

# GENERIC PHARMACEUTICAL REGULATION IN THE UNITED STATES WITH COMPARISON TO EUROPE: INNOVATION AND COMPETITION

## I. INTRODUCTION

The debate over health care expenditures rages in America. As presidential candidates discussed their plans for revamping the health care system, the United States makes the largest health expenditures in the world, both per capita and as a percentage of gross domestic product.<sup>1</sup> Health care costs constitute an increasing percentage of household expenditures, particularly for the elderly.<sup>2</sup> While health care costs climb, prescription drug costs represent an expanding percentage of the health care budget.<sup>3</sup> Prescription drug prices thus remain a central concern in the health care debate.<sup>4</sup> For many of their prescriptions, Americans purchase generic versions of prescription drugs, certified by the Food and Drug

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1. By 2000, the United States “spent the highest amount on health care in the world (\$4,499 per capita).” NECLAM SEKHRI & WILLIAM SAVEDOFF, WORLD HEALTH ORG., DISCUSSION PAPER NO. 3, PRIVATE HEALTH INSURANCE: IMPLICATIONS FOR DEVELOPING COUNTRIES (2004), available at [http://www.who.int/health\\_financing/private\\_health\\_in\\_dp\\_04\\_3.pdf](http://www.who.int/health_financing/private_health_in_dp_04_3.pdf); see also M. L. Burstall, *How Do They Do It Elsewhere in Europe*, in SHOULD PHARMACEUTICAL PRICES BE REGULATED? THE STRENGTHS AND WEAKNESSES OF THE BRITISH PHARMACEUTICAL PRICE REGULATION SCHEME 72, 72 (David Green ed., 1997) (explaining that “spending on health care has tended to rise more rapidly than national income, driven by aging populations, rising expectations and above all by the progress of medical science.” (footnote omitted)).

2. See Milt Freudenheim, *Drug Prices for Elderly Surge Ahead in America*, INT’L HERALD TRIB., Aug. 17, 2005, at 15; see also Gerard F. Anderson et al., *It’s the Prices, Stupid: Why the United States Is So Different from Other Countries*, 22 HEALTH AFF. 89 (2003), available at <http://content.healthaffairs.org/cgi/content/full/22/3/89>.

3. Prescription drugs are the most rapidly increasing expenditure of the entire health care system. Kaiser Family Foundation, Trends and Indicators in the Changing Health Care Marketplace: National Health Expenditures and Their Share of Gross Domestic Product, 1960–2004, <http://www.kff.org/insurance/7031/ti2004-1-1.cfm>. The Kaiser Family Foundation estimates that from 1993–2004, national health expenditures doubled to represent nearly sixteen percent of the gross domestic product. *Id.* For a definition of what constitutes a “drug,” see Federal Food, Drug, and Cosmetic Act, 21(g)(1), 21 U.S.C. § 321(g)(1) (2000) (explaining that a drug is a substance that exerts an action on the structure or function of the body by chemical action and that is intended for use in the treatment or prevention of disease).

4. Zvi Griliches & Iain M. Cockburn, *Generics and the Producer Price Index for Pharmaceuticals*, in COMPETITIVE STRATEGIES IN THE PHARMACEUTICAL INDUSTRY 19, 19 (Robert B. Helms ed., 1996). See also David Green, *Editor’s Introduction: Is Price Regulation Necessary?*, in SHOULD PHARMACEUTICAL PRICES BE REGULATED? *supra* note 1, at 1 (explaining that “in America about 60 percent of pharmaceutical spending is out-of-pocket”). Studies indicate that consumers could have saved as much as twenty billion dollars in 2004 by switching to generics. Kirsty Barnes, \$20 Billion in Untapped Generic Drug Savings, Nov. 2, 2005, <http://www.in-pharmatechnologist.com/layout/set/print/content/view/print/91166>.

Administration (“FDA”) to be sufficient therapeutic substitutes for brand-name versions of the same chemical compound.<sup>5</sup> Economists estimate that Americans save eight to ten billion dollars annually by purchasing generic alternatives to brand-name pharmaceuticals.<sup>6</sup>

In both the United States and Europe, the pharmaceutical industry has become a unique regulatory animal. Government agencies hold pharmaceutical manufacturers to rigorous evidentiary showings of the quality of their products. In the United States, the FDA requires pharmaceutical manufacturers to document “proof of safety and efficacy.”<sup>7</sup> Evidentiary showings necessitate significant pre-market testing expenses; when coupled with research and development costs, they mandate a huge capital investment to produce innovative drugs. To protect this investment and prevent unsafe drugs from entering the market, the FDA maintains an exclusivity system—market protections that insulate brand-name pharmaceuticals from generic competition for a term, typically three or five years.

The FDA has been criticized for the length of its exclusivity periods, which essentially maintain the large pharmaceutical companies’ abilities to sell branded medications at a monopoly price for an extended period of time. Supporters of the current system have suggested that an alternative system would be deleterious to research and safety, permitting pharmaceuticals of unknown effectiveness onto the market. Indeed, the FDA requires a laborious approval process and years of legal wrangling before a generic prescription drug enters the marketplace.

The European prescription drug regulatory system provides an interesting contrast to the American process. Despite its comprehensive regulatory framework in which a centralized regulatory body mandates drug regulations, the European system does not regulate a single market

5. Griliches & Cockburn, *supra* note 4, at 21. The FDA certifies products as “therapeutically equivalent” if they are:

1) pharmaceutically equivalent, in that they contain the same active ingredient(s), are of the same dosage form, are identical in strength and route of administration, and meet applicable standards of purity and quality; 2) bioequivalent, in that *in vivo* or *in vitro* tests show that a product meets statistical criteria for equivalence to . . . [the] extent of absorption of the active ingredient and its availability at the site of action; 3) adequately labeled; and 4) manufactured in compliance with Current Good Manufacturing Practice regulations.

*Id.*

6. U.S. Food & Drug Admin., Ctr. for Drug Evaluation and Research, Office of Generic Drugs, What Are Generic Drugs?, <http://www.fda.gov/cder/ogd> (scroll down to “What are Generic Drugs?”) (last visited Sept. 5, 2008).

7. HENRY G. GRABOWSKI & JOHN M. VERNON, THE REGULATION OF PHARMACEUTICALS: BALANCING THE BENEFITS AND RISKS 9 (1983) (explaining the loss of efficiency due to stringent approval procedures).

for pharmaceuticals.<sup>8</sup> Unlike the United States, which lets the open market determine prices, individual European states regulate the prices of pharmaceuticals through single-payer state health systems.<sup>9</sup> But while EU countries set the market prices for pharmaceuticals by setting the amounts their state health systems will pay, the Europeans maintain longer exclusivity protections for innovator pharmaceuticals. Due to the unique subsidization of the European pharmaceutical industry, Europe has been criticized as creating a lack of pricing competence at the Community level, leading to a less robust, less competitive pharmaceuticals market.<sup>10</sup>

## II. BACKGROUND OF PHARMACEUTICAL REGULATION IN THE UNITED STATES

Consciousness-raising during the Progressive Era regarding the poor state of food and drug quality led to the early twentieth century development of federal regulatory bodies and the modern tort system.<sup>11</sup> The 1906 passage of the Federal Food and Drugs Act began the modern era of pharmaceutical regulation in the United States.<sup>12</sup> The Act created the Bureau of Chemistry, the predecessor to the modern FDA, which took its current name in 1930.<sup>13</sup> For the first three decades of its existence, the FDA primarily regulated the labeling of medications, gearing enforcement against product misrepresentation.<sup>14</sup> However, in 1937, a fatal and largely

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8. GOVIN PERMANAND, *EU PHARMACEUTICAL REGULATION: THE POLITICS OF POLICY-MAKING* 6 (2006) [hereinafter *EU PHARMACEUTICAL REGULATION*]. Govin Permanand explains a political rationale behind the fragmentation of the pharmaceutical market in Europe, as a centralization thereof would mean “industry rationalisation and job losses—undoubtedly favouring the more established and global-oriented member state industries . . . .” *Id.* See also Govin Permanand, *Regulating Under Constraint: The Case of European Union Pharmaceutical Policy* (2002) (unpublished Ph.D. Dissertation, University of London: London School of Economics & Political Science) (on file with author).

