
FDA MODERNIZATION AND  
ACCOUNTABILITY ACT OF 1997

by

Nathan A. Brown

Introduction

For much of the history of food and drug law in the United States, the protection of children has served as the impetus behind significant and beneficial reforms. Prior to 1902, Congress had been unable to pass federal legislation regulating food and drugs. However, after several children died from a tetanus-infected diphtheria antitoxin, Congress promptly enacted The Biologics Act of 1902,<sup>1</sup> implementing licensing requirements for biological drugs sold in interstate commerce.<sup>2</sup> Later, during the New Deal, Congress attempted unsuccessfully to strengthen the Food and Drug Administration (FDA).<sup>3</sup> Then, after more than one hundred children died from the ingestion of Elixir Sulfanilamide, Congress passed the 1938 Food, Drug and Cosmetic Act.<sup>4</sup> Finally, in

<sup>1</sup>32 Stat. 728 (1902).

<sup>2</sup>PETER BARTON HUN & RICHARD A. MERRILL, FOOD AND DRUG LAW 8 (2d ed.

1991).

<sup>3</sup>The FDA began in 1927 as the Food, Drug, and Insecticide Administration; its name was changed to the Food and Drug Administration in 1931. See Beth B. Myers, *The Food and Drug Administration's Experimental Drug Approval System: Is it Good for Your Health?*, 28 HOUS. L. REV. 309, 311 (1991).

<sup>4</sup>52 Stat. 1040 (1938) (current version at 21 U.S.C. § 301 et seq. (1996)). The stronger legislation required drug manufacturers to prove a drug's safety before marketing it. See Anne B. Wells, *Regulating Experimental AIDS Drugs: A Comparison of the United States and France*, 13 LOY. L.A. INT'L & COMP. L.J. 393, 397 (1990).

1962, Congress successfully passed the Kefauver-Harris Amendments<sup>5</sup> to the Food, Drug and Cosmetics Act only after the use of thalidomide by pregnant women caused deformed children.<sup>6</sup>

The Food and Drug Modernization Act of 1997<sup>7</sup> (the Act) has the opportunity to provide a fourth episode in this series. As part of a long-debated reform of the FDA aimed in part at facilitating drug approval, the Act attempts to provide a market-based incentive for drug companies to test drugs for pediatric use for drugs that have been or will be approved for adult use. Specifically, Section 111 of the Act creates a new Section 505A of the Food, Drug and Cosmetic Act (505A) that provides for six months of additional market exclusivity, beyond both the market exclusivity already provided by

8

statute and that provided by patent protection, when a drug company, upon request by

the FDA, tests its product, whether already approved or not, for use by children.<sup>9</sup> 505A attempts to remedy the general lack of information about pediatric drug

use.<sup>10</sup> According to the American Academy of Pediatrics, roughly eighty percent of drug

Drug Amendments of 1962, Pub. L. No. 87-781, (codified at 21 U.S.C. §§ 321-81 (1996).

<sup>6</sup> the FDA never approved thalidomide in the United States, it had been distributed to women in the U.S. as an investigational new drug (IND). The 1962 Amendments broadened the definition of new drug and repealed the sixty-day automatic approval for new drugs. See Myers, *supra* note 3, at 312 n.17.

<sup>7</sup> 111 Stat. 2296 (1997).

<sup>8</sup> Part II, *infra*, which discusses the 1984 Drug Price Competition Act, 98 Stat. 1585.

<sup>9</sup>ii 1 Stat. 2296.

<sup>10</sup> See, e.g., David A. Kessler, M.D., *Remarks by the Commissioner of Food and Drugs*,

50 FOOD & DRUG L.J. 327, 330 (1995) (noting that information about a drug's safety and effectiveness in adults is insufficient for use in children, who are not miniature adults).

2

2

prescriptions for children are off-label. This situation results from a combination of factors: first, physicians are free to prescribe drugs according to their approved uses or for off-label uses;<sup>2</sup> second, pharmaceutical companies may generally only promote drugs for their FDA-approved uses, even if evidence of other uses is available;<sup>3</sup> third, companies often have little incentive to test and seek approval of already-approved drugs for additional uses;<sup>4</sup> and, fourth, companies have even less incentive to test for pediatric use, as children provide a smaller product market.<sup>5</sup>

See Congressional Testimony of Sarah F. Jagger, Director of Health Services Quality and Public Health Issues (Sept. 12, 1996), *available in* 1996 WL 10830746 [hereinafter Jagger Testimony]. Off-label refers to the prescription of a drug for any unapproved use, either in the way the drug is prescribed or to whom it is prescribed.

12

See 37 Fed. Reg. 16,503 (1972).

See, e.g., 21 C.F.R. §§ 310.3(h)(4), 312.7(a), 314.70(b)(3) (1996). The Act loosens restrictions on promotion of information about unapproved uses. See *infra* note 30, and accompanying text.

See Richard M. Cooper, *Unapproved Uses of Drugs: An Analysis and Some Proposals*, 49 Food & Drug L.J. 533, 535 (1994) (noting that although manufacturers are in the best position to provide information to physicians regarding drug treatment, a manufacturer has little or no incentive to generate information on the safety and effectiveness of the unapproved use). See also ROBERT HIGGS, HAZARDOUS TO OUR HEALTH? FDA REGULATION OF HEALTH CARE PRODUCTS 17 (1995) (reasoning that even if a new use for a drug is discovered, if the patent is about to expire the firm may have little incentive to finance these additional tests); Congressional Testimony of Dr. Sanford N. Cohen, American Academy of Pediatrics, House Subcommittee on Health and Environment (Apr. 23, 1997), *available in* 1997 WL 208511 [hereinafter Cohen Testimony] (Once a drug is marketed for an adult indication, the economic incentive to do additional studies to include pediatric labeling is markedly reduced because the drug may be prescribed off label.).

<sup>5</sup>See Cohen Testimony, *supra* note 14 (explaining that, with a few exceptions such as antibiotics, pediatric use of a drug makes up a small proportion of the total market).

However, questions remain regarding both the interpretation and future effectiveness of 505A. This paper attempts to analyze these issues, attempting to anticipate ways of improving the statute and making recommendations for the provision's effectiveness. Part I of this paper reviews the perceived need for greater pediatric drug information and previous attempts at improving pediatric pharmaceutical treatment. Part II summarizes SOSA itself in relation to current patent and exclusivity provisions. Part III examines 505A in light of the current regulatory system and financial incentives, arguing that greater FDA discretion in implementing the provision and/or greater reliance on market forces would make SOSA more effective. Finally, Part IV argues that SOSA should be expanded beyond pediatric studies, to provide incentive for further drug studies for adult indications as well.

