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### Pharmaceutical Patents after *Actavis*: The Challenge of Promoting Innovation in the Pharmaceutical Industry

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**Pharmaceutical Patents After *Actavis*: The Challenge of Promoting  
Innovation in the Pharmaceutical Industry**

By Emilia Rinaldi

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## I. INTRODUCTION

Patents are a powerful tool because they allow their owners to exclude others from the use of the patented technology and charge prices well above competitive levels. In the pharmaceutical industry, patents have long created contention between drug manufacturers, who regard them as essential to protect their investments in the development of new drugs, and consumer advocates, who regard the inflated prices as an obstacle to widespread drug access. In recent years, settlements to pharmaceutical patent infringement litigation, and specifically the so-called “reverse payment” settlements, have provided a new battleground for this debate.

The Supreme Court recently confronted the issue of reverse payment settlements in *F.T.C. v. Actavis*. The Court’s decision has once again raised the question of whether patents are the most appropriate form of intellectual property protection for the pharmaceutical industry. Technological innovation is a key aspect of the pharmaceutical sector from both an economic and a medical perspective. Promoting innovation in the pharmaceutical industry benefits both drug manufacturers and consumers, but finding the correct balance between the interests of those two groups has proven to be a challenge. This paper seeks to explore these challenges. The paper proceeds as follows. Section II provides the necessary regulatory and judicial background surrounding pharmaceutical patents and reverse payment settlements to understand pharmaceutical patent litigation. Section III describes the process of pharmaceutical innovation, the effects of generic

competition, and the role of pharmaceutical patents. Finally, section IV highlights some of the effects of the current regulatory scheme on the rate of pharmaceutical innovation and presents some alternative incentive structures that could substitute or augment the intellectual property protection given by pharmaceutical patents.

## II. AN OVERVIEW OF THE PHARMACEUTICAL INDUSTRY

### A. Statutory regulation of the pharmaceutical market

The pharmaceutical market is one of the most regulated industries in the United States.<sup>1</sup> No one can legally sell a new drug without first gaining the approval of the Food and Drug Administration (“FDA”).<sup>2</sup> In order to gain FDA approval for a pioneer drug – that is one that has never before received FDA approval – an applicant must file a New Drug Application (“NDA”).<sup>3</sup> The NDA must contain detailed information about the new drug – including its chemical composition, its method of production, and the reports of the clinical trials showing its safety and efficacy – as well as information on any patent related to it.<sup>4</sup> If the FDA approves the NDA, it publishes the drug and patent information in the Approved Drug Products with Therapeutic Equivalence and Evaluations or what is commonly referred to as the “Orange Book.”<sup>5</sup>

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1. Emily M. Morris, *The Myth of Generic Pharmaceutical Competition Under the Hatch-Waxman Act*, 22 FORDHAM INTELL. PROP. MEDIA & ENT. L. J. 245, 251 (2012).

2. 21 U.S.C. § 355(a) (2006).

3. *Id.* at § 355(b)(1).

4. *Id.*

5. *Id.* at § 355(j)(7)(A)(i)-(iii).

## B. The Hatch-Waxman Act

In an effort to promote competition, Congress enacted in 1984 the Drug Price Competition and Patent Term Restoration Act, commonly known as the Hatch-Waxman Act.<sup>6</sup> The Act streamlined the approval process for generic versions of pioneer drugs already approved and included in the Orange Book.<sup>7</sup> Specifically, generic firms can elect to file an Abbreviated New Drug Application (“ANDA”) which simply requires that the applicant prove the generic drug’s “bioequivalence”<sup>8</sup> with the branded product.<sup>9</sup> Generic firms, therefore, no longer have to reproduce the lengthy and costly clinical trials needed to prove the safety and efficacy of their products.<sup>10</sup> Rather, they can capitalize on the information submitted by the brand-name manufacturer in the original NDA application.<sup>11</sup> Consequently, the Hatch-Waxman Act aids competition in that it reduces the time and cost of bringing new generic drugs to the market.<sup>12</sup>

The Hatch-Waxman Act awards a five-year period of data exclusivity during

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6. 21 U.S.C. § 355.

7. *Id.* at § 355(j).

8. Bioequivalence refers to “the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.” *Id.* at § 355 (j)(8)(A)(i).

9. Henry G. Grabowski & Margaret Kyle, *Generic Competition and Market Exclusivity Periods in Pharmaceuticals*, 28 *MANAGERIAL AND DECISION ECON.* 491, 491-492 (2007).

10. Lee Branstetter et al., *Starving (or Fattening) the Golden Goose?: Generic Entry and the Incentives for Early-Stage Pharmaceutical Innovation*, (August 1, 2012) (unpublished manuscript), [http://faculty.haas.berkeley.edu/jeffrey\\_kuhn/Innovation\\_Seminar/Papers/Branstetter\\_Chatterjee\\_Higgins\\_2.pdf](http://faculty.haas.berkeley.edu/jeffrey_kuhn/Innovation_Seminar/Papers/Branstetter_Chatterjee_Higgins_2.pdf).

11. Grabowski, *supra* note 9, at 492.

12. Bret Dickey et al., *An Economic Assessment of Patent Settlements in the Pharmaceutical Industry*, 19 *ANNALS HEALTH L.* 367, 371 (2010).

which generic drugs may not be marketed.<sup>13</sup> However, the Act – through what are known as Paragraph IV certifications – allows generic manufacturers to file an ANDA after only four years from the brand-name drug’s approval and well before the expiration of the patents on the brand-name product.<sup>14</sup> Notably, the first generic manufacturer to file a Paragraph IV certification receives a 180-day market exclusivity period.<sup>15</sup> This timeframe provides a powerful incentive for generic manufacturers to challenge, or invent around, brand-name patents because the profits available during the 180-day exclusivity period can be substantial.<sup>16</sup>

### **C. Patent litigation in the context of the Hatch-Waxman Act**

An ANDA filer that makes a Paragraph IV certification commits a constructive act of patent infringement.<sup>17</sup> The Hatch-Waxman Act requires the filer to notify the patent holder of the filing of the Paragraph IV certification and provides the brand-name manufacturer 45 days to bring an action for patent infringement.<sup>18</sup> If an action is brought within this time period, the patent holder is

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13. 21 U.S.C. § 355 (c)(3)(E)(ii). Data exclusivity refers to the period of time a generic manufacturer has to wait before being allowed access to the clinical trial data submitted as part of the pioneer drug’s NDA.

14. *Id.*; *id.* at § 355 (j)(2)(A)(vii)(IV).

