



# BIOSIMILARS AFTER ACTAVIS: SIMILAR CONSIDERATIONS, SIMILAR RESULTS

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## I. INTRODUCTION

On September 3, 2015, the United States watched as the first “generic-like” biologic drug<sup>1</sup> entered the market ushering in a new era for the pharmaceutical industry.<sup>2</sup> In tow, the hopes of the American people and the promise of lower-priced, life-altering medication. This entry comes at a time when the lower courts and the pharmaceutical industry are wrestling with the Supreme Court’s decision in *FTC v. Actavis*,<sup>3</sup> which one commentator has called “one of the most important business cases in the past generation.”<sup>4</sup> In *Actavis*, the U.S. Supreme Court held that “reverse payment settlements”<sup>5</sup>—payments made by brand-name drug manufacturers to generic drug companies to delay entry—could sometimes fail to pass antitrust muster and are subject to “rule-of-reason” analysis.<sup>6</sup> While *Actavis* and subsequent lower court cases have addressed reverse payment settlements in the context of generic small-molecule drugs and their respective statutory scheme, the Drug Price Competition and Patent Term Restoration Act (informally known as the Hatch-Waxman Act),<sup>7</sup> a question that remains

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<sup>1</sup> See FDA.gov, *What are “Biologics” Questions and Answers*, CTR. FOR BIOLOGICS EVALUATION AND RES. (last visited Mar. 6, 2017), <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm133077.htm>

(Biological products include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins . . . Biologics are isolated from a variety of natural sources - human, animal, or microorganism - and may be produced by biotechnology methods and other cutting-edge technologies).

<sup>2</sup> See Media Release, Novartis AG, Sandoz Launches Zarxio™ (filgrastim-sndz), First Biosimilar in the United States (Sept. 3, 2015), <https://www.novartis.com/news/media-releases/sandoz-launches-zarxiotm-filgrastim-sndz-first-biosimilar-united-states>.

<sup>3</sup> See *FTC v. Actavis*, 133 S. Ct. 2223, 2229 (2013).

<sup>4</sup> Michael A. Carrier, *How Not to Apply Actavis*, 109 NW. U. L. REV. 113, 113 (2014).

<sup>5</sup> *Id.* at n.1. “Payments from brands to generics are often called ‘reverse payments’ because the payment flows from patentee to alleged infringer.” *Id.* Notice that unlike a typical patent litigation settlement, the accused infringer—the party normally on the hook for damages—instead receives payment from the injured party, the patentee.

<sup>6</sup> *Actavis*, 133 S. Ct. at 2229 (quoting *Schering-Plough Corp. v. F.T.C.*, 402 F.3d 1056, 1058 (11th Cir. 2005)). The rule of reason analysis requires a fact finder to “weigh all of the circumstances of a case in deciding whether a restrictive practice should be prohibited as imposing an unreasonable restraint on competition.” *Cont’l T.V., Inc. v. GTE Sylvania, Inc.*, 433 U.S. 36, 49 (1977).

<sup>7</sup> Pub. L. No. 98–417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. §§ 355, 360 (cc) (2000), 35 U.S.C. §§ 156, 271, 282 (2000)), as amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108–173, 117 Stat. 2066 (2003). The Hatch–Waxman Act is the name commonly used to refer to the Drug Price Competition and Patent Term Restoration Act. *Janssen Pharmaceutica, N.V. v. Apotex, Inc.*, 540 F.3d 1353, 1355 (Fed. Cir. 2008).

unanswered, is how the decision might apply to *generic-like* or *follow-on* biologic drugs<sup>8</sup> and their respective statutory scheme.<sup>9</sup>

By way of background, and to better understand the need for separate statutory schemes for the abbreviated approval of small molecule and biologic drugs, a look at the inherent differences between the two drug classes is necessary. The majority of pharmaceuticals are considered small-molecule drugs.<sup>10</sup> Small molecule drugs are very much what they sound like – low-weight inorganic compounds created from “standard chemicals and reagents.”<sup>11</sup> In contrast, biologics are high molecular weight compounds created through complicated production processes involving living cells.<sup>12</sup>