## I. History of SOSA:

### a. Children as Therapeutic Orphans

The lack of prescription drugs approved and labeled for pediatric use, and the lack of information about the effectiveness on children of drugs developed for adults, has lead some to call America's children therapeutic orphans.<sup>16</sup> Roughly eighty percent of prescription drugs marketed in the United States contain a disclaimer that the drug has not been tested for pediatric use.<sup>17</sup> In many cases, however, the dearth of available drug products approved for pediatric uses forces physicians to prescribe drugs off-label, despite any disclaimers. The lack of approved drugs in pediatric cancer treatment is

<sup>16</sup> See, e.g., S. REP. No. 105-43, at 51(1997).

especially revealing. While physicians have been successful in improving the rates of cure, virtually every therapy available., involves the off-label use of approved anticancer drugs.<sup>18</sup> Cancer treatment is by no means the only area for concern. For instance, there is no migraine drug that has been approved for pediatric use by the FDA;

consequently, doctors often recommend Excedrin for children, even though it contains

j9

aspirin.

While physicians do treat children by prescribing drugs off-label, this measure is not a panacea, and can be dangerous. Animal models and trials in adults cannot accurately predict the effect of a drug on children, a group that encompasses a wide range of developmental stages.<sup>20</sup> To determine accurately the safety and effectiveness of a drug, the great diversity within the pediatric population might even necessitate the study of a drug in various pediatric groups, ranging from neonates to adolescents.<sup>21</sup>

<sup>17</sup> See Cohen Testimony, *supra* note 14.

*Changes in the FDA.* Hearings on More information for Better Patient Care Before the Senate Labor and Human Resources Comm., 104th Cong. (1996) (statement of Gregory H. Reaman, M.D., Chairman, Dep't of Hematology/Oncology, Children's National Medical Center) available in 1996 WL 75269 [hereinafter Reaman Testimony] (If physicians were restricted to using anticancer agents only for the purposes approved by the FDA, the success of pediatric cancer treatment would not be what it is today).

<sup>18</sup> While Excedrin is now available over the counter, it is still intended only for people over twelve years old, due to its aspirin content. See *Migraines: FDA OKs Excedrin as 1st Over-the-Counter Treatment*, CHI. TRIB., Jan. 16, 1998, (News), at 7.

<sup>20</sup> See Cohen Testimony, *supra* note 14.

<sup>21</sup> See *id* (recommending the study of neonates, infants, young children, and adolescents as distinct subpopulations to determine a drug's efficacy, toxicity, dosing, and appropriate formulations for each group).

Furthermore, drugs unapproved for pediatric use typically lack dosage recommendations for children, and often are manufactured in dosage forms not accessible to children.<sup>22</sup>

Even when off-label uses of drugs are seemingly safe and effective, physicians often fail to receive information about these treatment options. Typically, while physicians in academic research hospitals may be privy to innovative treatment possibilities, community physicians are unlikely to be sufficiently informed and to remain

23

up to date about treatment options. Moreover, the lack of accurate, controlled studies and FDA's approval may lead even those informed physicians to hesitate in prescribing

treatments off-label. Their hesitancy stems naturally from their duty to provide safe and effective patient care and from the threat of liability for medical malpractice.<sup>24</sup>

Thus, lack of FDA approval for pediatric use forces physicians to choose between prescribing with imperfect labeling and inadequate understanding of the drug's efficacy, or denying children access to potentially life-saving or therapeutic drugs. Yet, the potential solution— increasing studies for pediatric indications— has more obstacles than just the lack of financial incentive among manufacturers. For instance, the study of new drugs on children, for whom the risks may be greater due to organ development, poses

22 For instance, many drugs are manufactured in capsules or tablets that cannot be swallowed by children or are unavailable in small enough dosage increments to give the proper amount to a child. *See id*

23 *See* Reaman Testimony, *supra* note 18 (explaining that community physicians have busy practices and are simply unable to remain aware of current off-label treatment options; consequently, while a young child with cancer will often be treated in a major institution, a teenager with cancer is likely to be treated in a community setting where information is lacking).

<sup>2</sup> *See* S. REP. No. 105-43, at 57(1997).

ethical issues.<sup>25</sup> Moreover, pediatric patients are more difficult to attract into studies.<sup>26</sup> For these reasons and others, the FDA has been reluctant to require pediatric studies for a new drug unless the primary use of the drug will be for children.<sup>27</sup>

Various solutions have been offered to improve pediatric drug treatment, including requiring pediatric studies. Unfortunately, these proposals have significant drawbacks. Some of the more common proposals will be analyzed in turn:

1) Loosening restrictions on pharmaceutical companies concerning dissemination of data: Prior to the FDA Modernization and Accountability Act, the FDA restricted pharmaceutical companies to promoting their drug products only for approved uses.<sup>28</sup> However, the new legislation amends the Food Drug & Cosmetic Act by specifically allowing manufacturers to disseminate information on unapproved uses of approved

<sup>29</sup>

drugs, subject to certain restrictions. Allowing manufacturers to publicize

<sup>25</sup> *See id*

<sup>26</sup> *See id*

<sup>27</sup> *See* Cohen Testimony, *supra* note 14.

<sup>28</sup> 21 C.F.R. 202.1 (e)(4) (1997). However, manufacturers could supply physicians with independent studies if they were requested. *See* Jagger Testimony, *supra* note 11.

<sup>29</sup> 111 Stat. 2296, § 401 (1997). Information can be distributed only if: the product is approved; in the case of information produced by a manufacturer, the manufacturer has given permission; the information is submitted to the FDA sixty days before distribution; a supplemental application covering the new use is filed with the FDA; and, the information contains a prominent statement that the use has not been approved. *See id.* (new section 551(b) of the Food, Drug and Cosmetic Act). The information can be distributed to practitioners, health care professionals, and governmental agencies, but not to patients. *See id.* (new section 551(a) of the Food, Drug and Cosmetic Act). Finally, the only information that a manufacturer may distribute is an unabridged reprint of a peerreviewed, scientifically sound article published in a scientific or medical journal, or a reference publication, produced independently of the manufacturer, containing similar information. *Id.* (new section 552 of the Food, Drug and Cosmetic Act).



independently-produced information about their products may aid physicians in treating

children. Arguably, physicians are adequately trained to assess the literature in light of

<sup>30</sup>

their training. Furthermore, pharmaceutical companies are in the best position, and have the financial incentive, to provide treatment information to physicians quickly.<sup>31</sup>

Proponents of liberalizing the dissemination rules regarding unapproved uses note that the current system ignores the reality that a great deal of treatments, including virtually all treatments for diseases such as cancer, are prescribed off-label.<sup>32</sup>

Loosening the restrictions on drug promotion also has significant drawbacks. First, allowing companies to provide information directly to physicians or health professionals for off-label pediatric use is likely to reduce substantially the incentive for companies to conduct the scientific trials necessary for additional approvals.<sup>33</sup> This, in turn, may actually reduce the amount of reliable information about the safety and effectiveness of drugs. Second, studies by peer-review journals may be limited in scope and insufficient according to FDA standards of approval.<sup>34</sup> In addition, journals only

<sup>30</sup> See Reaman Testimony, *supra* note 18 (arguing that peer-reviewed journal studies generally include adequate detail to allow physicians to understand dosing requirements, methods of administration, toxicity, and other variables necessary to treat patients to a greater extent than does the information provided in FDA-approved labeling).