9. Burstall, *supra* note 1, at 73.

10. *EU PHARMACEUTICAL REGULATION*, *supra* note 8, at 195. See also ALFONSO GAMBARDILLA ET AL., *EUROPEAN COMM’N, ENTERPRISE DIRECTORATE-GEN., GLOBAL COMPETITIVENESS IN PHARMACEUTICALS: A EUROPEAN PERSPECTIVE* 7 (2000), available at [http://ec.europa.eu/enterprise/library/enterprise-papers/pdf/enterprise\\_paper\\_01\\_2001.pdf](http://ec.europa.eu/enterprise/library/enterprise-papers/pdf/enterprise_paper_01_2001.pdf).

11. See PHILIP J. HILTS, *PROTECTING AMERICA’S HEALTH: THE FDA, BUSINESS, AND ONE HUNDRED YEARS OF REGULATION* 35–71 (2003).

12. For a complete discussion of the history of the FDA, see *id.* at 53 (explaining that the Act was the first to require pharmaceutical manufacturers to label their medications correctly in an attempt to make sure that the contents were not “adulterated or impure”).

13. John P. Swann, *History of the FDA: The 1906 Food and Drugs Act and Its Enforcement*, Food & Drug Admin., <http://www.fda.gov/oc/history/historyoffda/fulltext.html> (last visited Jan. 13, 2009).

14. *Id.* See *United States v. Johnson*, 221 U.S. 488 (1911) (holding that a label claiming a tonic to be cancer-curing is not “misbranding” under the meaning of the Food and Drug Act; this case

untested new cough syrup, Elixir Sulfanilamide, led to the deaths of over 107 Americans.<sup>15</sup> This nationally publicized tragedy led to the passage of the Food, Drug and Cosmetic Act in 1938, which provided the framework for comprehensive regulation of pharmaceutical production and sales in the United States.<sup>16</sup> This Act and its later amendments create a lengthy regulatory approval process for new drugs to pass before being placed on the market.<sup>17</sup> For a new drug, this process requires FDA approval through a process now called the New Drug Application (“NDA”).

In the United States, private pharmaceutical companies and universities became the primary producers of new chemical entities (“NCEs”).<sup>18</sup> Pharmaceuticals, like any other new product, are eligible for patent protection under American patent law, ensuring a legal remedy against infringement.<sup>19</sup> Patent protection requires that the inventor apply within one year of the new creation entering the public domain; for pharmaceuticals, this means that the manufacturer must apply for patent protection within one year of beginning the FDA regulatory process.<sup>20</sup> Once a new pharmaceutical has been discovered and has gone through pre-clinical trials, the manufacturer must file an investigational NDA with the FDA.<sup>21</sup> Then a series of human testing programs take place in three categories: toxicology, effectiveness, and—finally—human testing on a

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demonstrated the continuation of the status quo of *caveat emptor* in the pharmaceutical industry, despite Progressive attempts to regulate the industry).

15. HILTS, *supra* note 11, at 89–93.

16. *Id.* at 93.

17. See 21 U.S.C. § 355(a)-(b) (2000), providing that the FDA must have sufficient information to determine the drug’s safety and efficacy through both preclinical and clinical studies; see also DOUGLAS J. PISANO & DAVID MANTUS, FDA REGULATORY AFFAIRS: A GUIDE FOR PRESCRIPTION DRUGS, MEDICAL DEVICES, AND BIOLOGICS 7 (2004) (explaining the FDA’s modern orientation: “It is a scientifically based law enforcement agency whose mission is to safeguard public health and to ensure honesty and fairness between the consumer and health-regulated industries, involved with pharmaceuticals, devices, and biologics” (citing S. STRAUSS, FOOD AND DRUG ADMINISTRATION: AN OVERVIEW, STRAUSS’ FEDERAL DRUG LAWS AND EXAMINATION REVIEW 323 (5th ed. 1999))).

18. GRABOWSKI, *supra* note 7, at 18–19 (explaining that since the early 1950s American pharmaceutical firms have produced over ninety percent of the nation’s NCEs, and from 1963 to 1975 they produced over fifty percent of the world’s total).

19. See 35 U.S.C. § 154(a)(1) (2000) (“Every patent shall contain a short title of the invention and a grant to the patentee, his heirs or assigns, of the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States . . .”).

20. Mary Atkinson, *Patent Protection for Pharmaceuticals: A Comparative Study of the Law in the United States and Canada*, 11 PAC. RIM L. & POL’Y J. 181, 184 n.18 (2002).

21. GRABOWSKI & VERNON *supra* note 7, at 22 (“The FDA’s decision to permit clinical testing is based on the following considerations: (1) the protection of the human research subject, (2) the adequacy of animal studies already completed, (3) the scientific merits of the research plan, and (4) the qualifications of the investigator.”).

large patient population.<sup>22</sup> These tests can take as long as four to six years.<sup>23</sup> Having passed that series of testing, the drug manufacturer has to submit a new drug application for review by the FDA, a process which in itself can require additional time.<sup>24</sup> In all, the regulatory process, from product creation to the marketplace, entails laborious and time-consuming testing and regulation.

The pioneering pharmaceuticals of the 1960s and 1970s were given long exclusivity protection terms; yet, as development time increased, exclusivity periods were decreased.<sup>25</sup> Generic pharmaceuticals present a different regulatory issue—they contain the same active ingredients as pioneer drugs already tested and reviewed by the FDA.<sup>26</sup> However, into the 1980s, manufacturers of generic pharmaceuticals were required to perform the same expensive testing that the pioneer drug makers had already undergone.<sup>27</sup> These barriers perhaps contributed to the public scandals in the 1970s and 1980s of generic manufacturers cutting corners and attempting to bribe FDA officials to gain entry into the market.<sup>28</sup>

As a result, Congress attempted to level the playing field for generic pharmaceuticals and encourage competition through the Drug Price Competition and Patent Term Restoration Act of 1984 (the “Hatch-Waxman Act”).<sup>29</sup> The Act established a new process for generic drugs to enter the market, the Abbreviated New Drug Application (“ANDA”).<sup>30</sup> Congress intended the Act to “make available more low-cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962.”<sup>31</sup> However, with the Hatch-Waxman Act, Congress also sought to balance the ability of competitors to bring cheap generics to the marketplace with the need for companies producing brand-name drugs

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22. *Id.*

23. *Id.* at 23.

24. *Id.* at 22–23.

25. *Id.* at 22–24 (explaining that patent lives decreased on average 4.3 years between 1966 and 1979).

26. *United States v. Generix Drug Corp.*, 460 U.S. 453, 454–55 (1983) (noting that the Supreme Court defined a generic as “a product that contains the same active ingredients but not necessarily the same excipients as a so-called ‘pioneer drug’ that is marketed under a brand name”).

27. H.R. REP. NO. 98-857, Part I, at 16–17 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647.

28. PISANO & MANTUS, *supra* note 17, at 5.

29. *See* Federal Food, Drug, and Cosmetic Act, § 21 U.S.C. 355(j) (2000).