15. *Id.* at § 355 (j)(5)(B)(iii)(IV)(iv)(I). This exclusivity period is triggered by the marketing of the first filer’s generic product. Dickey, *supra* note 12, at 373.

16. Dickey, *supra* note 12, at 373. During those 180 days the brand-name and the first generic filer will partake in a duopoly, allowing the first generic filer (1) to set prices only slightly below monopolistic values; and (2) to capture a much larger share of the market than it would if facing competition from multiple generics.

17. Bruce R. Genderson, *Settlements in Hatch-Waxman Act Patent Litigation: Resolving Conflicting Intellectual Property and Antitrust Concerns*, 3 SEDONA CONF. J. 43, 45 (2002).

18. 21 U.S.C. § 355 (j)(5)(B)(iii).

granted an automatic stay of the ANDA approval, which prevents the generic drug from entering the market.<sup>19</sup> The stay will last until the litigation is resolved in favor of the ANDA filer or the end of a 30-month period from the Paragraph IV notification, whichever comes first.<sup>20</sup> Because of the automatic stay, the patent litigation will take place before the generic drug is allowed to enter the market.<sup>21</sup> This situation differs drastically from the more typical patent dispute. Commonly, a patent holder brings an action against an alleged infringer that is actively utilizing the patented technology without the consent of the patent holder.<sup>22</sup> Under the Hatch-Waxman Act, however, a generic manufacturer can challenge the validity of a brand-name patent without the risk of being liable for the damages caused by actual infringement.<sup>23</sup>

#### **D. “Reverse payment” settlements agreements**

A great number of patent litigations result in settlements.<sup>24</sup> The litigation risks involved are extremely high for both the alleged infringer, who risks treble damages that can reach hundreds of millions of dollars, and the patent holder, who risks an equally costly finding of patent invalidity.<sup>25</sup> Also, because of the complexity of the technologies and of the legal issues involved, the outcome of patent litigation is remarkably uncertain – not only at trial but also on appeal, where reversal rates

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19. *Id.* at § 355 (j)(5)(B)(iii)(I)(aa).

20. *Id.*

21. Marc G. Schildkraut, *Patent-Splitting Settlements and the Reverse Payment Fallacy*, 71 ANTITRUST L. J. 1033 (2004).

22. *Id.* at 1036

23. Genderson, *supra* note 17, at 45.

24. *Id.*

25. *Id.*



are quite high.<sup>26</sup>

In a Hatch-Waxman context, parties have an even greater incentive to settle.<sup>27</sup> The peculiar nature of a Paragraph IV-induced litigation gives rise to a situation of exceptionally asymmetric risks between the litigants. On the one hand, the generic manufacturer has a strong economic incentive to adopt risk-seeking behavior.<sup>28</sup> It faces the possibility of enormous gains in the event of a successful challenge for a relatively small price – because there have yet to be any sales of the generic drug, damages will be minimal, leaving litigation costs as the only expense.<sup>29</sup> On the other hand, the brand name is often risk-averse because it has much to lose and nothing to gain.<sup>30</sup> If it prevails, it will be left in essentially the same economic position it had before the litigation, while if it loses its patent-granted monopoly profits will be lost.<sup>31</sup>

Furthermore, parties in a Hatch-Waxman Act patent litigation have, for the most part, an incentive to settle on monetary terms.<sup>32</sup> Such incentive originates from the fact that, holding constant the value received by the generic manufacturer, a settlement based on a license will cost the patent holder much more than a

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26. *Id.* at 46. Depending on the type of claim, patent litigation reversal rates range between 10 and 38% against an average for all areas of federal civil litigation of 18%. Ted Sichelman, *Myths of (Un)Certainty at the Federal Circuit*, 43 LOY. L.A. L. REV. 1161, 1172-1173 (2010).

27. Genderson, *supra* note 10, at 46.

28. Xiang Yu & Anjan Chatterji, *Why Brand Pharmaceutical Companies Choose to Pay Generics in Settling Patent Disputes: A Systematic Evaluation of the Asymmetric Risks in Litigation*, 10 NW. J. TECH. AND INTELL. PROP. 19, 21 (2011).

29. *Id.*

30. *Id.*

31. *Id.*

32. Genderson, *supra* note 10, at 47.

monetary settlement.<sup>33</sup> In contrast to the typical patent litigation settlement, however, in the Hatch-Waxman context the payment often flows from the patent holder to the alleged infringer – hence the name “reverse payment.”<sup>34</sup> These settlements have raised much debate and many economists have written on the issue. Numerous economists agree that, when real-world complexities are taken into account, reverse payments provide the parties in the litigation the negotiation flexibility necessary to reach pro-consumer settlements.<sup>35</sup> The Federal Trade Commission (“F.T.C.”) and several consumer advocacy groups, on the other hand, have challenged the legality of reverse payment agreements.<sup>36</sup> The F.T.C. regards a reverse payment as the parties’ effort to conspire to monopolize the market for a

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33. *Id.* at 46. A license to the generic would immediately lower the price at which the brand name is able to sell its product. This loss of monopolistic profits would unlikely be matched by any royalties agreed to as part of the settlement.

34. *Id.*

35. Dickey, *supra* note 12, at 392-393. *See also* Yu & Chatterji, *supra* note 28, at 31 (noting that reverse payments are, in large part, a byproduct of the asymmetric litigation risks between the parties); Henry N. Butler & Jeffrey Jarosch, *Policy Reversal on Reverse Payments: Why Courts Should Not Follow the New DOJ Position on Reverse-Payment Settlements of Pharmaceutical Patent Litigation*, 96 IOWA L. R. 101, 156 (2010)(concluding that reverse payment can have anticompetitive as well as procompetitive outcomes depending on the surrounding circumstances). *But see* Carl Shapiro, *Antitrust Limits to Patent Settlements*, 34 RAND J. ECON. 391, 395 (2003)(claiming that reverse payments can never produce pro-consumer outcomes). There is, however, a profound difference in the methodology employed by Shapiro and those following his model. This group of scholars reaches their conclusions by using the concept of “probabilistic patents.” Because, they say, there is always a chance that a jury would invalidate a patent, a patent does not confer a right to exclude but rather a right to *try* to exclude by asserting the patent in court. While intriguing from a mathematical perspective, the concept of “probabilistic rights” has serious flaws when confronted with the rule of law. A very good discussion on the topic can be found in Kevin D. McDonald, *Hatch-Waxman Patent Settlements and Antitrust: On “Probabilistic” Patent Rights and False Positives*, 17 ANTITRUST 68, 71-72 (2003).