<sup>31</sup> See *id.*

<sup>32</sup> *Changes in the FDA*. • *Hearing Before the Senate Comm. on Labor and Human Resources*, 104th Cong. (1996) (statement of Bruce A. Chabner, M.D., Clinical Director of the Cancer Center of the Massachusetts General Hospital) available in 1996 WL 77253 [hereinafter Chabner Testimony].

<sup>33</sup> See Cohen Testimony, *supra* note 14.

For instance, peer-review studies may use an insufficient number of subjects, collect incomplete data, or fail to account for interaction of the tested drug with other

publish a limited number of articles; even if the studies are comprehensive, the peer-review forum is too limited to report all the information potentially available and useful in pediatric treatment. Third, non-pediatric practitioners often prescribe drugs to children.<sup>35</sup> Insufficient or incomplete information places children at an even greater risk in the hands of physicians inexperienced with pediatric care. Thus, in light of the significant questions surrounding these less restrictive dissemination provisions, the provisions clearly are not an adequate substitute for increasing the amount of FDA-approved pediatric uses available to physicians.

2) Requiring pediatric studies of drugs likely to be used in treating children:

Under this approach, an independent panel of advisors may advise the FDA in determining which new drugs might have pediatric applications, what types of studies should be required, and which previously approved drugs should also be tested for pediatric use.<sup>36</sup> Proponents of requiring pediatric studies usually favor the maintenance of tight restrictions on the promotion of off-label use.<sup>37</sup> Those in favor of mandatory testing note that the FDA's attempts at obtaining pediatric prescribing information from

compounds. *See id* The new dissemination provisions in the Act also increase the FDA's policing responsibilities, as the agency will have to make an individual determination about the scientific soundness of each article to be distributed.

<sup>35</sup> *See* Cohen Testimony, *supra* note 14.

<sup>36</sup> *See id*

<sup>37</sup> *See id*

drug manufacturers on a voluntary basis have failed; most new drugs are still being approved without pediatric information.<sup>38</sup>

However, mandatory testing also has significant disadvantages. Mandatory testing is likely to result in disincentives for drug development. Due to the significant cost of trial studies,<sup>39</sup> anticipation of mandatory pediatric studies in addition to adult studies could impede research on drug therapies for both children and adults.<sup>40</sup> Testing experimental drugs on children also poses ethical dilemmas related to the effect of these trials on a child's organ development and to issues of informed consent.<sup>41</sup> Furthermore, opponents question whether the FDA has legal authority to force a drug sponsor to test

<sup>38</sup> See Joseph K. Zanga, M.D., *Testing Drugs for Kids.* Pro, DALLAS MORNING NEWS, Dec. 21, 1997, at 1 J (stating, in reference to the s proposed rule, that of the seven new drugs proposed in 1991 for which pediatric studies were promised, only one ultimately had pediatric labeling).

~ estimates place the research and development costs of developing a new drug between \$359 million (see PHARMACEUTICAL RESEARCH & MANUFACTURERS OF AMERICA, INDUSTRY PROFILE 1996 at 13) and \$500 million (see STANDARD & Poor's, INDUSTRY SURVEYS- HEALTH-CARE: PHARMACEUTICALS 19 (1997)). One of the main sources of development costs is clinical trials. See Boston Consulting Group, *The Contribution of Pharmaceutical Companies.* What's at Stake for America, Sept. 1993.

~ *Prescription Drugs and FDA Overhaul.* Hearing before the Health and

*Environment Subcomm. of the House Commerce Comm.*, 105th Cong. (1997) (statement

of Susan L. Weiner, North American Brain Tumor Coalition) available in 1997 WL 228096 [hereinafter Weiner Testimony].

<sup>41</sup> See Chabner Testimony, *supra* note 32. The pharmaceutical industry has raised the ethical dilemma of testing children in its protest against the proposed FDA regulations requiring drug companies to test products for pediatric use. See Robert Pear, *Testing Drugs in Children Opposed.* Clinton Proposal is Raising All Sorts of Ethical Questions, SEATTLE TIMES, Nov. 30, 1997, at A1. The same ethical dilemma should apply to voluntary testing under the new Section 505A as well. However, given that drugs without pediatric testing are already being used in children, and will continue to be used in children, there seems to be little added risk in testing these drugs on a limited sample of children. Actually, testing a limited sample before doctors across the country start experimenting on their own likely is a safer alternative.

and label a drug for an age group for which it does not intend to market the product.<sup>42</sup> Whether or not the FDA has authority, Congress' recent push to ease the regulatory burden on pharmaceutical companies indicates that it is unlikely to support mandatory testing either.

3) More funding to independent organizations like NIH to research pediatric therapies:

Despite disagreement over the previous two proposals, virtually all quarters in the debate support funding more research into treating children.<sup>43</sup> While increasing pediatric research is a commendable goal, any increase in funding successfully passed into law would not be sufficient to address the significant lack of information regarding pediatric drug treatment. Thus, while additional funding could increase information about pediatric drug treatment, by itself it is insufficient to address the problem.

4) Providing economic incentives to drug manufacturers to conduct studies of their products

Congress ultimately adopted an economic incentive approach in 505A. First proposed in 1994 as the Better Pharmaceuticals for Children Act, the proposal was supported by many in the children's health care community.<sup>45</sup>

<sup>42</sup> See *Rx Makers Challenge FDA on Pediatric Studies*, DRUG TOPICS, Dec. 8, 1997, at 26, available in 1997 WL 13740742.

<sup>43</sup> See, e.g., Weiner Testimony, *supra* note 40 (arguing for federal financial support for pediatric research). See also *National Institutes of Health Reauthorization: Hearing Before the Senate Labor Public Health and Safety Comm.*, 105th Cong. (1997) (statement of Sen. DeWine) (arguing for greater investment in innovations in children's health care).

See *infra* note 56 and accompanying text.