30. *The Generic Drug Maze: Speeding Access to Affordable Life-Saving Drugs: Hearing Before the S. Special Comm. on Aging*, 109th Cong. 83 (2006) (statement of Mark Merritt, President and Chief Executive Officer, Pharmaceutical Care Management Association) [hereinafter *Hearing*]. For the text of the Hatch–Waxman Amendments to the Act in 1984, called the Drug Price Competition and Patent Term Restoration Act of 1984, see Pub. L. No. 98–417, 98 Stat. 1585 (1984) (codified in relevant part at 21 U.S.C. § 355 and 35 U.S.C. § 271(e) (2000)).

31. H.R. REP. NO. 98-857, *supra* note 27, at 14.

to research and develop new pharmaceuticals.<sup>32</sup> To accomplish the first objective, the Hatch-Waxman Act's ANDA provided generics with a new approval process, during which generic producers need only prove the equivalency of their generic product to the pioneer drug on which FDA testing and approval had already taken place.<sup>33</sup> This was intended to allow generic manufacturers to avoid the enormous costs inherent in duplicating the NDA process, particularly the expensive data on human subjects.<sup>34</sup> The Act also gave generic manufacturers the opportunity to petition for generic drugs that list different drugs as the active ingredient or have a different dosage or strength, provided that the change does not require a separate review of clinical data.<sup>35</sup> Additionally, Hatch-Waxman aimed to maintain investment in research and development of new innovator pharmaceuticals.<sup>36</sup> To this end, the Act established two new FDA pharmaceutical approval processes: the ANDA and the Section 505(b)(2) application.<sup>37</sup> These approval processes allow manufacturers of equivalent pharmaceuticals, similar but non-equivalent pharmaceuticals, and pharmaceuticals for which significant safety and efficacy testing have been heretofore conducted by third parties to avoid duplicative innovator research and to develop products during innovator exclusivity periods.<sup>38</sup>

To aid concurrent development of generics, the Hatch-Waxman Amendments also allowed generic manufacturers to use the patented pioneer drug during the patent life to test and develop generics, which might otherwise be patent infringement.<sup>39</sup> Thus, proprietary pioneer drugs

32. *aaPharma Inc. v. Thompson*, 296 F.3d 227, 230 (4th Cir. 2002). For a discussion of the rationale behind the Hatch-Waxman Act, see RICHARD A. EPSTEIN, *OVERDOSE: HOW EXCESSIVE GOVERNMENT REGULATION STIFLES PHARMACEUTICAL INNOVATION* 56 (2006) (explaining that, through Hatch-Waxman, Congress sought to accomplish its objectives by better coordinating the patent system and the FDA's regulatory system, and by limiting "the dangers of monopoly associated with both systems of regulation").

33. Holly Soehnge, *The Drug Price Competition and Patent Term Restoration Act of 1984: Fine-Tuning the Balance Between the Interests of Pioneer and Generic Drug Manufacturers*, 58 *FOOD & DRUG L.J.* 51, 54 (2003). The FDA maintains a list of its already approved branded and generic pharmaceuticals. This list, *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly known as the "Orange Book," is available at <http://www.fda.gov/cder/orange/default.htm>. See also *Watson Pharms., Inc. v. Henney*, 194 F. Supp. 2d 442, 445 (D. Md. 2001) (explaining that federal courts have ruled that the FDA plays merely a "ministerial" role in creating the Orange Book, rather than acting as the arbiter of the scope or validity of patent claims).

34. Mary W. Bourke & M. Edward Danberg, *Current Trends in Hatch-Waxman Patent Litigation: A System Still in Flux*, in *PHARMACEUTICAL LAW 2006: ACROSS THE PRODUCT LIFE CYCLE* 939, 952-53 (Practicing Law Inst. ed., 2006).

35. See 21 U.S.C. § 355(j)(2)(C).

36. See *aaPharma Inc.*, 296 F.3d at 230.

37. See *Hearing*, *supra* note 30, at 83.

38. *Id.* at 74.

39. Soehnge, *supra* note 33, at 54.

and their testing data were made available to generic manufacturers, allowing the manufacturers to put a competitor pharmaceutical on the market sooner.

However, in accordance with the first goal of maintaining the incentives for research and development, several restrictions on competition were included in the Hatch-Waxman Act. First, pioneer drugs, those with NCEs new to the market, receive a five-year exclusivity period, during which time no ANDA may be submitted.<sup>40</sup> When generic manufacturers wish to market a bioequivalent, the Act requires that producers notify the corresponding pioneer pharmaceutical's patent owners of a possible exclusivity infringement so that the issue may be litigated promptly.<sup>41</sup>

Once a generic manufacturer files an ANDA, if a patent infringement action is brought within forty-five days after notice of final certification, approval is stayed for thirty months, or until a court decides that the patent is not infringed.<sup>42</sup> If after thirty months no federal court has ruled on the validity of the patent infringement, the generic manufacturer who filed the ANDA may distribute and market the drug; however, the ANDA filer that chooses to follow this course may thereafter become liable for infringement damages if infringement is found later by a court.<sup>43</sup>

Once a generic pharmaceutical has filed for final ANDA certification, the Hatch-Waxman Act gives the marketer of the generic drug 180 days of

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40. See Bourke & Danberg, *supra* note 34, at 968. See also 21 C.F.R. § 314.108 (2008) ("New chemical entity means a drug that contains no active moiety that has been approved by FDA in any other application . . .").

41. See Federal Food, Drug, and Cosmetic Act 21 U.S.C. § 355(j)(5)(B) (2000).

42. 21 U.S.C. § 355(j)(5)(B)(iii).

43. *In re Ciprofloxacin Hydrochloride Antitrust Litigation (Cipro I)*, 166 F. Supp. 2d 740, 744 (E.D.N.Y. 2001). The courts have also ruled that even if litigation over the patent infringement extends for longer than the thirty-month protection provided by the statute, the generic drug may nevertheless enter the market. See *Roche Prods., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 856 (1984) (citing 21 U.S.C. § 355(j)(5)(B)(iii)) (upholding a generic manufacturer's use of a patented brand-name prescription for research purposes during the patent term, so as to not create a de facto patent term extension in which time the generic would be developed). See also *In re Terazosin Hydrochloride Antitrust Litigation*, 352 F. Supp. 2d 1279 (S.D. Fla. 2005). For a complete discussion of the *Bolar* decision, see James J. Wheaton, *Generic Competition and Pharmaceutical Innovation: The Drug Price Competition and Patent Term Restoration Act of 1984*, 35 CATH. U. L. REV. 433, 447–48, 462–63 (1986). However, note that the federal courts have also held that a generic manufacturer's exclusivity period could not prevent competition from the brand-name manufacturer producing its own, unbranded generic version of the pioneer drug to compete with its own drug as well as with the competitor's generic. *Mylan Pharm., Inc. v. U.S. FDA*, 454 F.3d 270 (4th Cir. 2006). The Fourth Circuit held that the Hatch-Waxman Act did not prohibit the manufacturer of a brand-name drug from marketing an authorized generic version of the drug through a third-party licensee during the 180-day exclusivity period afforded to the first generic manufacturer under paragraph IV of the ANDA. *Id.* at 276.

market exclusivity for that generic.<sup>44</sup> In implementing this provision of the Hatch-Waxman Act, however, the FDA determined that the provision could not be read literally; it then added the requirement that the first applicant must have “successfully defended against a suit for patent infringement” before the exclusivity period can begin to run.<sup>45</sup> Thus the FDA inserted an additional hurdle of litigation before the generic manufacturer can enjoy the 180-day exclusivity period.<sup>46</sup> Furthermore, federal courts have limited the 180-day generic exclusivity period, allowing the producer of the innovator drug (the NDA holder) to market its own generic version of the drug during the ANDA holder’s 180-day exclusivity period.<sup>47</sup> Thus, during their period of supposed exclusivity, generic manufacturers may have to defend patent infringement suits and face generic competition from the innovator drug producer, a company already equipped and engaged in the manufacture of the same pharmaceutical.