36. Yu & Chatterji, *supra* note 28, at 22.

particular drug and considers them a violation of the Sherman Act.<sup>37</sup>

### **E. Challenges to the legality of reverse payment settlements**

Reverse settlement agreements have been challenged under antitrust principles in various federal courts. The challenges resulted in conflicting opinions from different circuit courts. The Second Circuit adopted a policy in favor of settlement; the Federal Circuit concluded that the agreements are presumed lawful unless they extend beyond the patent exclusivity zone; the Eleventh Circuit developed a framework intended to ascertain the appropriate exclusionary zone of the patent; while the Third Circuit adopted a “quick look” rule of reason analysis.<sup>38</sup>

#### **1. Second Circuit: *In re Tamoxifen***

The Second Circuit considered the issue of reverse payment settlements in *In*

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37. The Sherman Act imputes criminal and civil liability to any person who “shall monopolize, or attempt to monopolize, or combine or conspire with any other person or persons, to monopolize any part of the trade or commerce among the several States, or with foreign nations . . .” 15 U.S.C. § 2 (2006).

38. Antitrust analysis distinguishes between certain types of practices considered inherently anticompetitive, such as price fixing, and “per se” illegal and other practices analyzed under a more flexible balancing test known as the “rule of reason.” WILLIAM C. HOLMES, ANTITRUST LAW HANDBOOK, §2:9 (2008). The rule of reason is a totality of the circumstances analysis aimed at ascertaining whether the challenged practice imposes unreasonable restraints on competition. *Id.* at §2:10. Relevant factors can include the defendants’ intent, the structure of the relevant market, or the market power of the defendants. *Id.* An abbreviated version of the rule of reason, the “quick look” approach, is used in circumstances when the anticompetitive effects of the practice are so intuitively obvious as to be clear without a detailed market analysis. *Id.* Primarily, the quick look approach relieves the government from rigorously identifying the relevant market, the defendants’ market power, or the anticompetitive effects of the practice. *Id.*

*re Tamoxifen Citrate Antitrust Litigation*.<sup>39</sup> The litigation involved a patent held by Zeneca covering Tamoxifen, a widely-prescribed drug for the treatment of breast cancer.<sup>40</sup> The district court ruled in favor of the Paragraph IV filer, Barr, based on fraud against the Patent and Trademark Office.<sup>41</sup> While the appeal was pending, the parties agreed to a settlement in which Barr would receive \$21 million and a non-exclusive license to sell Zeneca-manufactured Tamoxifen under Barr's label, and Barr's supplier, Heumann, would receive payments of over \$45 million over ten years.<sup>42</sup> In return, Barr agreed to change its Paragraph IV certification to a Paragraph III certification – thereby agreeing not to enter the market until Zeneca's patent expired unless the patent was subsequently declared invalid due to litigation with another challenger.<sup>43</sup>

The agreement was challenged by various consumers, providers of medical benefits, and consumer advocacy groups.<sup>44</sup> The district court rejected the charges and granted the defendants' motion to dismiss.<sup>45</sup> In affirming the district court's

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39. 466 F.3d 187 (2d Cir. 2006).

40. *Id.* at 193.

41. *Id.* A finding of fraud against the PTO bars enforcement of a patent thereby effectively invalidating the patent. *See e.g.* *Therasense, Inc. v. Becton, Dickinson & Co.*, 649 F.3d 1276, 1295 (Fed. Cir. 2011).

42. *Id.* at 193-194.

43. *Id.* Over the years following the agreement, three other generic manufacturers challenged the patent by filing a Paragraph IV certification, but each time the courts upheld the validity of Zeneca's patent. *See Zeneca Ltd. v. Novopharm Ltd.*, 111 F.3d 144, 1997 WL 168318, at \*2-\*4 (Fed. Cir. Apr. 10, 1997)(unpublished opinion); *Zeneca Ltd. v. Pharmachemie B.V.*, 2000 WL 34335805, at \*15 (D.Mass. Sept. 11, 2000); *AstraZeneca UK Ltd. v. Mylan Pharms., Inc.*, No. 00-2239, slip op. at 2-3 (W.D.Pa. Nov. 30, 2000).

44. *Id.* at 196.

45. *Id.* at 197.

decision, the Second Circuit stressed how courts must encourage the settlement of litigation and noted that restricting patent settlements might be contrary to the goals of patent laws since increased uncertainty surrounding patents might harm innovation.<sup>46</sup> The court also rejected the argument that the settlements would allow an invalid patent to remain in force and that reverse payments are inherently anticompetitive.<sup>47</sup> The court reasoned that, due to the inherent risk of litigation, settlements of legitimate disputes intended to eliminate that risk should be allowed and that a patent holder paying to protect its patent-granted monopoly, without more, is not a violation of the Sherman Act.<sup>48</sup>

## 2. Federal Circuit: *In re Ciprofloxacin*

The Federal Circuit considered the issue of reverse payment settlements in *In re Ciprofloxacin Hydrochloride Antitrust Litigation*.<sup>49</sup> Just before trial, the parties agreed to a settlement in which the generic manufacturer, Barr, agreed to cease challenging the patent and delay market entry until six months prior to patent expiration.<sup>50</sup> In exchange, the patent owner, Bayer, agreed to pay Barr \$49.1 million and either supply it with the drug for resale or make quarterly payments for a period of seven years.<sup>51</sup> Advocacy groups challenged the agreement on antitrust

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46. *Id.* at 202-203.

47. *Id.* at 204.

48. *Id.* at 205.

49. 544 F.3d 1323 (Fed. Cir. 2008).

50. *Id.* at 1328-1329.

51. *Id.* at 1329. In subsequent years, the validity of the patent was upheld in court four times after other generic manufactures filed Paragraph IV ANDAs.

grounds.<sup>52</sup>

The district court granted summary judgment for the defendants and the Federal Circuit affirmed.<sup>53</sup> In doing so, the Federal Circuit distinguished the *Ciprofloxacin* agreement from others where the restraints on the generic manufacturer extended the patent exclusivity zone.<sup>54</sup> The court concluded that, when the anticompetitive effects of the settlement are “within the exclusionary power of the patent,” the application of the rule of reason under antitrust law must produce the same outcome as an analysis of the right to exclude granted by the patent under patent law.<sup>55</sup>

### 3. Eleventh Circuit: *Watson Pharmaceuticals*

The most recent appellate decision on reverse payments in the Eleventh Circuit is the ruling in *F.T.C. v. Watson Pharmaceuticals*.<sup>56</sup> The original litigation involved a Paragraph IV challenge to Solvay’s patent on AndroGel, a topical gel used to treat low testosterone in men, by two generic manufacturers.<sup>57</sup> The litigation ended when the parties agreed to a settlement providing that the generic manufacturers would (1) refrain from marketing their generic version of the drug for a period of nine years; (2) promote the branded AndroGel to urologists; and (3)

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52. *Id.*

53. *Id.* at 1330, 1340.