<sup>45</sup> See, e.g., Cohen Testimony, *supra* note 14; Chabner Testimony, *supra* note 32.

However, detractors doubt that six months of market exclusivity will provide enough incentive to drug manufacturers.<sup>46</sup>

b. **Unsuccessful Regulatory Efforts to Require Labeling and Encourage Testing** The current legislation is only the latest in recent governmental attempts to

improve pharmaceutical care for children. Previously, FDA regulations have aimed at either expanding labeling or requiring some degree of clinical testing. In 1979, the FDA published regulations specifying the content and format of prescription drug labeling, including a stipulation that pediatric labeling be based on adequate, controlled studies involving children.<sup>47</sup> The FDA intended that these regulations would lead to the provision of adequate information about the use of drugs in children.<sup>48</sup> Instead, drug makers began adding to labels a disclaimer that the safety and effectiveness of the drug in children had not been established.<sup>49</sup>

<sup>46</sup> See e.g., Weiner Testimony, *supra* note 40. Skeptics of the financial incentive approach seemingly prefer a stick approach (requiring testing) to a carrot approach (encouraging testing), as the carrot approach has not been successful so far. For further analysis of the potential drawbacks of this approach, see *infra* Part 111(a).

See 44 Fed. Reg. 37,462 (1979); 21 C.F.R. § 201.57 (1996). In 1974, the FDA had revised the general labeling requirements by prohibiting label statements describing differences of opinion among experts regarding product warnings. See 39 Fed.Reg. 33,229 (1974). Note, however, that the FDA does permit labels to state differences of opinion with respect to effectiveness if the opinions are supported by substantial evidence as defined by sections 505(d) and 5 12(d) of the Act. In 1975, the FDA had amended the over the counter (OTC) regulations by requiring a label on all OTC drugs that warned against accessibility to children. See 40 Fed.Reg. 11,717 (1975); 21 C.F.R. § 330.1(g).

<sup>48</sup> See Cohen Testimony *supra* note 14.

<sup>49</sup> See *id*

The FDA attempted to take corrective action in 1994. In an effort to increase pediatric information in drug labeling, the FDA published regulations that accepted several methods of establishing substantial evidence supporting pediatric labeling claims.<sup>50</sup> However, according to one observer, two years after the regulations had gone into effect, it was not yet apparent that they [had] resulted in any increase in new drug labeling for children.<sup>51</sup>

Most recently, President Clinton announced proposed FDA regulations that would require drug makers to test their products in children if the drugs were used or were likely to be used in a substantial number of children, or if they potentially provided a significant therapeutic benefit over existing pediatric treatments.<sup>52</sup> Despite the FDA's efforts, few substantial advances in improving pediatric drug treatment have been made. According to a survey by the American Academy of Pediatrics, in 1995 only three of the twenty-five new drugs approved had pediatric labeling.<sup>53</sup> Between 1984 and 1995, approximately 80% of approved new molecular entities contained no labeling for pediatric use, even though many of them have been used widely in treating children.<sup>54</sup> By utilizing market incentives, 505A represents a different approach to a lingering problem.

<sup>50</sup> See 59 Fed. Reg. 64,240; 65,738 (1994). Acceptable labeling claims can include published pediatric information or approval of pediatric use based on adult efficacy studies where the disease for which the drug is to be used is substantially the same in children and adults. See *id.*

<sup>51</sup> Cohen Testimony, *supra* note 14.

<sup>52</sup> See Pear, *supra* note 41. See also 62 Fed. Reg. 43,900; 51,071 (1997).

<sup>53</sup> Cohen Testimony, *supra* note 14.

<sup>54</sup> *id.*

## II. Section 505A: Offering a Carrot to Industry

Section 505A of the FDA Modernization and Accountability Act of 1997<sup>56</sup> was first introduced in similar form in 1992 as the Better Pharmaceuticals for Children Act. 56 Congress approved overwhelmingly the Act as a whole,<sup>57</sup> with market incentives for pediatric studies under Section 505A considered to be one of the Act's central achievements.<sup>58</sup>

A review of the system of exclusivity existing prior to the 1997 Act is useful in analyzing the incentive system implemented by 505A. 505A amends the exclusivity provisions of the Food Drug and Cosmetic Act that were established in 1984 under the Drug Price Competition and Patent Term Restoration Act (Waxman-Hatch Act).<sup>59</sup> The Waxman-Hatch Act protects drug manufacturers by providing periods of market exclusivity and patent protection. Once a new drug application (NDA) for a new

~ Ill Stat. 2296 (1997). Section 3 of the Act amends Chapter V (21 U.S.C 351 et. seq.) of the Food Drug & Cosmetic Act by creating a new section, 505A, Pediatric Studies of Drugs [hereinafter 505A].

<sup>56</sup>It was originally introduced by Senator Nancy Kassebaum as S3337. *See* 138 CONG. REC. S 16979-02 (daily ed. Oct. 5, 1992) (statement of Sen. Kassebaum).

<sup>57</sup>The Act passed the Senate by a 98 - 2 margin. *See* 143 CoNG. REC. 5 12241-02 (daily ed. Nov. 9, 1997) (statement of Sen. Dodd). The Act passed the House by voice-vote. *See* CONGRESS DAILY (Oct. 7, 1997) *available in* 1997 WL 11443852.

<sup>58</sup>*See, e.g.*, 143 CoNG. REC. H10531-01 (daily ed. Nov. 9, 1997) (statement of Rep. Dingell) (touting the provision of market incentives for pediatric studies). *See also id* (statement of Rep. Waxman) (same); 143 CoNG. REC. 5 12241-02 (daily ed. Nov. 9, 1997) (statement of Sen. Dodd) (same).

<sup>59</sup>Pub.L. 98-417, 1984; 98 Stat. 1585 (1984).

chemical entity (NCE) is approved, an abbreviated NDA<sup>60</sup> will not be accepted by the FDA for five years from the date of approval.<sup>61</sup> After the FDA has approved an NDA or supplemental NDA for a new indication or other variation of an already-approved drug, an abbreviated NDA for the same variation will not be approved for three years.<sup>62</sup> Regarding patents, if the applicant of an abbreviated NDA is not challenging the patent on a drug, the FDA cannot approve an abbreviated NDA until the patent has expired.<sup>63</sup> Finally, if the applicant is challenging a patent, the FDA cannot approve the abbreviated NDA for two and a half years.<sup>64</sup> The three- and five-year exclusivity provisions and the patent provisions are independent of one another; in any given situation, the longer of the two will be operative in determining the permissibility of subsequent abbreviated NDA approvals.<sup>65</sup>

<sup>60</sup>An abbreviated NDA is an NDA that lacks the safety and effectiveness data for approval of a full NDA, because the drug seeking approval is the same in its indications and effects as a previously approved drug or is so similar that use of the data on the previously approved drug is appropriate to approve the generic copy. *See* FD&CA § 505(j)(2)(A), 21 U.S.C. § 355(j)(2)(A).