The Hatch-Waxman Act also provides the section 505(b)(2) application for innovative pharmaceuticals that offer a new therapeutic benefit or alternative for consumers.<sup>48</sup> In essence, section 505(b)(2) constitutes a hybrid between the NDA and ANDA processes, allowing applicants to avoid duplicative research for drugs that would not qualify as bioequivalents for the ANDA process. Section 505(b)(2) provides this alternative for two types of drugs: drugs that cannot be approved solely on the basis of studies conducted or compensated by the applicant and drugs that are similar to innovators but not sufficiently similar to constitute therapeutic equivalents.<sup>49</sup> In practice, section 505(b)(2) applications are used by producers of NCEs and new molecular entities (“NMEs”) that rely

44. See 21 U.S.C. § 355 (j)(5)(B)(iv) (2000, Supp. III, 2003):

[F]or a drug for which a first applicant has submitted an application containing such a certification, the application shall be made effective on the date that is 180 days after the date of the first commercial marketing of the drug (including the commercial marketing of the listed drug) by any first applicant.

45. See 21 C.F.R. § 314.107(c)(1), the FDA regulations in addition to the Hatch-Waxman Act, implementing 21 U.S.C. § 355(j)(5)(B)(iv).

46. See *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060 (D.C. Cir. 1998) (citing former 21 C.F.R. § 314.107(c)(1)).

47. See *Mylan Pharm.*, 454 F.3d at 276; *Abbreviated New Drug Application*, 21 U.S.C. § 355(j)(5)(B)(iv); see also *Teva Pharm. Indus. Ltd. v. Crawford*, 410 F.3d 51 (D.C. Cir. 2005).

48. Julie Dohm, *Expanding the Scope of Hatch-Waxman Act’s Patent Carve-out Exception to the Identical Drug Labeling Requirement: Closing the Patent Litigation Loophole*, 156 U. PA. L. REV. 151, 155 (2007).

49. See U.S. FOOD & DRUG ADMIN., CTR. FOR DRUG EVALUATION & RESEARCH, GUIDANCE FOR INDUSTRY APPLICATIONS COVERED BY SECTION 505(b)(2), DRAFT GUIDANCE (1999), available at <http://www.fda.gov/Cder/Guidance/2853dft.htm> [hereinafter DRAFT GUIDANCE].

on FDA findings or studies to which the applicant has not been afforded a right of reference.<sup>50</sup> Also, section 505(b)(2) applications are used by producers of pharmaceuticals that modify previously approved drugs, creating equivalents not similar enough to warrant the approval of an ANDA.<sup>51</sup> A section 505(b)(2) applicant pharmaceutical may receive a five-year exclusivity period for an NCE or NME; if the drug is not an NCE, and one or more of the clinical studies was conducted or sponsored by the applicant, the section 505(b)(2) applicant can receive a three-year exclusivity period.<sup>52</sup> The section 505(b)(2) applicant may also be eligible for orphan drug or pediatric exclusivity.<sup>53</sup>

Furthermore, a brand-name drug manufacturer that takes anticompetitive measures beyond the FDA-prescribed windows of market exclusivity can face antitrust liability in the American system. The Sherman Act punishes all behavior that “attempt[s] to monopolize” in restraint of trade, aiming to protect competition in a market, and thus the consumer, rather than merely the rights of the competitor.<sup>54</sup> In this regard, federal courts have found that brand-name drug manufacturers attempting to block generic entry through unfounded lawsuits would be guilty of antitrust violations.<sup>55</sup> Holding that filing frivolous lawsuits constitutes an

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50. *Id.*; see also 21 C.F.R. § 314.3(b) (text of definition added by Applications for Approval to Market a New Drug, Fed. Reg. 39, 588, 39, 607 (July 10, 2008)) (“Right of reference or use means the authority to rely upon, and otherwise use, an investigation for the purpose of obtaining approval of an application, including the ability to make available the underlying raw data from the investigation for FDA audit, if necessary.”). A right of reference is a written statement signed by the owner of the referenced raw data that authorizes the applicant to use, in support of its submission to the FDA, data that provide the basis for each investigation submitted in its application. See DONALD O. BEERS, *GENERIC AND INNOVATOR DRUGS: A GUIDE TO FDA APPROVAL REQUIREMENTS*, app. 34 (2004).

51. Equivalent to the NDA process, section 505(b)(2) applicants must demonstrate the safety and efficacy of their pharmaceuticals. However, as with the ANDA process, a section 505(b)(2) application may “piggyback” on existing studies and FDA findings for similar pharmaceuticals. Dohm, *supra* note 48, at 155. Section 505(b)(2) applications may rely on “one or more” studies which “were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.” DRAFT GUIDANCE, *supra* note 49; 21 U.S.C. § 355(b)(2) (2000). Section 505(b)(2) expressly permits the applicant and FDA to rely on data not developed by the applicant, and to which the applicant does not possess a right of reference. According to the FDA, this information may include published literature or general information when an applicant has not obtained a right of reference, or the FDA’s “previous finding of safety and effectiveness” for an approved drug. DRAFT GUIDANCE, *supra* note 49.

52. 21 C.F.R. § 314.108(b)(4)(iv); 21 C.F.R. § 314.108(b)(2).

53. 21 U.S.C. §§ 360aa–ee (2000); 21 U.S.C. § 355a(d)(23).

54. 15 U.S.C. §§ 1–2 (2000). American antitrust law is governed by the Sherman Act, 15 U.S.C. §§ 1–7 (2000).

55. See *In re Buspirone Antitrust Litigation*, 185 F. Supp. 2d 363 (S.D.N.Y. 2002) (finding that the brand-name drug maker filed patent suits against generic competitors merely as a sham to delay generic competition; antitrust liability and treble damages were upheld in a \$220 million settlement against Bristol-Myers Squibb).

antitrust violation rather than a minor violation of the Federal Rules of Civil Procedure perhaps demonstrates the federal judiciary's acknowledgement of the time required for effective marketing and for a consumer to switch to generics.

### III. DISCUSSION OF THE EFFECTS OF AMERICAN GENERIC PHARMACEUTICAL REGULATION

In the manufacture of pharmaceuticals, initial research and development is a highly inefficient and prohibitively expensive process; required pharmaceutical testing and human studies can take upwards of several years and are extremely expensive.<sup>56</sup> The cost required for a pioneer manufacturer to research and develop a new pharmaceutical, much less an NCE, is substantial. The vast majority of money spent on research and development of new pharmaceuticals results in the creation of unusable, unmarketable chemicals.<sup>57</sup> Thus, only a small minority of the pharmaceuticals that reach the marketplace turn a profit.<sup>58</sup> Furthermore, while a company is attempting to find one of the few NCEs that will be therapeutically effective and marketable for a relatively common ailment, other companies may be working concurrently, winning the race to get the drugs in clinical trials and patented. Even those drugs that are successfully

However, the Second Circuit in *In re Tamoxifen Citrate Antitrust Litigation* declared a "reverse payment" in a patent litigation settlement agreement—that is, an exchange of money from a brand-name pharmaceutical manufacturer to a generic competitor that effectively ends the generic manufacturer's ANDA application—to be legitimate and not in violation of the Sherman Act. 466 F.3d 187, 206 (2d Cir. 2006). The court held that reverse payments are not "*per se* violations of the Sherman Act such that an allegation of an agreement to make reverse payments suffices to assert an antitrust violation." *Id.* The court ruled that it "[did] not think the fact that the patent holder is paying to protect its patent monopoly, without more, establishes a Sherman Act violation." *Id.* See also Thomas F. Cotter, *Refining the "Presumptive Illegality" Approach to Settlements of Patent Disputes Involving Reverse Payments: A Commentary on Hovenkamp, Janis & Lemley*, 87 MINN. L. REV. 1789, 1807 (2003).