54. *Id.* at 1335. The court cited *In re Cardizem CD Antitrust Litig.* where (1) the generic manufacturer had not relinquished the 180-day exclusivity period, thereby preventing other generic manufacturer from entering the market; and (2) the generic agreed not to market non-infringing versions of the generic drug. 332 F.3d 896 (6th Cir. 2003).

55. *Id.* at 1336.

56. 677 F.3d 1298 (11th Cir. 2012).

57. *Id.* at 1303-1304.

serve as backup manufacturers.<sup>58</sup> In exchange, Solvay agreed to pay \$10 million a year for six years – plus an additional \$2 million a year for the backup manufacturing – to one of the generic manufacturers and share some of its AndroGel profits with the other.<sup>59</sup> The F.T.C. filed an antitrust suit claiming the settlement was an agreement not to compete and the district court granted the defendants’ motion to dismiss.<sup>60</sup>

The Eleventh Circuit affirmed the rule it developed in three previous decisions<sup>61</sup> that, absent sham litigation of fraud, reverse payment settlements that remain within the exclusionary zone of the patent are immune from antitrust attacks.<sup>62</sup> Furthermore, the court firmly rejected the F.T.C. argument that an antitrust claim could be based on allegations that the patent holder was “not likely to prevail” in the patent infringement action.<sup>63</sup> Describing the F.T.C. argument as equating a likely result – the invalidation of the patent – with an actual result, the court remarked that “[p]redicting the future is precarious at best; retroactively predicting from a past perspective a future that never occurred is even more perilous.”<sup>64</sup>

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58. *Id.* at 1305.

59. *Id.*

60. *Id.* at 1306.

61. The three decisions were: *Valley Drug Co. v. Geneva Pharm., Inc.*, 344 F.3d 1294 (11th Cir. 2003); *Schering–Plough Corp. v. F.T.C.*, 402 F.3d 1056 (11th Cir. 2005); and *Andrx Pharm., Inc. v. Elan Corp.*, 421 F.3d 1227 (11th Cir. 2005).

62. *Watson Pharm.*, 677 F.3d at 1312.

63. *Id.*

64. *Id.* at 1313.

#### 4. Third Circuit: *In re K-Dur*

The Third Circuit addressed reverse payments in *In re K-Dur Antitrust Litigation*.<sup>65</sup> The brand manufacturer, Schering, held a patent on the controlled-release coating used in K-Dur, its potassium chloride supplement.<sup>66</sup> Two generic manufacturers, Upsher and ESI Lederle, filed ANDAs providing Paragraph IV certification compelling Schering to file suit to defend its patent.<sup>67</sup> Both litigations terminated with reverse payment agreements. The Schering-Upsher agreement provided that Upsher would refrain from marketing its generic version of K-Dur, or any similar product, for four years in exchange for a payment of \$60 million.<sup>68</sup> The Schering-ESI agreement provided that ESI would not develop a potassium chloride product and would receive in return \$15 million and a non-exclusive license to K-Dur starting eight years following the agreement.<sup>69</sup>

The F.T.C. filed a complaint against Schering, Upsher and ESI alleging that the settlements unreasonably restrained commerce and that the reverse payments intended to preserve Schering's monopoly by delaying generic entry.<sup>70</sup> In ruling in favor of the F.T.C., the Third Circuit rejected the "scope of the patent" test as granting an almost un rebuttable presumption of patent validity.<sup>71</sup> Instead, the court adopted a "quick look" rule of reason analysis in which a reverse payment

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65. 686 F.3d 197 (3d Cir. 2012).

66. *Id.* at 203.

67. *Id.* at 205.

68. *Id.* at 205-206.

69. *Id.* at 206.

70. *Id.* at 206-207.

71. *Id.* at 214.



constitutes *prima facie* evidence of an unreasonable restraint of trade, rebuttable only “by showing that the payment (1) was for a purpose other than delayed entry or (2) offers some pro-competitive benefit.”<sup>72</sup>

#### **F. The Supreme Court’s response in *Actavis***

In response to a deepening split among the circuits, the Supreme Court granted a writ of *certiorari* in *F.T.C. v. Watson Pharmaceuticals*.<sup>73</sup> The Court reversed the near-automatic antitrust immunity provided by the Eleventh Circuit.<sup>74</sup> Rather, the Court concluded that reverse payment settlements should be reviewed under a full rule of reason analysis.<sup>75</sup>

The Court based the ruling that reverse settlements should be subject to antitrust scrutiny on five sets of considerations.<sup>76</sup> First, the Court noted that these types of agreements have “the potential for genuine adverse effects on competition.”<sup>77</sup> Second, while sometimes the agreements are justified – such as when the payment is an approximation of litigation expenses saved through the settlement, or reflects compensation for other services offered by the generic manufacturer – when no such redeeming qualities are present the anticompetitive effects might prove unduly harmful.<sup>78</sup> Third, firms willing to make large payments may possess market power – the ability to charge prices higher than the competitive

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72. *Id.* at 218.

73. *F.T.C. v. Actavis, Inc.*, \_\_\_ U.S. \_\_\_, 133 S. Ct. 2223, 2230 (2013).

74. *Id.* at 2237.

75. *Id.*

76. *Id.* at 2234.

77. *Id.*

78. *Id.* at 2236.

level.<sup>79</sup> Fourth, normally there would be no need to litigate the patent’s validity in order to answer the antitrust question because an “unexplained large reverse payment” in itself can provide a proxy for an invalid patent.<sup>80</sup> Fifth, the parties have other means to settle the litigation that do not involve large and unjustified reverse payments and are, therefore, not at risk of antitrust liability.<sup>81</sup>

Further, the Court refused the F.T.C.’s argument that reverse payment settlements should be presumed unlawful. Rather than a “quick look” approach, the Court held that reverse payments must be reviewed under a full rule of reason analysis.<sup>82</sup> A “quick look” approach, the Court reasoned, is appropriate only when “an observer with even a rudimentary understanding of economics could conclude that the agreements in question would have an anticompetitive effect on consumers and market.”<sup>83</sup> Therefore, because of the inherent complexities of reverse payment settlements in the Hatch-Waxman Act context, the Court concluded that the settlement challenger should prove its case under a full rule of reason analysis.<sup>84</sup>

The Supreme Court created an approach that will be difficult to apply in practice because is unclear how a full rule of reason analysis can be performed without attempting to assess patent validity.<sup>85</sup> It is also unclear what means for reverse payments to be “large” and “unjustified,” the telltale signs of

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79. *Id.*

80. *Id.*

81. *Id.* at 2237

82. *Id.*

83. *Id.*

84. *Id.*

85. The Court remarked that it is “normally not necessary to litigate patent validity to answer the antitrust question[.]” *Actavis*, 133 S. Ct. at 2236.

anticompetitive agreements according to the Court.<sup>86</sup> The resulting high level of uncertainty leaves the parties two equally undesirable choices: litigate the patent dispute until a final judgment or risk highly uncertain and complex post-settlement antitrust litigation. This situation can severely affect the economic choices of innovator drug manufacturers and have serious repercussions on the pharmaceutical industry. Of particular concern are the negative effects on the rate of pharmaceutical innovation that result from insufficient patent protection.