<sup>61</sup>*See* FD&CA § 505(j)(4)(D)(ii). However, if the applicant is seeking to challenge a patent on the drug, it can submit an abbreviated NDA after four years. If a patent infringement suit is brought, on the other hand, the FDA cannot approve the abbreviated NDA for seven and a half years after NDA approval.

<sup>62</sup> FD&CA §§ 505(j)(4)(D)(iii), (iv).

<sup>63</sup>*See* FD&CA § 505(j)(4)(B)(ii). If the patent has expired, the applicant's abbreviated NDA can be approved with no waiting period. FD&CA §§ 505(j)(2)(A)(vii), (j)(4)(B)(i).

<sup>64</sup>*See* FD&CA § 505(j)(4)(B)(iii). If the patent holder wins, the FDA cannot approve the abbreviated NDA until after the patent expires. *See id*

<sup>65</sup>Paper NDAs are subject to the same patent and exclusivity provisions that restrict approval of abbreviated NDAs. *See* FD&CA § 505A. Although a paper NDA does require safety and effectiveness studies, similar to an abbreviated NDA it may rely on published reports of studies without actual submission of data. *See* FD&CA § 505(b)(2).



In short, 505A provides an incentive for pediatric studies by extending exclusivity to both the original market exclusivity provisions and the patent protection provisions under the Waxman-Hatch Act. Furthermore, the extended exclusivity applies to adult and pediatric indications and variations alike.<sup>66</sup> Each subsection of Section 505A is summarized below:

Subsection (a): Provides that, prior to approval of a new drug, if the FDA determines that information about the drug will produce pediatric health benefits, and makes a written request for pediatric studies, and the studies are completed and accepted by the FDA, then

<sup>67</sup>

the sponsor can receive six months of extra market exclusivity.

Subsection (b): Directs the FDA to produce a list of already-approved drugs for which additional pediatric information may be useful in producing health benefits. The list is to be updated annually.<sup>68</sup>

Subsection (c): Authorizes the FDA to apply exclusivity to already-approved drugs that are on the list created under subsection (b). After the list has been published, the process mirrors that for new drugs: the FDA requests pediatric studies, and if the FDA is

<sup>66</sup>Extending exclusivity only for pediatric uses would not be a sufficient inducement to carry out pediatric studies due to the small pediatric market; if it were, this provision likely would not be necessary.

<sup>67</sup>FD&CA § 505A(a).

•For an NCE, the period during which an abbreviated NDA cannot be submitted is extended from five to five and a half years. If the applicant is challenging a patent, the period of patent protection is extended from four to four and a half years, and if litigation is brought the period is extended from seven and a half to eight years. *See* FD&CA §505A(a)(1)(A)(i).

~For a drug that does not qualify as an NCE, the exclusivity period is extended from three to three and a half years. *See* FD&CA § 505A(a)(1)(A)(ii).

Any applicable orphan drug exclusivity period is extended from seven to seven and a half years. *See* FD&CA § 505A(a)(1)(B).

~For drugs subject to a patent not being challenged, the exclusivity period is extended six months beyond the patent expiration. *See* FD&CA §505A(a)(2)(A).

~For drugs subject to a patent that is being challenged, the exclusivity period is extended six months beyond the patent expiration. *See* FD&CA §505A(a)(2)(B).

<sup>68</sup> FD&CA § 505A(b) (1997)

satisfied that the manufacturer has completed the studies, it may award six months of additional exclusivity.<sup>69</sup>

Subsection (d): Specifies the procedures for conducting requested pediatric studies. If the FDA and sponsor agree on written protocols, those protocols satisfy the requirements. However, if they cannot agree on written protocols, the FDA must determine whether the studies conducted fairly respond to the request, have been carried out in accordance with commonly accepted scientific principles, and have been properly reported.<sup>70</sup>

Subsection (e): Addresses situations in which a study report has been submitted before the expiration of a patent (or other form of exclusivity), but has not been accepted or rejected by the Secretary at the time of expiration. In such circumstances, the FDA is to delay acceptance of an abbreviated NDA for another drug while it determines whether the study is accepted. This delay may not exceed 90 days. If the pediatric study is subsequently accepted and exclusivity is granted, the period of additional exclusivity will be considered to have begun on the date of the expiration of the previous exclusivity.<sup>71</sup>

Subsection (f): Requires the FDA to publish a notice of the acceptance of pediatric studies under subsection (d) and granting of additional exclusivity.<sup>72</sup>

Subsection (g): Defines the term pediatric studies to mean at least one clinical investigation in appropriate age groups, according to how the drug is expected to be used.<sup>73</sup>

Subsection (h): Limits the availability of exclusivity to one award per product, except in the case of a drug supplemental application for a new use. In that case, the FDA may award another six months of exclusivity to be added to any exclusivity for the use of the drug that is available under Waxman-Hatch authorities, but not for additional exclusivity beyond patent expiration.<sup>74</sup>

<sup>69</sup>FD&CA § 505A(c) (1997). As noted above, the additional exclusivity applies whether derived from patent or Waxman-Hatch exclusivity. *See* (HR 105-3 10, p. 53) <sup>70</sup>FD&CA § 505A(d) (1997). According to the Conference Committee Managers Statement (p. 3), qualifying studies can be conducted either before or after a request from the FDA has been made.

<sup>71</sup>FD&CA § 505A(e) (1997).

<sup>72</sup>FD&CA § 505A(f) (1997). This will notify potential applicants of abbreviated NDAs

that an additional six months of exclusivity will apply.

<sup>73</sup>FD&CA § 505A(g) (1997). One purpose of this provision is to ensure that the studies requested will not merely review existing data. *See* H.R. REP. 105-310, at 54 (1997).

<sup>74</sup>FD&CA § 505A(h) (1997).

Subsection (F): Provides that if, under any proposed regulations, the Secretary requires pediatric studies, those studies are to be deemed to satisfy the requirements under 505A and to be the basis for the award of exclusivity.<sup>75</sup>

Subsection (F): Terminates the FDA's authority to grant additional exclusivity under this section on January 1, 2002. After that, exclusivity is available only if (1) the drug was in commercial circulation when the FDA Modernization Act went into effect; (2) the drug was on the FDA's subsection (b) list by January 1, 2002; (3) the FDA determines there is a continuing need for pediatric information and that the drug may provide health benefits to children; and, (4) all of the requirements of 505A have been met.<sup>76</sup>

Subsection (k): Requires the FDA to conduct a study on the program and submit a report to Congress by January 1, 2001. The study must include all aspects of the program, as well as the impact of the program on the price and availability of drugs, including generic drugs.