As biologic drugs are created in living organisms, there are greater difficulties in their production as compared to small molecule drugs.<sup>13</sup> The slightest variation in these living cells can affect the make-up of the drug molecule and can significantly impact the way in which the molecule interacts with its intended target in the human body.<sup>14</sup> Often, variability exists amongst living organisms.<sup>15</sup> The inherent variations between living organisms mean that no two manufacturers will have the same collection of cells by which the biologic is produced.<sup>16</sup> Therefore, *similar*, rather than identical, products will be created.<sup>17</sup> For this reason, follow-on biologics are commonly referred to as

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<sup>8</sup> See JUDITH A. JOHNSON, CONG. RESEARCH SERV., RL 41483, FDA REGULATION OF FOLLOW-ON BIOLOGICS 1 (2010) (*generic-like* versions of biologic drugs are referred to as “follow-on” biologics because they follow the brand-name version); see also JOHN R. THOMAS, CONG. RESEARCH SERV., RL 34045, FOLLOW-ON BIOLOGICS: THE LAW AND INTELLECTUAL PROPERTY ISSUES 1 (2014) (following this naming convention and explains the rationale behind the departure from the classifications “brand” and “generic” as used to describe small-molecule drugs).

<sup>9</sup> See Carrier, *supra* note 4, at 113 (“in ensuring a robust role for antitrust analysis . . . [the Actavis Court] articulated a blueprint for future analysis based on antitrust law’s ‘rule of reason.’ But the Court did not specify every step in the analysis or consider every type of settlement. Instead, it called on ‘lower courts . . . to structure . . . the present rule-of-reason antitrust litigation.’”).

<sup>10</sup> See generally PHARMACY PRACTICE NEWS & SPECIALTY PHARMACY CONTINUUM, SPECIAL REPORT: UNDERSTANDING KEY DIFFERENCES BETWEEN BIOSIMILARS AND SMALL MOLECULE GENERICS (May 2013), [http://www.pharmacypracticenews.com/download/sr1229\\_wm.pdf](http://www.pharmacypracticenews.com/download/sr1229_wm.pdf).

<sup>11</sup> Simon D. Roger, *Biosimilars: How Similar or Dissimilar Are They?*, 11 NEPHROLOGY 341, 341 (2006).

<sup>12</sup> *Id.* Biologics are complex protein products created in living organisms such as “plant and animal cells, bacteria, viruses, and yeasts.” *Id.* To create the biologic molecule, the DNA sequence of the desired protein product is transferred into an appropriate organism cell line and a “master cell bank” is derived. *Id.* at 342.

<sup>13</sup> See generally, *id.*

<sup>14</sup> *Id.* “Slight differences in a biologic or its in a manufacturing process may produce a biological drug with small but critical differences as compared to its reference product.” Kate S. Gaudry, *Exclusivity Strategies and Opportunities in View of the Biologics Price Competition and Innovation Act*, 66 FOOD & DRUG L. J. 587, 588-89 (2011). These slight differences may “even be difficult to detect” and may affect the product’s effectiveness, safety or potential for adverse effects. *Id.* at 589.

<sup>15</sup> Roger, *supra* note 11, at 342-43.

<sup>16</sup> *Id.* at 342.

<sup>17</sup> *Id.*

“biosimilars.”<sup>18</sup>

This characteristic of biologic drugs is significant because the Hatch-Waxman Act only allows for the approval of generic drugs demonstrating that the generic product contains the same active ingredient.<sup>19</sup> This showing is impossible to make when comparing follow-on biologics to the reference product.<sup>20</sup> For this reason, follow-on biologics require a different statutory pathway to allow for their abbreviated approval. After much deliberation, Congress addressed this issue and formally passed the Biologics Price Competition and Innovation Act (“BPCIA”).<sup>21</sup> The BPCIA was passed along with the Patient Protection and Affordable Care Act in 2010 and provides follow-on biologics with their own mechanism for abbreviated FDA approval.<sup>22</sup>

The uncertainty surrounding *Actavis*’ applicability to reverse payment settlements in the BPCIA context is largely founded upon the great extent to which the Court’s opinion focused on the Hatch-Waxman statutory scheme.<sup>23</sup> As the Court noted, “most if not all reverse payment settlement agreements arise in the context of . . . suits brought under statutory provisions allowing a generic drug manufacturer to challenge the validity of a patent owned by an already-approved brand-name drug owner.”<sup>24</sup> While this may be true, both the majority and dissenting opinions recognized that reverse payment settlements may occur outside of Hatch-Waxman litigation.<sup>25</sup>