55. *Competition in the Pharmaceutical Marketplace: Antitrust Implications of Patent Settlements: Hearing Before the S. Comm. on the Judiciary*, 107th Cong. (2002) (statement of the Fed. Trade Comm., Molly Boast, Dir., Bureau of Competition), available at <http://www.ftc.gov/05/2001/05/pharmtstmy.htm>. See generally EPSTEIN, *supra* note 32, at 237–40.

56. See U.S. CONGRESS, OFFICE OF TECH. ASSESSMENT, PHARMACEUTICAL R&D: COSTS, RISKS, AND REWARDS 39–46 (1993).

57. GRABOWSKI & VERNON *supra* note 7, at 22, fig.4. Scholars estimate attrition rates in the chemical lab, before any preclinical animal studies, to be at least ten to one. This means that for every ten NCEs contrived and created for the first time, nine are eliminated as ineffective before any studies on their therapeutic effectiveness have begun. *Id.*

58. See generally EPSTEIN, *supra* note 32, at 237–40.

developed and have passed clinical trials may fail to be the first of their kind.<sup>59</sup>

Pharmaceutical companies often point to a Tufts University study that found the pre-tax cost of new drug development to be \$897 million, including \$403 million of purported “opportunity costs” of drug development.<sup>60</sup> In addition, the research and development process has become increasingly expensive over time, as costs have risen dramatically without a proportional increase in the number of new drugs.<sup>61</sup>

Once development, success in the regulatory process, and patent protection of a new drug have been achieved, the pharmaceutical companies must bring the drug to market—often facing the prospect of creating a new market for the drug.<sup>62</sup> It is estimated that only three of ten pharmaceuticals even earn back the average cost of research and development.<sup>63</sup> This market environment has created such a large upfront

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59. *Id.* at 68 (noting that initial investments are made by a firm attempting to create innovative pharmaceutical products without knowing whether or not it would “win the patent race” by getting its products through the FDA approval process before other companies developing similar new pharmaceuticals get theirs patented).

60. Tufts Ctr. for the Study of Drug Dev., Total Cost to Develop a New Prescription Drug, Including Cost of Post-Approval Research, Is \$897 Million (May 13, 2003), <http://csdd.tufts.edu/NewsEvents/RecentNews.asp?newsid=29>. “Some estimates exceed 300 million required to produce a marketable drug that will take eight to twelve years to produce.” Griliches & Cockburn, *supra* note 4, at 19. *But see* Daniel L. Pollock, *Blame Canada (and the Rest of the World): The Twenty-Year War on Imported Prescription Drugs*, 30 SETON HALL LEGIS. J. 331, 345 (2006) (explaining that other studies have noted that “U.S. taxpayer-funded researchers conducted 55 percent of the published research projects leading to the discovery and development of” top selling pharmaceuticals (citing BOB YOUNG ET AL., PUBLIC CITIZEN’S CONGRESS WATCH, RX R&D MYTHS: THE CASE AGAINST THE DRUG INDUSTRY’S R&D “SCARE CARD” 7–8 (July 2001), available at <http://www.citizen.org/documents/acfdc.pdf>)). *See also* *The Pharmaceutical Industry: Beyond the Pill*, THE ECONOMIST, Oct. 27, 2007, at 76 [hereinafter ECONOMIST] (stating that research & development expenditures on pharmaceuticals were sixty-four billion dollars in 2006, with only thirteen new pharmaceuticals approved by the regulator).

61. Rebecca Henderson & Iain M. Cockburn, *The Determinants of Research Productivity in Ethical Drug Discovery*, in COMPETITIVE STRATEGIES, *supra* note 4, at 167.

62. BERNICE SCHACTER, THE NEW MEDICINES: HOW DRUGS ARE CREATED, APPROVED, MARKETED, AND SOLD, 181–93 (2006). *See also* EPSTEIN, *supra* note 32, at 144–45 (explaining that marketing costs often double the cost of research and development). These expenditures are spent both on physician marketing (i.e., marketing to those professionals and institutions that prescribe pharmaceuticals to their patients) and on direct-to-consumer marketing (i.e., marketing by those whose efforts promote pharmaceuticals directly to the consumer). *Id.* at 154–64. *See also* Jim Edwards, *Where There’s a Pill, There’s a Way*, BRAND WEEK, May 16, 2005, [http://www.brandweek.com/bw/research/article\\_display.jsp?vnu\\_content\\_Id=1000920676](http://www.brandweek.com/bw/research/article_display.jsp?vnu_content_Id=1000920676) (stating that four billion dollars are spent on consumer advertisements each year, not including the large amount spent on free samples of the medications). *See also* James Kanter, *Free-for-All over Generic Drugs in Europe*, INT’L HERALD TRIB., Nov. 15, 2005, at 15 (according to Stewart Adkins of Lehman Brothers, “[o]n both sides of the Atlantic, drug companies spend about 50 percent more promoting product awareness than they do for research and development”).

63. Griliches & Cockburn, *supra* note 4, at 19.

cost for developing pharmaceuticals and bringing them to the marketplace that manufacturers have come to believe only top-selling drugs are “worth the investment.”<sup>64</sup> Sales of the top fifteen drugs are heavily dominated by American companies, controlling some eighty-eight percent of the market.<sup>65</sup>

Perhaps because the FDA encourages the fungible image of pharmaceuticals through its aforementioned process of certifying generics as therapeutic bioequivalents to their Orange Book brand-name drugs, the majority of consumers internalize this message and eventually switch from a branded pharmaceutical to a generic.<sup>66</sup> This may be expected of any rational consumer, “considering that generic versions sell at discounts of 30 percent to 50 percent below the price of the branded products.”<sup>67</sup> Generic producers often reach a fifty percent quantity share of a pharmaceutical market within a year after the exclusivity period expires.<sup>68</sup> However, the fact that brand-name pharmaceutical manufacturers maintain as significant a market share as they do presents an interesting problem: why would consumers continue to purchase a pioneer drug if they can buy the generic for half the price?<sup>69</sup> The answer lies in the economic factors underlying the market for pharmaceuticals, and the failure of the regulatory regime to effect a transition to less expensive generics in the face of a favorable demand environment.

Clearly, as with the market for any other product, NDA holders possess a first-mover advantage in the marketplace, which helps them retain a large market share; first-movers benefit from brand loyalty and the price insensitivity inherent in the prescribing physician’s choice of the original

64. SCHACTER, *supra* note 62, at 224 (explaining that drug manufacturers since the 1980s have come to believe that only a drug—such as a Celebrex, Viagra, or Lipitor—“bringing in \$300 million in sales by the third year of marketing is worth the investment”).

65. *See* GAMBARDILLA ET AL., *supra* note 10, at 36. American dominance in the top-fifteen drug market greatly exceeds that of pharmaceutical patents (by around thirty percent) or top fifty NCE creation (by around fifty percent). *Id.*

66. Griliches & Cockburn, *supra* note 4, at 19, 21.

67. *Id.* at 19. *See also* *Hearing*, *supra* note 30, at 79 (explaining that “the brand and generic differential is on average \$60–\$80 per prescription”). However a patient’s adoption of a generic bioequivalent may be the result of the impetus of the insurance provider, pharmacy, or prescribing physician instead of merely the patient’s personal preference towards purchasing a less expensive brand of pharmaceutical.