### III. Strategies for Optimizing the Effectiveness of 505A:

The success of 505A remains to a large degree contingent upon as yet unresolved issues. This is due in part to the interpretative ambiguities in the statute and Congress' requirement of a report within a few years. Thus, 505A is experimental and should be treated as a work in progress. Problems may arise with the statute, most notably whether six months of extra market exclusivity is the proper inducement to testing. Consequently, in applying the statute, and with an eye toward its possible modification in a number of

FD&CA § 505A(i) (1997). Subsection (i) directly addresses the FDA's proposed regulations, announced by President Clinton, under which the agency could require pediatric studies to be performed. *See* 62 Fed. Reg. 43,900 (1997). In effect, subsection (i) provides six months of market exclusivity even if the sponsor *is forced to* carry out pediatric studies, rather than doing so voluntarily under 505A.

<sup>75</sup>FD&CA § 505A(j) (1997).

<sup>76</sup>FD&CA § 505A(k) (1997).

years, two primary principles relied on within 505A should be further embraced: agency discretion and utilization of market forces.

a. Expanding Agency Discretion

(i): *Interpreting* the Statute Currently to Give the FDA More Discretion:

Unlike much of the Act, which forces the FDA to act in a certain manner,<sup>78</sup> 505A actually gives the FDA greater discretion by expanding its authority over exclusivity. Previously, the terms of exclusivity were codified; now, the FDA has the authority, albeit limited, to add to those terms based on its discretion.<sup>79</sup> In implementing 505A, the FDA will have to interpret parts of the provision that Congress left unclear. For instance, 505A(a) authorizes the Secretary to request pediatric studies;<sup>80</sup> the FDA will have to determine which officials have the authority to request pediatric studies. Moreover, 505A(g) defines pediatric studies as clinical investigations in pediatric age groups in which the drug is anticipated to be used;<sup>81</sup> yet, the age groups themselves are undefined.

Regarding the request for pediatric studies, allowing review officers to make individual assessments of the usefulness of pediatric studies would maximize the effectiveness of the statute. The drugs in question have not yet been approved, and the

<sup>78</sup> *See, e.g.*, 111 Stat. 2296, § 401 (authorizing dissemination of information about unapproved uses of approved drugs); § 502(a) (requiring that health care economic information be based on competent and reliable scientific evidence, a more lenient standard than that previously imposed by the FDA).

<sup>79</sup> *See* § 505A.

<sup>80</sup> § 505A(a)

<sup>81</sup> §505A(g)

average time for a drug to gain approval is over nineteen months.<sup>82</sup> By decentralizing the decision to request studies under 505A, requests will be made faster, manufacturers can begin more promptly, and the product and/or additional pediatric information will be available sooner.

In specifying what age groups need to be tested as part of a manufacturer's pediatric studies under 505A(g), the FDA should define precisely the group or groups

83

being targeted. The American Academy of Pediatrics has emphasized the importance of differentiating children in different developmental stages when considering

pharmaceutical indications.<sup>84</sup> It has recommended five categories of children: neonate, infant, toddler, young child, child, and adolescent, defined by age.<sup>85</sup> Attempting to assess pediatric indications from overly general studies could produce misleading information that may be harmful to children. Moreover, overly general studies could obfuscate data wherein a drug is actually effective for a subpopulation of ages within the pediatric range, but not for other children; a generalized experimental design would average out the effects and make the drug appear to be ineffective. Thus, the FDA should determine if more than one category of child could benefit from pediatric studies, and request clinical studies accordingly.

<sup>82</sup> PHARMACEUTICAL RESEARCH & MANUFACTURERS OF AMERICA, *supra* note 39, at

15 (citing the United States Food & Drug Administration).

Currently, the FDA only defines pediatric patients as ranging from birth to sixteen years of age. *See* 21 C.F.R. § 201.57(f)(9) (1996). The FDA defines infant as a child not more than twelve months old for dietary foods, *see* 21 C.F.R. § 105.3(e) (1996), but has not defined infant for drugs. *See* 21 C.F.R. § 201.19 (1996).

<sup>84</sup> *See* Cohen Testimony, *supra* note 14.

<sup>85</sup> *See id*

(ii): *Revising the Statute to Give the FDA More Discretion:*

The provision of six months of extra market exclusivity clearly is not subject to FDA interpretation under 505A; it can grant it or not. However, the FDA is required to report back to Congress by January 1, 2001 on the effectiveness of the program, the adequacy of the incentives, and the economic impact of the program.<sup>86</sup> While the effect of the provision is unpredictable, the market exclusivity program would benefit from giving the FDA discretion to alter and fine-tune the amount of exclusivity awarded.

Giving the FDA discretion to determine, within reason, the amount of exclusivity would produce a more efficient system for gaining information about pediatric drug indications. Congress could grant discretion in a number of ways. For instance, the FDA could be required to utilize rulemaking proceedings to determine categories of exclusivity based on the potential value of the category of drugs in question. For a potential pediatric AIDS treatment, providing more than six months of exclusivity might be a socially valuable investment. For other drugs, less than six months might be a sufficient inducement to conduct further studies; in this case granting six months is socially wasteful and needlessly prevents the introduction of new drug products onto the market.

Another alternative would be for the FDA to determine appropriate amounts of additional exclusivity on a case by case basis in adjudicatory proceedings. While this would be more time consuming for the agency and carry the potential for arbitrary or inconsistent decisionmaking, it would allow for more input from manufacturers. Because

<sup>86</sup> See § 505A(k)

manufacturers are in the best position to gauge the value of their products, their input would allow the FDA to optimize social utility by measuring the value of information about individual drugs.

Either alternative goes a long way towards eliminating the disadvantage of 505A as currently written. That is, Congress has determined, rather arbitrarily, that the information to be gained from additional studies of pediatric drug use is, on average, worth six months of exclusivity. By quantifying the value of this information, manufacturers will be able to determine whether the studies will be economically advantageous. Essentially, Congress is gambling that the *average* utility of information gained about pediatric use of drugs will equal or exceed the *average* value of six months of additional market exclusivity. However, many of the individual drugs will produce

information below the value of six months of exclusivity.<sup>87</sup> More importantly, the

88

tradeoff is a six month delay in new products, including much cheaper generic versions,

entering the market. Granting the FDA discretion over the grant of exclusivity avoids this outcome.