This note is not intended to scrutinize the Supreme Court’s reasoning in *Actavis*, because, for better or for worse, the decision now serves as controlling authority for the lower courts when faced with reverse payment settlement. Rather, it argues that in following *Actavis*’ teachings, *Actavis*’ holding will extend to settlements occurring outside of Hatch-Waxman litigation and should apply to settlements arising from BPCIA litigation because both share the same propensity for anti-competitive harm. Part I will discuss the statutory scheme under the Hatch-Waxman Act, and outline the relevant provisions that incentivized reverse payment settlements. Part II will discuss, in relevant part, the statutory scheme under the BPCIA as it relates to follow-on biologics. Part III will provide a brief overview of the lower courts handling of reverse payment settlements leading up to *Actavis*, the *Actavis* decision itself, and a brief survey of relevant post-*Actavis* developments. Lastly, part IV will show how under certain circumstances the BPCIA may be susceptible to reverse payment settlements and that

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<sup>18</sup> JOHNSON, *supra* note 8, at 1.

<sup>19</sup> See 21 U.S.C. § 355(j)(2)(A); 21 U.S.C. § 355(j)(8).

<sup>20</sup> See Gaudry, *supra* note 14, at 589; see also Huub Schellekens, *How Similar do ‘Biosimilars’ Need to Be?*, 22 NAT. BIOTECHNOLOGY 1357, 1358-59 (2004).

<sup>21</sup> The Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119, §§7001 – 7003 (2010).

<sup>22</sup> *Id.*

<sup>23</sup> See *FTC v. Actavis*, 133 S. Ct. 2223, 2227-30 (2013) (describing “four key features” of the Hatch-Waxman Act that creates incentives for parties to enter into reverse payment settlements).

<sup>24</sup> *Id.* at 2227-28 (internal parentheticals omitted).

<sup>25</sup> *Id.* at 2227 & 2242-43 (Roberts, J., dissenting).

these settlements have the potential to work the type of unjustified anticompetitive harm addressed in *Actavis*.

## II. THE HATCH-WAXMAN ACT

As the Supreme Court's reasoning in *Actavis* relied on the Hatch-Waxman's statutory scheme, a brief overview of the act's pertinent provisions is helpful. The Hatch-Waxman Act's statutory scheme encourages manufacturers to create generic versions of already-approved small-molecule drugs by providing for an expedited approval process, known as the Abbreviated New Drug Application (ANDA).<sup>26</sup> Unlike a full New Drug Application (NDA), under the Hatch-Waxman Act, "[g]eneric drug companies are not required to conduct their own independent clinical trials to prove safety and efficacy, but can instead rely on the research of the [brand-name] pharmaceutical companies."<sup>27</sup> This allows the generic manufacturer to bypass the costly and time-consuming clinical trials<sup>28</sup> by only requiring a showing that the generic drug contains the same active ingredient and is bioequivalent<sup>29</sup> to the brand-name product.<sup>30</sup>

Generally, all new drugs containing chemical entities never previously approved by the FDA (either alone or in combination) are granted a five-year period of exclusivity in which no ANDA may be submitted.<sup>31</sup> This exclusivity provision does not prevent other manufacturers from marketing a duplicate version of the same drug product so long as the duplicate version is the subject of a NDA containing a full set of safety and efficacy data.<sup>32</sup> Essentially, these provisions provide for a period of data exclusivity. Despite the Hatch-Waxman Act's limited protection for brand-name products, even if a competitor filed their own NDA, they would likely run head-first into the drug's patent.

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<sup>26</sup> *Id.* at 2228; Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified at 21 U.S.C. §§ 355, 360(cc) (2000), 35 U.S.C. §§ 156, 271, 282 (2000)), as amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003).

<sup>27</sup> *Janssen Pharmaceutica, N.V. v. Apotex, Inc.*, 540 F.3d 1353, 1356 (Fed. Cir. 2008) (citing 21 U.S.C. § 355(j)(2)(A)(iv), (j)(8)(B)).