68. Griliches & Cockburn, *supra* note 4, at 19. Because the pharmaceuticals are selling for thirty to fifty percent less, reaching a fifty percent quantity share of the market is distinguished from reaching a majority of the profits in the market.

69. *See id.* at 25–26. Even after three years on the market (1990–1992) generic Prazosin had yet to reach a sixty percent quantity share of the market, despite the fact that the price of the generic was at that point on average seventy-five percent less than that of its brand-name counterpart. *Id.*

brand-name drug.<sup>70</sup> Loyal customers then reward branded drugs for their first-mover advantage by continuing to pay higher prices after the entry of generics into the market.<sup>71</sup> For these reasons, establishing a reputation—among doctors, pharmacists, and patients—as the first pharmaceutical to treat a therapeutic need has been historically as important for the pioneer manufacturer in securing profits as maintaining a patent.<sup>72</sup> Thus, this first-mover advantage helps retain market share in spite of the fact that, having succeeded in the ANDA process, a generic drug has been certified to be equally as safe and effective as the pioneer drug of whose chemical ingredients it often consists.<sup>73</sup>

While the familiarity and loyalty of physicians and patients to a pioneer drug may be an important factor, a large part of the pioneer pharmaceuticals' market retention may stem from the success of their manufacturers' rent-seeking behavior. Brand-name pharmaceutical manufacturers invest in some of America's most expensive marketing campaigns to create an illusion that the brand-name drug, despite being declared a bioequivalent of the generic by the FDA, remains a superior product with a greater therapeutic quality in the eyes of the consumer.<sup>74</sup> Rent-seeking behavior as a means of maintaining a first-mover advantage after the introduction of generic competitors may help explain pioneer manufacturers' widely disproportionate rate of advertising to research and development expenditures.<sup>75</sup>

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70. Lacy Glen Thomas III, *Industrial Policy and International Competitiveness in the Pharmaceutical Industry*, in COMPETITIVE STRATEGIES, *supra* note 4, at 107, 121. This provides a "regime of appropriation" that allows pioneer drug manufacturers to gather significant rents from their innovations, allowing for returns above and beyond their investment in research and development. *Id.*

71. *See id.*

72. *Id.* at 127.

73. For a comparison with over-the-counter drugs, see *Analgesic Markers in a Battle*, N.Y. TIMES, Feb. 18, 1986, at D1. While this market effect can be difficult to conceptualize, an analogy could easily be made to over-the-counter pain relievers—despite the introduction of lower-cost generic competitors, acetaminophen purchasers remained loyal to Tylenol. *Id.* *See also* Griliches & Cockburn, *supra* note 4, at 25. Given the difference in price between a brand-name and generic product, the continued purchasing of the branded product suggests that many consumers have different expectations of a generic drug, despite the FDA's certification of its bioequivalence. *Id.*

74. Joseph M. Jadow, *Commentary*, in COMPETITIVE STRATEGIES, *supra* note 4, at 76, 78. For a recent example of such a campaign, see Pfizer's recent use of Dr. Robert Jarvik to help fend off the projected losses to generic rivals of the cholesterol fighter Lipitor, its most widely prescribed and profitable drug, whose patent is scheduled to expire by 2010. Stephanie Saul & Alex Berenson, *Lipitor Maker Digs in to Fight Generic Rival*, N.Y. TIMES, Nov. 3, 2007, at A1. *The Economist* estimates Pfizer will lose some thirteen billion dollars in revenue a year from generic competition biting into its Lipitor profits, despite this campaign. ECONOMIST, *supra* note 60, at 76.

75. *See id.* (estimating that twenty percent of revenues are spent on research and development, while over one-third of revenues are spent on marketing efforts).

By contrast, generic manufacturers seldom advertise their products because generics cannot be marketed under the branded pharmaceutical's trade name, which remains with the original patent holder; instead generics must use the chemical name.<sup>76</sup> Because generic manufacturers are given such a short window in which they have a monopoly over the generic drug, generic manufacturers face a collective action problem in advertising—were a generic manufacturer to launch a series of advertisements for its product, other generic manufacturers, including the branded drug manufacturer producing its own generic, would be able to “free ride” on the publicity given that pharmaceutical by the advertising campaign.<sup>77</sup> Predictably, the length of the monopolization period for brand-name drug manufacturers results in colossal advertising expenditures, while the short exclusivity period (during which the first generic manufacturer can still face competition from both the initial producer's brand-name drug and its generic equivalent) available to the generic manufacturer results in minimal advertising and the maintenance of a considerable percentage of the market going to the brand-name pharmaceutical, despite the fact that the FDA has certified the generic as the therapeutic equivalent to the brand-name drug. The system of regulatory controls pushes valuable social resources into rent-seeking prospective marketing by the brand-name drug manufacturers to maintain monopoly pricing, squandering those funds available for further research and development.

Because of the regulatory and market incentives given to the innovator, pharmaceutical companies benefit far more by developing their own NCEs and new categories of products than by creating competitive products similar to those already in the marketplace.<sup>78</sup> For this reason, American firms are the first to enter most new lines of pharmaceutical products.<sup>79</sup> The regulatory environment incentivizes lateral innovation, pushing drug manufacturers into new lines of products to sell to much the same market of patients.

However, creating these new categories of pharmaceutical products ignores the possibility that alternative products may function more

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76. EPSTEIN, *supra* note 32, at 153.

77. *Id.*

78. Thomas, *supra* note 70, at 120. A case involving some of the most commonly prescribed pharmaceuticals in the country exhibited this phenomenon: in the market for cardiovascular products, the prior cementation of the extremely lucrative beta-blocker markets by a handful of big pharmaceutical products led to very limited competition in terms of new beta-blockers, but fueled the development of new fields of cardiovascular products to treat heart failure, such as ACE inhibitors. *Id.*

79. *Id.*

effectively at controlling the same problem. The efficacy and safety of these product categories has already been approved in the NDA process by the FDA, suggesting that development in this category would require less expense and less testing to create an effective and safe product. The competition between various pharmaceuticals in the same product category would increase competition, reduce prices for consumers, and provide consumers greater utility from their chosen pharmaceuticals; consumers could choose, from among similar products, those that better fit their medication regimen or result in fewer undesirable side effects.<sup>80</sup> A socially beneficial regulatory regime may concentrate on developing the value of this intra-market regulation for consumers.<sup>81</sup>

The system of generic pharmaceutical regulation in the United States seems to exaggerate the first-mover advantages of brand-name manufacturers, but does so in a rapidly changing environment. These manufacturers face rising costs for the production of innovative products.<sup>82</sup> Yet some argue that because of the poor average returns in the pharmaceutical market, surviving in that market requires the accumulation of skill and knowledge in a brand-name pharmaceutical manufacturer, resulting in a more efficient industry.<sup>83</sup> Every exclusivity system values innovation and the production of new products and categories of products; yet, in a declining profitability environment for NCEs, manufacturers of branded pharmaceuticals seem to be entering into a new era in which most profits will be driven by innovations in marketing drugs for new therapeutic uses and to new demographics rather than through research and development towards the creation of new “wonder drugs” that cure widespread, currently perceived medical problems.<sup>84</sup> The American regulatory system is not designed for this new environment—the regime protects brand-name manufacturers with long exclusivity periods to shield

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80. EPSTEIN, *supra* note 32, at 56 (“Me-too products reflect and create competition among drug and device manufacturers, and that competition is also a powerful driver of better quality and lower cost.” (quoting Thomas H. Lee, *Me-Too Products—Friend or Foe?*, 360 *NEW ENG. J. MED.* 211 (2004))).

81. *See id.* at 125 (discussing that an appropriate industrial policy encourages firms to adopt strategies that create value for consumers in the long run and punishes firms that offer inferior or uninnovative products).