~ Significantly, drugs receive the additional market exclusivity regardless of whether the

clinical studies indicate that the drug actually is safe and effective for children. *See* §

505A.

88 Generic drugs have been known to enter the market at a 90% discount compared with the name brand. *See* STANDARD & POOR'S, *supra* note 39, at 11.

b. Relying More Heavily on the Market

While giving the FDA more discretion, 505A also departs from other recent drug law reforms by concentrating on market forces.<sup>89</sup> Notably, utilization of financial incentives, voluntarily complied with, also reduces the need for significant enforcement responsibility and resource allocation by the FDA. Conversely, while previous FDA reforms have been successful, they have also increased the FDA's enforcement responsibilities.<sup>90</sup> In 2001, when Congress reexamines the program, it should consider relying even more heavily on market forces. For instance, it should consider implementing a pilot program that releases the FDA from any responsibility for annually making a list of previously approved drugs for which additional pediatric information

would be useful,<sup>91</sup> or from determining on a case by case basis whether such information

92

would be useful regarding a drug awaiting approval. Instead, the pilot program should

leave the decision to invest in pediatric studies entirely up to individual manufacturers. Because manufacturers are very familiar with their pharmaceutical products, they

will be in a position to determine the value of additional pediatric studies more easily than the overburdened FDA. However, because manufacturers would be free to conduct studies without waiting for a request, the FDA should only award additional market

<sup>89</sup> *See* HENRY G. GRABOWSKI & JOHN M. VERNON, THE REGULATION OF PHARMACEUTICALS: BALANCING THE BENEFITS AND RISKS 7-8 (1983) (noting that the history of U.S. pharmaceutical regulation is one of steady evolution away from attempting to make the market work better in favor of implementing strong, centralized regulatory control).

<sup>90</sup> *See infra* nn. 3-5 and accompanying text.

<sup>91</sup> As the FDA is now required to do under § 505A(b).

92 the FDA is now required to do under § 505A(a).



exclusivity for sufficient clinical studies that yielded valuable pediatric indications. This would serve to discourage manufacturers from over-investing in pediatric studies. For those manufacturers whose drugs are already being prescribed off-label, they would take the risk that their products are actually safe and effective, and would be rewarded for clinically demonstrating so. Moreover, reluctance on the part of a manufacturer to conduct the studies might indicate to practitioners that the drug in question is not necessarily safe and effective.

The FDA would still have to evaluate the results of studies, despite leaving manufacturers to initiate the action by rolling the dice for market exclusivity. However, because the FDA currently has to evaluate the completed studies under the current system, evaluating additional studies of a drug seeking initial approval should not add substantially to the approval time. Furthermore, this system would not preclude leaving in place the current system of requesting studies and guaranteeing exclusivity, regardless of the outcome of the clinical studies, if the FDA decided to do so.

#### IV. Expanding 505A Beyond Pediatric Studies

The history of drug law reforms indicates that reforms originally enacted in response to deficiencies in the pharmaceutical treatment and protection of children have

improved pharmaceutical standards of safety in general.<sup>93</sup> The case for attempting to

#### Q

improve pediatric care through financial incentives is strong. ~ However, further drug

<sup>93</sup> *See infra* Introduction.

<sup>94</sup> *See infra* Part I.

studies for adult indications would also provide valuable information in improving overall pharmaceutical care. Pending the success of *505A*, additional market exclusivity should be extended beyond the limited sphere of pediatric studies to encompass adult studies as well.

a. The Problem of Unapproved Drug Use in Treating the General Population

The FDA implements the world's most comprehensive new drug approval process.<sup>95</sup> Partly for this reason, however, off-label use of drugs is a substantial problem. Off-label uses include the use of a drug to treat an entirely different condition from what has been approved by the FDA, the varying of dosage of a prescription drug from the levels indicated on the drug's labeling, use of a different method of applying the treatment (e.g., injection into muscles instead of veins), or use of the drug for a different patient population from that for which the drug received approval.<sup>96</sup> While every prescription drug is sometimes, perhaps frequently, administered [off-label], off-label uses may represent sound medical care or represent recklessness.<sup>97</sup>

As is the case with pediatric treatment, practitioners treat some conditions overwhelmingly through off-label uses. In cancer treatment, off-label use is a prevalent

<sup>95</sup> See Wells, *supra* note 4, at 399 (noting that the 1938 and 1962 reforms have resulted in the world's most involved process for new drug approval).

<sup>96</sup> See Edmund Polubinski III, Note, *Closing the Channels of Communication.*' *A First Amendment Analysis of the FDA's Policy on Manufacturer Promotion of Off-Label Use*, VA. L. REV. 991, 997 (1990).

<sup>97</sup> HUTT & MERRILL, *supra* note 2, at 617. In some cases, a physician who fails to prescribe a drug off-label might be liable for malpractice. See Polubinski, *supra* note 96, at 998.

phenomenon.<sup>98</sup> According to a study of drug-prescription pattern among cancer specialists, approximately one third of all prescriptions were off-label.<sup>99</sup> Furthermore, of the approved anticancer drugs prescribed by oncologists during the study, ninety six percent were prescribed at least once to treat an off-label indication. ~ Overall, fifty six percent of cancer patients were the recipients of off-label prescriptions.<sup>101</sup> Evidence indicates that off-label use is even more prevalent in AIDS treatment.<sup>102</sup>

Just as the phenomenon of extensive off-label use in general is similar to that in pediatric treatment, i 03 the problems created by off-label use are also similar. Even though off-label use may represent the best treatment available, concerns over liability or managed care oversight may prevent physicians from prescribing drugs for unapproved uses.<sup>104</sup> Of course, the best way to determine the safety and effectiveness of a drug is to go through the FDA approval process. While adults provide an adequate market, if a drug is already being prescribed widely off-label, manufacturers have little reason to

<sup>98</sup> Jagger Testimony, *supra* note 11.

~ *See id.*

~ *id* (compilation mine).

~ *See id*

<sup>102</sup> *id*

<sup>103</sup> The degree of off-label use in pediatric treatment seems to be greater than overall offlabel use, as health authorities often single out pediatric treatment for special attention. *See, e.g.*, Cohen Testimony, *supra* note 14; Jagger Testimony, *supra* note 11.