<sup>28</sup> The average total clinical trial cost for a drug in development (phase I through phase IV clinical studies) is nearly \$60 million. AYLIN SERTKAYA ET AL., U.S. DEPT. OF HEALTH & HUM. SERV., EXAMINATION OF CLINICAL TRIAL COSTS AND BARRIERS FOR DRUG DEVELOPMENT § 3.2 (2014), <https://aspe.hhs.gov/report/examination-clinical-trial-costs-and-barriers-drug-development>.

<sup>29</sup> Bioequivalence is found when the rate and extent of the generic drugs absorption into the human body is not significantly different from that of the branded or reference product. *See* 21 C.F.R. § 320.23(a)(1).

<sup>30</sup> 21 U.S.C. § 355(j)(2)(A), (j)(8).

<sup>31</sup> *Small Business Assistance: Frequently Asked Questions for New Drug Product Exclusivity*, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069962.htm> (last visited Mar. 6, 2017). Additionally, a drug product containing a previously approved active ingredient may be granted a three-year period of exclusivity for changes in the approved drug product that affect the "active ingredient(s), strength, dosage form, route of administration or conditions of use." *Id.*

<sup>32</sup> *Id.* As an exception to this provision, an ANDA containing a paragraph IV certification (described in detail below) may be submitted after four years. *Id.*

Small-molecule drugs are typically protected by a small number of patents, and some drugs even rely on a single patent for protection.<sup>33</sup> “Any single pharmaceutical patent is . . . likely to cover most (if not all) aspects of a drug product, and therefore c[an] be used to exclude all competitors from the market for that product.”<sup>34</sup> Therefore, pharmaceutical patents often provide brand-name manufacturers with an effective monopoly.<sup>35</sup>

The Hatch-Waxman Act also provides mechanisms to facilitate patent litigation between brand-manufacturers and generic manufacturers. The act requires brand-manufacturers to list all patent numbers and expiration dates in its NDA and requires generic manufacturers, in their ANDA, to “assure the FDA that the generic will not infringe the brand-name’s patents.”<sup>36</sup> Generic manufacturers can provide this assurance in one of four ways. It can: (1) certify that the brand-manufacturer has not listed any relevant patents; (2) certify that any relevant patents have expired; (3) request approval to market beginning when any still-in-force patents expire; or (4) certify that any listed, relevant patent “is invalid or will not be infringed by the manufacture, use, or sale” of the generic drug.<sup>37</sup>

The fourth option is often referred to as the “paragraph IV” route, and the mere act of making such a certification constitutes patent infringement often triggering litigation.<sup>38</sup> If the brand-name manufacturer brings a patent infringement suit within forty-five days after receiving the required paragraph IV notice from the generic manufacturer, the Hatch-Waxman Act provides for a thirty-month stay period in which the FDA may not approve the generic drug.<sup>39</sup> The Hatch-Waxman Act provides an incentive for generic manufacturers to go the paragraph IV route, encouraging the challenging of weak patents.<sup>40</sup> The first successful paragraph IV challenger is rewarded with a 180-day period of exclusivity in which no other generic manufactures may enter the market.<sup>41</sup> This is an enticing and sizeable reward because this period is where the

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<sup>33</sup> Lauren Krickl & Matthew Avery, *Roberts was Wrong: Increased Antitrust Scrutiny After FTC v. Actavis has Accelerated Generic Competition*, 19 VA. J. L. & TECH. 509, 521 (2015), <http://www.american.com/archive/2008/January-february-magazine-contents/patents-pending> (noting that a small number of patents can provide the foundation for years of research and development in the pharmaceutical industry).

<sup>34</sup> *Id.* at 522.

<sup>35</sup> *Id.*

<sup>36</sup> *Actavis*, 133 S. Ct. 2223 at 2228.

<sup>37</sup> *Id.*

<sup>38</sup> *Id.* at 2228; *see also* 21 U.S.C. § 355(c)(3)(C).

<sup>39</sup> U.S. FEDERAL TRADE COMMISSION, AUTHORIZED GENERIC DRUGS: SHORT-TERM EFFECTS AND LONG-TERM IMPACT 3 (2011). The stay period provides that the FDA may not approve the generic drug until the earlier of: (1) thirty months from the date that the required paragraph IV notice is provided to the brand-manufacturer; or (2) a decision is rendered finding the patent invalid or not infringed. *Id.*

<sup>40</sup> *See* MICHAEL A. CARRIER, INNOVATION FOR THE 21<sup>ST</sup> CENTURY: HARNESSING THE POWER OF INTELLECTUAL PROPERTY AND ANTITRUST LAW 347 (2009) (explaining that one of the goals of the Hatch-Waxman Act was to provide incentives for generics to challenge brand-name patents).