### **III. INNOVATION IN THE PHARMACEUTICAL INDUSTRY**

One of the goals of the Hatch-Waxman Act was to balance an increase in generic competition with adequate incentives that would encourage the continued innovation of new drugs.<sup>87</sup> However, the Supreme Court's decision is oddly devoid of any consideration regarding the effects of increased uncertainty on future innovation in the pharmaceutical industry.

#### **A. Pharmaceutical research and development**

Technological innovation is the essence of the pharmaceutical industry — one of the most research-intensive sectors in the United States.<sup>88</sup> The industry's focus on innovation is aptly illustrated by the estimated \$48.5 billion spent on research and development ("R&D") by Pharmaceutical Research and Manufacturers of

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86. *Id.* at 2237.

87. Henry G. Grabowski et al., *Evolving Brand-Name and Generic Drug Competition May Warrant a Revision of the Hatch-Waxman Act*, 30 HEALTH AFFAIRS 2157, 2157 (2011).

88. Dickey, *supra* note 12, at 369 (citing CONG. BUDGET OFFICE, RESEARCH AND DEVELOPMENT IN THE PHARMACEUTICAL INDUSTRY 7-9 (2006)).

America (“PhRMA”) members in 2012.<sup>89</sup> Innovation in the pharmaceutical industry is a risky, costly, and time-consuming endeavor. Innovator firms place the largest portion of their R&D effort into developing new chemical entities (NCE).<sup>90</sup>

Typically, developing a NCE is a process that requires several years. First, considerable research is needed in order to synthesize a new compound.<sup>91</sup> Once a new promising compound is discovered, it will be subject to screening for pharmacological activity and toxicity, first in vitro and then in animals.<sup>92</sup> If the compound is still considered a promising candidate after the initial screening then clinical trials will begin. Human testing normally occurs over three phases with increasing numbers of test subjects. Phase I, designed to obtain toxicity information and safe dosage ranges, is conducted on a small number of healthy volunteers.<sup>93</sup> Phase II is aimed at proving the drug’s efficacy and is performed on a larger number of individuals, usually in the hundreds, selected among those patients for whom the drug is intended to be beneficial.<sup>94</sup> Lastly, Phase III involves large-scale testing on thousands of patients and is used to provide additional support to the previous efficacy findings, as well as to detect possible side-effects.<sup>95</sup>

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89. PHARM. RESEARCH AND MFR. OF AM., 2013 BIOPHARMACEUTICAL RESEARCH INDUSTRY PROFILE, 30 [hereinafter PhRMA].

90. DiMasi et al., *Cost of Innovation in the Pharmaceutical Industry*, 10 J. HEALTH ECON. 107, 108 (1991)[hereinafter DiMasi I].

91. *Id.* at 110.

92. *Id.*

93. DiMasi et al., *The Price of Innovation: New Estimation of Drug Development Costs*, 22 J. HEALTH ECON. 151, 155 (2003)[hereinafter DiMasi II].

94. *Id.* at 156.

95. *Id.*

## B. Costs and success rates of pharmaceutical R&D

Typically, it takes about twelve years for a new medicine to complete the R&D cycle from initial discovery to market launch.<sup>96</sup> Further, only a small fraction of the promising compounds tested in the pretrial phase are eventually brought to market.<sup>97</sup> Indeed, for every 5,000 compounds tested, on average only five will be tested in clinical trials, and only one of those will receive final FDA approval.<sup>98</sup>

Given the complexity and length of the R&D effort, it is not surprising that the costs of such endeavors are extremely high. Several studies, over different time periods, have provided estimates of the R&D expenditures required to develop and bring to market a new drug. Although several of these studies were based on different data sources, taken together these studies point to a steeply rising cost of R&D.<sup>99</sup> After normalizing the various studies' results to 2011 prices for comparison purposes, the estimated cost of bringing a new drug to market was \$199 million in the late 1970s, \$451 million in the early 1990s, \$1,031 million in the early 2000s, and \$1,867 million in 2010.<sup>100</sup> Such drastic increase is due, in large part, to the

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96. Michael Dickson & Jean Paul Gagnon, *Key Factors in the Rising Cost of New Drug Discovery and Development*, 3 NATURE REVIEWS DRUG DISCOVERY 417, 418 (2004)(citing the Tufts Center for the Study of Drug Development, *infra* note 97). The latest estimate, however, suggests it might take as long as fifteen years to bring a new compound to market. PhRMA, *supra* note 89, at 32.

97. Dickey, *supra* note 12, at 369.

98. TUFTS CTR. FOR THE STUDY OF DRUG DEV., *Backgrounder: How New Drugs Move through the Development and approval Process* (2001), [http://csdd.tufts.edu/files/uploads/how\\_new\\_drugs\\_move.pdf](http://csdd.tufts.edu/files/uploads/how_new_drugs_move.pdf).