82. Barrie G. James, *The Pharmaceutical Industry in 2010*, in *HEALTH CARE 2010: HEALTH CARE DELIVERY, THERAPIES, AND THE PHARMACEUTICAL INDUSTRIES*, 49, 49–66 (C. Bezold & K. Knabner eds., 1994) (explaining that the pharmaceutical market is evolving into an industry in which “new” and “innovative” products that are more therapeutically effective might not boost profits; rather, the success of market actors is increasingly driven by cost containment in the production process and pricing).

83. Thomas, *supra* note 70, at 121.

84. James, *supra* note 82, at 54–56.

their flagship pioneer drugs. This entrenches brand-name manufacturers and supposed biochemical innovation, while in reality the pharmaceutical industry is transforming into a price- and marketing-driven environment. The protection of politically powerful drug manufacturers and the enshrinement of quasi-innovation necessarily comes at the expense of the consumer, who primarily seeks low-cost generic alternatives and innovative new applications for existing drugs in new populations.

#### IV. THE GENERIC PHARMACEUTICAL REGULATORY SCHEME IN EUROPE

The European Union has taken a markedly different approach to pharmaceutical regulation while facing many of the same social, political, economic, and scientific hurdles as the United States. As in the United States, health care costs have increased substantially in the European Union, driven by an extremely expansive, technologically sophisticated market for pharmaceuticals.<sup>85</sup> And perhaps more so than in the United States, European countries have sought to use pharmaceutical spending as a means of controlling these rising health care costs.<sup>86</sup> European state governments, like those of almost every First World country besides the United States, engage in heavy regulation of pharmaceutical prices; price regulation is more easily facilitated in a single-payer public health system through which almost all prescription drugs are publicly disseminated.<sup>87</sup> The European state governments, because they themselves are purchasing the drugs for their respective populations, have sought to cut down their own prescription drug bills through the purchase of generics, resulting in substantial savings for taxpayers.<sup>88</sup>

While policy decisions on health care spending are decidedly a Member State-dominated practice, an overarching regulatory body controls the licensing of pharmaceutical products across the common market.<sup>89</sup> The political rationale behind the creation of a common

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85. See also Burstall, *supra* note 1, at 72–87 (explaining that spending on health care in Europe has risen “more rapidly than national income, driven by aging populations, rising expectations and above all by the progress of medical science” (footnote omitted)).

86. Kanter, *supra* note 62.

87. Green, *supra* note 4, at 1. For a discussion of the varying forms of price regulation across the European Union, see PERMANAND, *supra* note 8, at 233 (citing Monique Mrazek & Elias Mossialos, *Regulating Pharmaceutical Prices in the European Union*, in *REGULATING PHARMACEUTICALS IN EUROPE: STRIVING FOR EFFICIENCY, EQUITY AND QUALITY* 114–29 (Elias Mossialos et al. eds., 2004)).

88. See Kanter, *supra* note 62 (explaining that France has reduced its annual drug bill by \$468 million over the last three years by purchasing more generic products).

89. See Burstall, *supra* note 1, at 72. The Treaty of Rome left the financing of health care to individual Member States, allowing them to act as they see fit within broad limits, as upheld by the

regulatory system mirrors that behind the American regulatory scheme: the system resulted from public outrage over the havoc caused by the use of an unsafe pharmaceutical (Thalidomide) in the early 1960s.<sup>90</sup>

The Thalidomide scare began a wave of regulation in Western Europe, resulting in the 1965 Guidelines for Medicines.<sup>91</sup> However, pharmaceutical companies hoping to license their products' safety and efficacy were encumbered by separate approval processes in the separate Member States.<sup>92</sup> The problem was rectified through the creation of a regulatory body for the entire European Economic Community, the European Agency for the Evaluation of Medicinal Products, known since 2004 as the European Medicines Agency ("EMA"), which is similar to the FDA but in a supranational regional conception.<sup>93</sup>

The European Commission provided the means through which manufacturers could certify the efficacy of their drugs with the EMA and present them to the marketplace.<sup>94</sup> Like in the United States, brand-name drugs were given exclusivity protection to allow their manufacturers to recoup the cost of research and development and reap profits.<sup>95</sup> In 1992, the Commission introduced the Supplementary Protection Certificate ("SPC") to extend the monopoly period of pioneer medications by an additional five years from their time of marketing, thereby allowing up to a fifteen-year effective monopoly period for pioneer drugs.<sup>96</sup>

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European Court of Justice. Case 181/82, Roussel Laboratories BV v. Netherlands, 1983 E.C.R. 03849; Case 238/82, Duphar v. Netherlands, 1984 E.C.R. 00523.

90. EU PHARMACEUTICAL REGULATION, *supra* note 8, at 1 (stating that Thalidomide was hailed as a breakthrough nausea aid, but reportedly led to birth defects in tens of thousands of infants).

91. Council Directive 65/65, On the Approximation of Provisions Laid Down by Law, Regulation or Administrative Action Relating to Medicinal Products, 1965 O.J. (L22) 369 (EC).

92. EU PHARMACEUTICAL REGULATION, *supra* note 8, at 5.

93. Commission Regulation 2309/93, Laying Down Community Procedures for the Authorization and Supervision of Medicinal Products for Human and Veterinary Use and Establishing a European Agency for the Evaluation of Medicinal Products, 1993 O.J. (L 214) 1 (EC); *see also* European Medicines Agency, *About the EMA—Structure*, <http://www.EMA.europa.eu/htms/aboutus/emeaoverview.htm>. To put pharmaceuticals on the market, manufacturers submit an application to the EMA for an evaluation, carried out by its subsidiary, the Committee for Medicinal Products for Human Use. The Committee requires tests for safety and efficacy, resulting in a "positive opinion" which then is sent to the European Commission to make the opinion into an authorization for the Common Market. For a more general discussion, see Mrazek & Mossialos, *supra* note 87.

94. Mrazek & Mossialos, *supra* note 87.

95. EU PHARMACEUTICAL REGULATION, *supra* note 8, at 121.

96. *Id.* *See also* Council Regulation 1768/92, O.J. (L 182) (EEC). For a recent update on changes in the statutory pharmaceutical regime in Europe, see Markus Hartmann & Florence Hartman-Vareilles, *Recent Developments in European Pharmaceutical Law 2004: A Legal Point of View*, 39 DRUG INFO. J. 193 (2005).

Also like the United States, the European Union has a strong system of competition laws, contained in articles 81 and 82 of the EC Treaty.<sup>97</sup> The Commission has become increasingly rigorous in its enforcement of competition laws in the pharmaceutical markets, particularly against pioneer drug manufacturers seeking to maintain their dominance against generic drug manufacturers in a manner the Commission finds unfair.<sup>98</sup>

In spite of a markedly different system that makes extensive use of price regulation, Europe has consistently been productive in the creation of many new pharmaceuticals.<sup>99</sup> However, the differential regulations across the Common Market have created a number of “low [research and development] intensive, ‘national’, small pharmaceutical companies.”<sup>100</sup> These small firms exist only in one Member State and do no research and development of their own, suggesting a fragmented market, lacking the competitive dynamics that promote pharmaceutical innovation.<sup>101</sup> These small companies exist only in European states as a result of the system of overregulation—price fixing that protects brand-name manufacturers by requiring pharmacies and consumers to buy the branded medications; their market share remains the same regardless of the expiration of patents that would produce generic competition in other Member States.<sup>102</sup>

97. Consolidated Version of the Treaty on European Union, Nov. 10, 1997, 1997 O.J. (C 340) 145, arts. 81–82. *See also* Commission Notice, Guidelines on the Effect on Trade Concept Contained in Articles 81 and 82 of the Treaty, 2004 O.J. (C 101) 81, available at [http://eur-lex.europa.eu/pri/en/oj/dat/2004/c\\_101/c\\_10120040427en00810096.pdf](http://eur-lex.europa.eu/pri/en/oj/dat/2004/c_101/c_10120040427en00810096.pdf).