<sup>41</sup> *Actavis*, 133 S. Ct. 2223, at 2228.

“vast majority of profits for a generic drug manufacturer materialize,”<sup>42</sup> and is often “worth several hundred million dollars.”<sup>43</sup> This period of exclusivity offers the largest amount of profits because the only competition during this period is with the brand-name drug, and potentially an authorized generic product produced by the brand-manufacturer.<sup>44</sup> The large profits in this 180-day period are due to the rapid shift from the brand-name drug to the generic drug.<sup>45</sup> This shift largely occurs because the majority of states allow pharmacists to automatically substitute the generic for the brand-name drug without consulting with the prescribing physician.<sup>46</sup> Additionally, third-party payers (or, health insurers) often drive substitution through their formulary and copayment structure.<sup>47</sup> Typically, after the period of exclusivity expires, several generic manufacturers enter the market significantly reducing the profits of the first generic manufacture through an increase in competition.

The interplay between the 180-day exclusivity period for paragraph IV challengers and the thirty-month stay of FDA approval creates an incentive for brand and generic manufacturers to enter into reverse-payment settlement agreements. As the Supreme Court described, under the Hatch-Waxman Act “only the first [paragraph IV] challenger gains the special advantage of 180 days of an exclusive right to sell a generic version of the brand-name product,” therefore, “the patentee’s payment to the initial challenger (in return for not pressing the patent challenge) will not necessarily provoke subsequent challenges.”<sup>48</sup> Further, even if the first paragraph IV filer is sued by the brand-manufacturer and subsequently settles their law suit, the second filer must wait out the thirty-month stay before the FDA can approve its application.<sup>49</sup> All Hatch-Waxman settlements, including reverse payment settlements, are required by the Medicare Modernization Act of 2003 (MMA) section 1112(a) to be reported to FTC.<sup>50</sup>

### III. THE BILOGICS PRICE COMPETITION AND INNOVATION ACT

Although the *Actavis* Court relied on the regulatory and statutory framework of the Hatch-Waxman Act in its decision, the Court recognized that reverse-payment

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<sup>42</sup> *Id.*

<sup>43</sup> C. Scott Hemphill, *Paying for Delay: Pharmaceutical Patent Settlement as a Regulatory Design Problem*, 81 N.Y.U. L. REV. 1553, 1579 (2006).

<sup>44</sup> The 180-day period of market exclusivity does not preclude competition from an authorized generic (“AG”). AUTHORIZED GENERIC DRUGS: SHORT-TERM EFFECTS AND LONG-TERM IMPACT, *supra* note 39, at 3. AGs are pharmaceutical products approved as brand-name drugs but marketed as generic drugs that are manufactured to the brand’s specifications but do not bear the trademark or brand-name. *Id.* at i.

<sup>45</sup> See Mr. Faden, *Patent Expirations Produce Top-selling Generic Drugs* (Aug. 1, 2006), <http://www.pharmacytimes.com/publications/issue/2006/2006-08/2006-08-5763>.

<sup>46</sup> *Id.*

<sup>47</sup> *Id.*

<sup>48</sup> *Actavis*, 133 S. Ct. 2223 at 2235.

<sup>49</sup> *Id.*

<sup>50</sup> Pub. L. No. 108-173, 117 Stat. 2066 (2003).

settlements may occur in other contexts.<sup>51</sup> Before applying *Actavis*' teachings to BPCIA settlements, a brief overview of the act is required. The BPCIA creates an abbreviated regulatory pathway for the approval of follow-on biologic drugs by allowing applicants to reply on the brand name or reference products clinical safety and efficacy data.<sup>52</sup>

Follow-on biologic applications are referred to as an abbreviated Biologics License Application ("aBLA").<sup>53</sup> Unlike the ANDA requirements under the Hatch-Waxman Act, which only require generic manufacturers to demonstrate that their product contains the same active ingredient as the brand-name drug,<sup>54</sup> aBLA applicants are required to conduct independent clinical studies demonstrating the safety and efficacy of their product.<sup>55</sup> Generally, under the BPCIA, aBLAs may be filed for two types of follow-on biologic products—biosimilars and interchangeable biologics.<sup>56</sup> Biosimilars are products that are highly similar to the already approved reference biologic.<sup>57</sup> In addition to meeting the same standards as biosimilar products, interchangeable biologics must also produce the same clinical results in patients as the reference product.<sup>58</sup>

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<sup>51</sup> *Id.* at 2227; *id.* at 2242-43 (Roberts, J. dissent).