99. DiMasi I, *supra* note 90, at 111.

100. Jorge Mestre-Ferrandiz et al., THE R&D COST OF A NEW MEDICINE, 11 (Office of Health Econ. ed., 2012)(summarizing, among others, the following earlier studies: R. HANSEN, *The pharmaceutical development process: Estimates of*

growth in the size and length of clinical trials and an increased failure rate.<sup>101</sup> In particular, research has focused increasingly on developing drugs for chronic illnesses that require prolonged clinical trials.<sup>102</sup>

### C. Effects of generic competition

Brand-name drugs lose the majority of their sales to their generic equivalent. The generic share of dispensed prescription drugs has steadily increased from the time the Hatch-Waxman Act was enacted, growing from 18.6% in 1984 to 74.5% in 2009.<sup>103</sup> Further, the rate of market-share erosion brand-name drugs suffer has greatly accelerated over time. In the years immediately following the enactment of the Hatch-Waxman Act, it took generic drugs about three to four years to obtain a dominant share of the market.<sup>104</sup> But by 2008, brand-name drugs on average retained a market share of only 37% merely one month after generic entry, a figure

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*development costs and times and the effect of proposed regulatory changes, in ISSUES IN PHARM. ECON.* 151 (Robert I. Chien, ed., Lexington 1979); DiMasi I, *supra* note 90; DiMasi II, *supra* note 93; Steven M. Paul et al., *How to improve R&D productivity: The pharmaceutical industry's grand challenge*, 9 *NATURE REVIEWS DRUG DISCOVERY*. 203 (2010)). All the studies mentioned included (1) discovery costs, i.e. costs incurred during the pre-clinical trial stage; (2) the costs of unsuccessful research projects, which accounted for the expenditures on projects that did not result in a marketable drug; and (3) capitalized average costs, which were used to calculate the opportunity cost of funds invested in the R&D process.

101. *Pharmaceutical R&D and the Evolving Market for Prescription Drugs, Economic and Budget Issue Brief*, CONG. BUDGET OFFICE at 4 (2009), <https://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/106xx/doc10681/10-26-drugr&d.pdf>

102. *Id.*

103. Ernst R. Berndt & Murray Aitken, *Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century after the 1984 Waxman-Hatch Legislation*, NBER Working Paper No. 16431, 4 (2010).

104. Henry G. Grabowski, *Are the Economies of Pharmaceutical Research and Development Changing?*, 22 *PHARMACOECONOMICS* 15, 19 (2004).

that rapidly declined to 19% six months following generic entry.<sup>105</sup> “Blockbuster” drugs – drugs with average annual sales of more than \$100 million – are even more affected, as they suffer even faster market-share erosion.<sup>106</sup> If on the one hand fast market penetration of generic drugs allows for a reduction in healthcare costs, on the other it produces undesirable results that, while difficult to quantify, might more than offset the welfare gains due to lower prices.<sup>107</sup> Specifically, one major concern is whether innovator-drug manufacturers have the opportunity to recuperate the costs of R&D, earn a positive return on that investment, and maintain a steady rate of innovation.

#### **D. Protecting investments in pharmaceutical innovation**

Patent laws are designed to encourage investments in research and innovation. They attempt to do so by providing the patent holder the right to exclude others from making, selling, or using the patented invention for a period of twenty years from the date the patent was filed.<sup>108</sup> Given the time, cost, and high risk of failure of the R&D process, pharmaceutical companies rely heavily on patents to protect their investment. The proceeds from the sale of a drug that is successfully brought to market will not only repay the company’s shareholders for

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105. Henry G. Grabowski, *The Evolution of the Pharmaceutical Industry Over the Past 50 Years: A Personal Reflection*, 18 INT. J. OF THE ECON. OF BUSINESS 161, 2162 (2011) [hereinafter Grabowski I].

106. *Id.*

107. Henry G. Grabowski et al., *Does Generic Entry Always Increase Consumer Welfare?*, 67 FOOD & DRUG L. J. 373, 391 (2012).

108. 35 U.S.C. §154(a)(2) (2006).

their investment, but also fund new research.<sup>109</sup> For this reason, the pharmaceutical industry is believed to depend on intellectual property rights more than every other industry.<sup>110</sup> Despite that, patents are a less effective method of protecting an innovator firm's investment in the pharmaceutical context than in other industries.

First, while nominally a patent provides protection for twenty years, the effective life of a patent<sup>111</sup> is often less because patents are frequently obtained before marketing.<sup>112</sup> Estimates indicate that on average a patent will provide 18.5 years of effective patent life.<sup>113</sup> The situation is even worse in the pharmaceutical industry. Innovator firms normally apply for patents soon after the non-clinical testing process; given the length of clinical trials and the time necessary to receive FDA approval, pharmaceutical patents lose much of their nominal life before marketing even begins.<sup>114</sup> Recognizing this problem, the Hatch-Waxman Act provides restoration of the patent time lost in the regulatory review and clinical testing.<sup>115</sup> The Act, however, caps the length of the restoration period at five years.<sup>116</sup> Estimates indicate that, even accounting for the patent restoration period,

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109. Robin J. Strongin, *Hatch-Waxman, Generics, and Patents: Balancing Prescription Drug Innovation, Competition, and Affordability*, NATIONAL HEALTH POLICY FORUM BACKGROUND PAPER, 3 (2002).

110. Morris, *supra* note 1, at 249.

111. Effective patent life is defined as the period in which the patent holder enjoys market exclusivity.

112. Strongin, *supra* note 109, at 5.

113. *Id.*

114. Morris, *supra* note 1, at 257-258.

115. 21 U.S.C. § 355(5)(F)(ii).

116. *Id.*



the average effective patent life for new drugs is only 13.5 years.<sup>117</sup> Furthermore, the average effective patent life on blockbuster drugs is even shorter: approximately 11 years.<sup>118</sup>

Second, Paragraph IV challenges are one of the main factors responsible for the discrepancy between nominal and effective patent life.<sup>119</sup> Drugs that face Paragraph IV challenges have an estimated reduction in effective patent life of two years.<sup>120</sup> Unsurprisingly, given the great economic incentives enjoyed by a generic challenger, Paragraph IV certifications have been increasing in number.<sup>121</sup> Furthermore, Paragraph IV challenges disproportionately target blockbuster drugs.<sup>122</sup> These drugs frequently have a great therapeutic value, as they are those most likely to be first-in-class or best-in-class products, providing care for otherwise unmet medical needs.<sup>123</sup> In addition, brand name manufacturers are critically dependent on the revenues from blockbuster drugs in order to earn positive returns on their R&D efforts.<sup>124</sup> Given their tremendous importance from both a medical

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117. Grabowski & Kyle, *supra* note 9, at 496. *See also* Strongin, *supra* note 109, at 5 (reporting similar results).

118. Grabowski & Kyle, *supra* note 9, at 496.

119. Scott C. Hemphill & Bhaven N. Sampat, *Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals*, 31 J. HEALTH ECON. 327, 18 (2012).

120. *Id.* Note that the author uses the term “market life” to describe what is here referred to as effective patent life.

121. *Id.* at 14.

122. Grabowski & Kyle, *supra* note 9, at 498. A behavior the author calls “prospecting,” where the economic rewards of successfully challenging a blockbuster drug are so large to offset the associated costs, even when the likelihood of invalidating the patent is low.