<sup>104</sup> HIOGS, *supra* note 14, at 17.

spend money for approval. In addition, if a drug's patent has expired or is near expiration, a manufacturer will have little incentive to finance more clinical studies.<sup>105</sup>

b. Additional Market Exclusivity as an Inducement to Additional Testing

Whether or not 505A succeeds in persuading manufacturers to test for pediatric indications, the program would likely succeed if applied to testing for off-label uses in the general population. Additional market exclusivity would help the pharmaceutical industry recoup a greater amount of its investments and increase the number of drugs that break even. Currently, it is estimated that only three out of every ten approved drugs ever recover their research and development expenditures.<sup>106</sup> This low yield for manufacturers is likely to continue, as research and development costs have continued to increase more rapidly than prices.<sup>107</sup> The average cost of developing a new drug has been estimated between \$359 million<sup>108</sup> and \$500 million.<sup>109</sup> Despite the FDA's efforts at speeding up the approval process, in 1995 the average approval time for a drug was over nineteen

<sup>105</sup> See *id.*

<sup>106</sup> PHARMACEUTICAL RESEARCH & MANUFACTURERS OF AMERICA, INDUSTRY PROFILE, *supra* note 39, at 13.

<sup>107</sup> See PHARMACEUTICAL MANUFACTURERS OF AMERICA, FACTS AT A GLANCE 27.15

(1993 ed.) [hereinafter FACTS AT A GLANCE].

<sup>108</sup> See PHARMACEUTICAL RESEARCH & MANUFACTURERS OF AMERICA, *supra* note 39, at

13.

<sup>109</sup> See STANDARD & POOR'S, *supra* note 39, at 19.

months.<sup>0</sup> The average development time for new molecular entities (NMEs) between 1986 and 1992 was 9.2 years.<sup>11'</sup>

Sales of individual drugs help to reveal valuable incentive of delaying competition through extended exclusivity. While many manufacturers do not release sales information for each of their products, information about many top-selling drugs is available.<sup>2</sup> In 1996, the top ten selling prescription drugs made between \$768 million and \$1.8 billion.<sup>'</sup> During the first quarter of 1997 alone, two cholesterol-lowering

drugs, Zocor and Mevacor, reported sales of \$805 million and \$275 million, 114

respectively. Crixivan, a protease inhibitor, registered \$123 million in first quarter

sales.<sup>5</sup> Even from these admittedly spotty figures, it is clear that six months of additional market exclusivity could produce substantial gains and provide a significant inducement to conduct further testing.

The true value of additional market exclusivity is reflected in the growing influence of competitor drugs, especially generic versions. Indeed, the reduced time

<sup>110</sup> See PHARMACEUTICAL RESEARCH & MANUFACTURERS OF AMERICA, *supra* note 39, at

15 (citing the U.S. Food & Drug Administration). In 1995, mean approval time for a drug was 19.2 months. However, between 1985 and 1983, drug approval times ranged from 26.5 to 34.1 months. *See id*

See FACTS AT A GLANCE, *supra* note 107, at 27.21.

<sup>112</sup> While top-selling drug data is made public, various business databases yielded little comprehensive industry data.

~ STANDARD & Poor's, *supra* note 39, at 12 (citing IMS America).

~ Matthew Lerner, *Pharma Earnings Surge on Healthy Drug Sales*, CHEMICAL MARKET REp., May 5, 1997, available in 1997 WL 8496865.

<sup>5</sup> See *id*

during which the first drug in a therapeutic class is the sole drug in that class reveals the intensifying competition.<sup>6</sup> The profitable lifetime of a drug is shrinking concomitantly.<sup>7</sup> On average, a drug company has less than twelve years to recoup research and development investment in a product.<sup>8</sup>

Increased generic drug competition, due in part to pressure by managed care organizations, has cut into the market of originator drugs.<sup>9</sup> For drugs whose patents expired in 1991-1992, generic competition claimed seventy two percent of the market within eighteen months.<sup>10</sup> Generic prescriptions are on the rise,<sup>11</sup> and generic competition begins immediately after a patent lapses, with discounts of up to ninety percent of the originator drug's price.<sup>12</sup> This creates pressure for manufacturers to maintain a full pipeline of new products in order to maintain profitability.<sup>13</sup> For instance, on the day that the patent on Capoten expired, the FDA approved thirteen new

<sup>116</sup> See PHARMACEUTICAL RESEARCH & MANUFACTURERS OF AMERICA, *supra* note 39, at

33 - 36 (charting the period of time before introduction of a competitor drug).

<sup>117</sup> See *id* This is due in large part to the Waxman-Hatch Act of 1984, 98 Stat. 1585, which reduced to zero the period between patent expiration and the entry of generic competitors into the market.

<sup>118</sup> PHARMACEUTICAL RESEARCH & MANUFACTURERS OF AMERICA, *supra* note 39, at

36.

<sup>119</sup> See *id*

<sup>120</sup> *id* Compare that with drugs first facing generic competition in 1989-1990:

generics gained 47% of the market after eighteen months. See *id*

<sup>121</sup> See STANDARD & POOR'S, *supra* note 39, at 10. Generics grew to 22% of the

prescription market from 19% in 1996. See Greg Muirhead, *Ups and Downs*, DRUG TOPICS, May 5, 1997.

<sup>122</sup> STANDARD & POOR'S, *supra* note 39, at 11.

generic competitors, most of which were reduced by ninety percent of the name brand

124

price.

According to estimates, once generic drugs hit the market, branded prescription

drugs have about ten years of profitability left.<sup>25</sup> Because [generic drugs.. . are unencumbered by the need to recover the high costs of researching and developing a drug,

moving it through the lengthy FDA approval process, and advertising it, they can reduce

126

their prices. Hence, staving off generic competition, even for six additional months, would be of significant value to pharmaceutical manufacturers, and would be a potent

incentive for manufacturers to provide important information regarding treatments.

#### Conclusion

The market exclusivity provisions in 505A, and any expansions or revisions as proposed in Parts III and IV, involve a tradeoff. Additional information about existing drugs is being weighed against the cost of delaying cheaper, innovative competitor products from entering the market. The FDA will report to Congress in a few short years as to whether this tradeoff has been worthwhile. This paper has attempted to argue that 505A has the potential to be a valuable, market-based innovation in pediatric treatment. However, the FDA should be given expanded authority to determine both the specificity of tests requested and the amount of exclusivity that should be awarded.

<sup>24</sup> See Lodewijk DeVink, *The Values of Trust: The Challenges Ahead for Innovation*,

VITAL SPEECHES OF THE DAY, Sept. 1, 1996.

<sup>25</sup> See STANDARD & POOR'S, *supra* note 39, at 15.

1261d

More significantly, 505A should be seen as an overly modest achievement. The provision is a commendable attempt to improve information about pediatric treatment. However, these are merely baby steps. Given a chance to reflect on the history of drug regulation, Congress should give the FDA authority to provide the same incentives across the industry, so as to gain crucial supplemental treatment information about cancer, AIDS, and other conditions that will continue to challenge us as patients, scientists, and policymakers.