98. By 1994, the Commission was willing to take on brand-name drug manufacturer Tetra Pak, a monopolist engaging in “egregious anti-competitive practices” in the pharmaceutical industry, but did not impose significant fines and limited its ruling to extreme circumstances. Case T-83/91, *Tetra Pak Int’l SA v. European Comm’n*, 1994 E.C.R. II-755, ¶ 244.

In 2005, the Commission prosecuted AstraZeneca for attempting to block or delay the entry into the market of a generic competitor to its anti-ulcer drug. Commission Decision 2004/310/EC (Case COMP/M.1806-AstraZeneca/Novartis) O.J. (L 110) 1. The Commission found AstraZeneca’s actions to be a violation of its dominant position in the market, explaining that

misleading regulators to gain longer protection acts as a disincentive to innovate, and is a serious infringement of European Union competition rules. Health care systems throughout Europe rely on generic drugs to keep costs down. Patients benefit from lower prices. By preventing generic competition, AstraZeneca kept Losec prices artificially high. Moreover, competition from generic products after a patent has expired itself encourages innovation in pharmaceuticals.

*Id.*

99. GAMBARDELLA ET AL., *supra* note 10, at 33–35 (explaining that Europe produced sixteen of the top fifty NCEs from 1996 to 1999, and that Europeans were also responsible for the filing of over forty percent of the patents for pharmaceuticals from 1988 to 1997).

100. *Id.* at 57.

101. *Id.* Also see generally Lacy Glenn Thomas, III, *Implicit Industrial Policy: The Triumph of Britain and the Failure of France in Global Pharmaceuticals*, 3 INDUS. & CORP. CHANGE 451 (1994).

102. *Id.* at 58.

V. COMPARING THE EFFECTS OF THE EUROPEAN UNION  
PHARMACEUTICAL REGULATION REGIME TO THAT OF THE UNITED  
STATES

The European example provides some insights into the American pharmaceutical regulatory regime when considering the possible effects of price regulation and the use of generics. The European regulatory scheme has approached the new marketing period of medicines with an increasing disparity of “innovation” compared to the United States, yet provides drugs to most consumers at significantly lower costs.<sup>103</sup> European price regulation stimulates the entry of generics into that market.<sup>104</sup> European legal constraints thus show a preference for low pharmaceutical prices, particularly in those states whose governments favor the purchasing of generic substitutes. In contrast, the American system lends itself to the consolidation of manufacturing behind the major brand-name drug producers, who invest the rents taken from exclusivity into marketing and innovation through re-marketing. If Europe is any guide, the operation of a pharmaceutical price control regime mandating the use of generics would provide immediate savings to American consumers.<sup>105</sup> A regime that requires generic substitutions from doctors or pharmacists may be the only way to aid a largely uninformed public that has been misguided by the branded pharmaceuticals’ advertising campaigns.

However, the economic competitiveness of the pharmaceutical markets in Europe may be curtailed by the wide range of industrial policies chosen by European states.<sup>106</sup> Relative prices across Europe have varied widely in response to different regulatory environments, making effective marketing of products exceedingly difficult and corresponding economic opportunities unpredictable.<sup>107</sup> Thus, these varying regimes led to an “incomplete market” whose status quo is retained for political fear of what

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103. ORGANISATION FOR ECONOMIC CO-OPERATION & DEVELOPMENT, OECD HEALTH DATA 2001: A COMPARATIVE ANALYSIS OF 30 COUNTRIES (2001), available at [http://www.oecd.org/document/61/0,3343,en\\_2649\\_34631\\_1913405\\_119690\\_1\\_1\\_1,00.html](http://www.oecd.org/document/61/0,3343,en_2649_34631_1913405_119690_1_1_1,00.html). While the number of NCEs being developed in the United States each year has stayed relatively stagnant, those being developed in Europe have decreased by fifty percent, falling behind the United States from 1999 to 2003. *Id.* Prescription drug prices are higher in the United States than in the United Kingdom, France, Germany, and Italy. By contrast, over-the-counter medications are cheaper in the United States than in those countries. SCHACTER, *supra* note 62, at 231.

104. GAMBARDELLA ET AL., *supra* note 10, at 26.

105. Burstall, *supra* note 1, at 72–81.

106. See GAMBARDELLA ET AL., *supra* note 10, at 66.

107. Burstall, *supra* note 1, at 78–79.

a more efficient, Europe-wide market could bring.<sup>108</sup> An inefficient pharmaceutical market resulting from differentiating industrial policy and mandatory pricing caused an inefficient and fragmented industry in Europe. This may provide a lesson to the United States that developing a sub-national, state-based industrial policy, under the backdrop of our current national generic regulatory system with its resulting price differentiation based on locality, would be a mistaken approach, providing dispersed short-term savings at the expense of market efficiency. Expanding the current approach to health care savings on a state-based system could result in many of the same inefficiencies and uncompetitive market players seen in Europe.<sup>109</sup>

Although the dominant trends in the pharmaceutical industry will remain economizing and cutting operational costs, the downsides of pharmaceutical price regulation are evident in the reduction in incentives to create those innovative NCEs and new medicines that might otherwise be possible. Because the public sector and universities are generally not equipped to be the sole promoters of product innovation, private industry must take the lead, be it within Europe or from the United States.<sup>110</sup> Thus a system that values price protection may not result in the same quantities of innovative products from a robust private sector in a price-competitive environment. The mere prospect of a comparable form of price regulation added to the American regulatory regime has elicited negative reactions, with suggestions of an instantaneous and irrevocable downturn in research and development.<sup>111</sup> Perhaps consumers in the deregulated American marketplace value innovative scientific cures at all cost and are unwilling to trade breakthrough cancer cures for lower prices in mandated generics.<sup>112</sup> More likely, however, American consumers would value a

108. EU PHARMACEUTICAL REGULATION, *supra* note 8, at 189–92, 208 (explaining that a single market would “more than likely result in increased prices,” but it would make a “stronger European industry in output and export terms . . . at the price of heavy streamlining”). In 2002, employment in the pharmaceutical industry was 553,906 in the European Union compared to 293,000 in the United States. *Id.* at 208.

109. See generally Pam Belluck, *Massachusetts Sets Benefits in Universal Health Care Plan*, N.Y. TIMES, Mar. 21, 2007, at A18.

110. SCHACTER, *supra* note 62, at 228.

111. EPSTEIN, *supra* note 32, at 68 (“The researchers found that R&D spending will drop by nearly 40% over the next two decades, resulting in a loss of nearly \$300 billion in R&D and 277 million life years.” (quoting *Examining the Price of Drug Reimportation, Focusing on Implications for United States Consumers, Pricing, Research and Development, and Innovation: Hearing Before the S. Comm. on Health, Education, Labor & Pensions*, 109th Cong. (2005) (statement of Robert M. Goldberg, Dir., Ctr. for Medical Progress, Manhattan Inst. for Policy Research)).

112. See generally SCHACTER, *supra* note 62, at 226 (citing Paul Calabresi & Bruce A. Chabner, *Chemotherapy of Neoplastic Disease: Introduction*, in GOODMAN AND GILMAN’S THE

major revamping of the pharmaceutical scheme, adopting models from Europe.

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PHARMACOLOGICAL BASIS OF THERAPEUTICS 1225 (Hardman et al. eds., 9th ed. 1996)).

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