123. Grabowski & Kyle, *supra* note 9, at 496.

124. *Id.*

and economic perspective then, blockbuster drugs are those most in need of effective intellectual property protection. Despite this, these drugs are 59% more likely to face Paragraph IV challenges than other drugs and are often challenged early on after their market launch.<sup>125</sup>

Therefore, patents in the pharmaceutical industry are a less effective method of protecting an innovator firm's investment than in other industries because they guarantee fewer years of market exclusivity. First, a good portion of a pharmaceutical patent's life is lost during the pre-marketing years of clinical trials and the FDA approval process. Second, the increasing number of Paragraph IV challenges further reduces the estimated market exclusivity period, especially for those drugs more likely to earn positive returns and fuel new investments in R&D.

#### **IV. PROMOTING PHARMACEUTICAL INNOVATION**

Because of the high costs and risks of developing new drugs, pharmaceutical manufacturers need reliable intellectual property protections. As we have seen, however, patents are not as effective a mean of protecting investments in pharmaceutical innovation as they are in other industries. The *Actavis* decision further diminishes the value provided by pharmaceutical patents because it increases the uncertainty tied to patent litigation in the Hatch-Waxman context. While the Hatch-Waxman Act intended to strike a balance between promoting competition and innovation, the interplay of the Act's provisions may have had the effect of tipping the scale too much in favor of the former. To avoid the consequence

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125. Hemphill & Sampat, *supra* note 119, at 13, 19.

of severely limiting new drug development, it may be necessary to rethink the incentive structure provided by the Hatch-Waxman Act.

**A. Effects of the Hatch-Waxman Act on the rate of innovation**

As we have seen, R&D of pharmaceuticals is a costly, lengthy, and risky process. For this reason, for every new drug successfully brought to market, manufacturers need a correspondingly lengthy period of time to earn a positive risk-adjusted return on the R&D investment.<sup>126</sup> For most drugs, the data exclusivity period of five years provided by the Hatch-Waxman Act is not enough to recuperate the R&D costs and earn a positive return.<sup>127</sup> In fact, it is estimated that it takes about six years for most drugs to start earning positive marginal returns.<sup>128</sup> As a consequence, only about 20% of brand name drugs earn sufficient revenues to recoup average R&D costs.<sup>129</sup> Therefore, the Hatch-Waxman Act – featuring a short data exclusivity period, a streamlined approval process favoring early generic entry, and substantial rewards to generic manufacturers who challenge patents – has created an even greater uncertainty as to whether innovators may recover an appropriate return on their research investments.

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126. Grabowski, *supra* note 87, at 2163.

127. Henry G. Grabowski & Jeffrey L. Moe, *Impact of Economic, Regulatory and Patent Policies on innovation in Cancer Chemoprevention*, ECON. DEPT' DUKE UNIV. (2007), <http://www.econ.duke.edu/Papers/PDF/BarrierWorkingPaper>.

128. Morris, *supra* note 1, at 258.

129. John A. Vernon et al., *Drug development costs when financial risk is measured using the Fama-French three-factor model*, 19 HEALTH ECON. LETTERS 1002, 1004 (2010).

Furthermore, pharmaceutical R&D is predominantly funded by internal financing sources.<sup>130</sup> That is because the combination of the length of the R&D process, the great uncertainty about the R&D outcomes, and the information asymmetries between drug manufacturers and outside investors make external funds difficult to obtain and extremely costly.<sup>131</sup> For this reason, two major factors affecting pharmaceutical manufacturers' R&D investment behavior are the availability of internal funds and the expected returns on the R&D investment.<sup>132</sup> By affecting both of these factors, the Hatch-Waxman Act has had the unintended consequence of severely limiting new drug development.<sup>133</sup> First, the Hatch-Waxman Act greatly facilitates early market entry of generics which, since the Act's enactment, have eroded brand manufacturers' revenues at an alarmingly increasing rate.<sup>134</sup> The reduction in brand manufacturers' cash flows resulting from generics' market penetration decreases the availability of internal funds used to finance new research. Empirically, experts have calculated that a 10% increase in generic penetration decreases the flow of early-stage innovation by 7.3%.<sup>135</sup> Second, by increasing the uncertainty concerning pharmaceutical patents, the Hatch-Waxman

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130. Henry G. Grabowski & John A. Vernon, *The Determinants of Pharmaceutical Research and Development Expenditures*, 10 J. EVOL. ECON. 201, 207 (2000).

131. *Id.*

132. *Id.* at 208.

133. Matthew J. Higgins & Stuart J. H. Graham, *Balancing Innovation and Access: Patent Challenges Tip the Scales*, 326 SCIENCE 370, 370 (2009).

134. Grabowski, *supra* note 87, at 2162.

135. Branstetter, *supra* note 10, at 18. The term "early-stage" refers to products in the initial phase of the drug development process. The number of such products is a suitable proxy for measuring pharmaceutical manufacturers' efforts to innovate.

Act lowers the expected return on R&D investments.<sup>136</sup> A reduction in the expected value of pharmaceutical patents decreases drug manufacturers' incentives to engage in the highly risky and expensive R&D process. Indeed, experts have estimated that a 10% increase in Paragraph IV challenges leads to a 3.9% decrease in early-stage innovation.<sup>137</sup>

### **B. Longer exclusivity periods: the case of biologics**

In recent years, advances in molecular biology have stimulated the development of large molecule biologic-based pharmaceutical products.<sup>138</sup> Pharmaceutical manufacturers increasingly have been attracted to biologics, not only because of their great potential to provide breakthrough therapies, but also for the economic benefits they offer.<sup>139</sup> In particular, unlike conventional chemical-based drugs, brand-name biologics face virtually no competition from generic imitations or biosimilars.<sup>140</sup> There are two main reasons contributing to the lack of generic competition. First, the manufacturing of biologics is more difficult and subject to greater regulatory requirements than the manufacturing of chemical-based drugs.<sup>141</sup> Second, while biosimilars can be close substitutes to the branded

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136. Morris, *supra* note 1, at 273

137. Branstetter, *supra* note 10, at 21.

138. Grabowski I, *supra* note 105, at 165.

139. *Id.* at 166.

140. Congressional Budget Office, *supra* note 101 at 7.

141. Henry G. Grabowski, *Patents and New Product Development in the Pharmaceutical and Biotechnology Industries*, 94 (2002)[hereinafter Grabowski II].

biologics of reference, they are not chemically identical and therefore not completely interchangeable.<sup>142</sup>

As part of the Patient Protection and Affordable Care Act (“ACA”), Congress created an abbreviated pathway for biosimilars, similar to the one for generic drugs under the Hatch-Waxman Act.<sup>143</sup> As Congress tried to balance proper incentives for innovation with consumer interests, it extensively debated the appropriate length of the data exclusivity period to be afforded to innovator manufacturers.<sup>144</sup> As a consequence of that debate, the ACA grants a new innovative biologic twelve years of data exclusivity.<sup>145</sup> Therefore, the data exclusivity period for biologics is now much longer than for new chemical entities.<sup>146</sup> Data exclusivity provides a form of intellectual property protection that is considerably stronger than patents because it is not subject to legal challenges.<sup>147</sup> Longer data exclusivity periods for biologics, coupled with the increasingly uncertain outcomes of Paragraph IV challenges, raise the question of whether the incentives for future innovation are artificially skewed in favor of biologics.

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142. Grabowski I, *supra* note 105, at 166.

143. 42 U.S.C. § 262 (2006).

144. Henry G. Grabowski et al., *Data Exclusivity for Biologics*, 10 NATURE REVIEWS 15, 15 (2011) [hereinafter Grabowski III].

145. 42 U.S.C. § 262(k)(7)(A).

146. Grabowski III, *supra* note 144, at 16.

147. Dana P. Goldman et al., *The Benefits from Giving Makers of Conventional ‘Small Molecule’ Drugs Longer Exclusivity Over Clinical Trial Data*, 30 HEALTH AFFAIRS 84, 85 (2011).

The current regulatory environment has produced strong economic incentives to shift the focus of research to biologics.<sup>148</sup> Pharmaceutical manufacturers already seem to be responding to these incentives, as biologics account for almost half of all drugs currently being tested in clinical trials.<sup>149</sup> In the long run this shift could have severe negative repercussions on healthcare costs because biologics are significantly more expensive to produce than chemical-based drugs.<sup>150</sup> Extending the period of data exclusivity for chemical-based drugs to match the period afforded to biologics might help to counterbalance these effects. Estimates indicate that increasing the data exclusivity period to twelve years would produce a 5% increase in the expected revenues generated over a drug's lifetime.<sup>151</sup> Empirical evidence strongly supports the notion that profits drive innovation.<sup>152</sup> Accordingly, experts estimate that a data exclusivity period for chemical-based drugs extended to twelve years could result in an additional 228 drug approvals between 2020 and 2060.<sup>153</sup> Therefore, when given longer data exclusivity periods, manufacturers would be more likely to pursue many promising new therapies that otherwise might not be developed.

**C. A system of combined incentives: the orphan drugs example**

Stimulating innovation was the primary motivation behind another widely debated legislation: the Orphan Drug Act of 1983 (“ODA”).<sup>154</sup> The ODA was

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148. Branstetter, *supra* note 10, at 20.  
149. Grabowski I, *supra* note 105, at 166.  
150. Branstetter, *supra* note 10, at 20.  
151. Goldman, *supra* note 147, at 87.  
152. *Id.* at 85.  
153. *Id.* at 87.  
154. 21 U.S.C. §§ 360aa-360ff (2006).

designed to encourage the development of so called “orphan drugs” – drugs that are useful for a rare disease or condition – by providing a series of economic incentives. The statute defines a rare condition as one (1) that affects fewer than 200,000 individuals within the United States; or (2) for which there is no reasonable expectation to recover the costs of making and marketing a drug.<sup>155</sup> An orphan drug is one that manufacturers were typically unwilling to take through the lengthy and costly FDA approval process because, given the rareness of the condition that it is meant to treat, has a very small likelihood to generate positive returns. To overcome such great economic deterrent, the ODA created a system combining four types of incentives. First, it makes available a grants program to help defray the costs of testing and clinical trials.<sup>156</sup> Second, it provides FDA advice and counseling on the protocol of tests and experiments the drug sponsor needs to complete to gain marketing approval.<sup>157</sup> Third, it establishes a tax credit for fifty percent of the

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155. 21 U.S.C. § 360bb(a)(2). The current definition is the product of the first of three amendments which, in 1984, expanded the original definition of a rare disease – one for which there is no reasonable expectation to recover the costs of making and marketing a drug – to include conditions affecting less than 200,000 people in the United States. Subsequently, the 1985 amendment extended the market exclusivity provision to patentable as well as unpatentable drugs and the 1988 amendment required sponsors to apply for orphan designation before submitting a market approval application. Gary A. Pulsinelli, *The Orphan Drug Act: What’s Right with It*, 15 SANTA CLARA COMPUTER & HIGH TECH. L. J. 299, 307-309 (1999).

156. 21 U.S.C. § 360ee.

157. 21 U.S.C. § 360aa(a).



amounts spent performing clinical trials.<sup>158</sup> Fourth, it guarantees a seven-year market exclusivity period.<sup>159</sup>

The ODA provisions stimulate investments in the development of orphan drugs in two ways. The first three ODA provisions effectively subsidize research inputs, thereby lowering the cost of pharmaceutical R&D. The last provision helps reduce the risk associated with pharmaceutical R&D because, by barring early generic entry, it guarantees manufacturers a longer period of time to earn positive returns on their investments. This combination of incentives has unquestionably been successful in stimulating the development of drugs for rare diseases. While only a handful of such drugs were available before the passage of the act, by 2007 the FDA had designated 1,793 orphan products; 322 of these having received marketing approval.<sup>160</sup>

## V. CONCLUSION

Balancing consumer interests with sufficient incentives to foster pharmaceutical innovation is not an easy task. On the one hand, there is a critical need to curtail healthcare costs and increase drug accessibility. On the other, regulatory policies that affect the returns of pharmaceuticals, and in particular of blockbuster drugs, can have significantly negative consequences on the rate of innovation in the industry. Long-term trends in the industry, as well as more recent

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158. 26 U.S.C. § 45c.

159. 21 U.S.C. § 360cc(a)(2).

160. Enrique Seoane-Vazquez et al., *Incentives for Orphan Drug Research and Development in the United States*, ORPHAN J. RARE DISEASES (2008), <http://www.ojrd.com/content/pdf/1750-1172-3-33.pdf>

developments, make it highly questionable whether patents remain the most appropriate form of intellectual property protection for pharmaceutical products. To avoid the consequence of severely limiting new drug development, it might be necessary to rethink the incentive structure provided by the Hatch-Waxman Act. A mixed-incentives system could be devised to replace what is currently in place. The new system could not only offer pharmaceutical innovator firms a greater likelihood of recovering R&D expenses – through longer statutorily-granted exclusivity periods – but also lower the costs of research by offering a tax credit for amounts spent on research. These types of incentives have proven to be extremely successful in niche areas of the pharmaceutical industry and could help restore the proper balance sought when the Hatch-Waxman Act was originally enacted.