<sup>52</sup> Pub. L. No. 111-148, §§ 7001-7003, 124 Stat. 119, 804-21 (2010) (codified as amended at 42 U.S.C. § 262, 35 U.S.C. § 271(e), 28 U.S.C. § 2201(b), 21 U.S.C. § 355 et seq.). Under the abbreviated regulatory pathway, an applicant is permitted to submit data demonstrating that its product is "highly similar" to a previously approved reference product together with "publicly-available information regarding the [FDA]'s previous determination that the reference product is safe, pure, and potent." 42 U.S.C. § 262(k)(2)-(5). Therefore, the BPCIA essentially permits a biosimilar applicant to rely in part on the approved reference product's application.

<sup>53</sup> *See* *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347, 1351 (Fed. Cir. 2015), *cert. granted*, No. 15-1039, 2017 WL 125661 (U.S. Jan. 13, 2017), and *cert. granted*, No. 15-1195, 2017 WL 125662 (U.S. Jan. 13, 2017) (Biologics applications filed pursuant to the BPCIA's abbreviated pathway, codified at 42 U.S.C. § 262(k), are referred to as "abbreviated biologics license applications" or "subsection (k) applications.").

<sup>54</sup> Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. 98-417, 98 Stat. 1585 (1984). *See also* 21 U.S.C. § 355(j)(2)(A); 21 U.S.C. § 355(j)(8).

<sup>55</sup> The FDA requires (1) "analytical studies demonstrating that the biological product is 'highly similar' to the reference product notwithstanding minor differences in clinically inactive components;" (2) "animal studies (including the assessment of toxicity);" and (3) "[a] clinical study or studies (including the assessment of immunogenicity and pharmacokinetics (PK) or pharmacodynamics (PD)) sufficient to demonstrate safety, purity, and potency in 1 or more appropriate conditions of use for which the reference product is licensed." *See Information for Industry (Biosimilar)*, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm241720.htm> (last updated May 10, 2016) [hereinafter FDA, *Info for Industry*].

<sup>56</sup> *See* 42 U.S.C. § 262(k); 42 U.S.C. § 262(n).

<sup>57</sup> 42 U.S.C. § 262(i)(2) (effective Jan. 7, 2011); *see Information for Consumers (Biosimilar)*, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm241718.htm> (last updated Aug 27, 2015) [hereinafter FDA, *Info for Consumers*] (A biosimilar product has "been shown to have no clinically meaningful differences from the reference product").

<sup>58</sup> 42 U.S.C. § 262(k)(4) (effective Jan. 7, 2011); *see* FDA, *Info for Consumers*, *supra* note 57.



Unlike the Hatch-Waxman Act, the BPCIA awards new biologic drugs not only with a period of data exclusivity, but also a period of market exclusivity.<sup>59</sup> The data exclusivity period prevents a follow-on biologic applicant from relying on the reference products clinical studies for four years from the FDA's approval of the reference product.<sup>60</sup> The market exclusivity period runs concurrently and lasts for twelve years from the date of FDA approval.<sup>61</sup> Accordingly, a follow-on biologic manufacturer may file an aBLA relying on the reference products clinical data after four years from the approval of the reference product, however, the application may not be approved until twelve years from the date of the reference product's licensing. In essence, these provisions could amount to a substitute for a patent regardless of whether the biologic is patent eligible.

An important distinction between generic drugs under the Hatch-Waxman Act and follow-on biologics under the BPCIA, is that, unlike generic drugs, follow-on biologics will not automatically be deemed interchangeable with the reference product. In order for a follow-on biologic drug to be considered interchangeable, it must file for interchangeable status in its aBLA.<sup>62</sup> Manufacturers wishing to do so must file along with their BLA, "information demonstrating biosimilarity, and include information to show that the proposed interchangeable product is expected to produce the same clinical result as the reference product in any given patient."<sup>63</sup>

This additional information requires more clinical trial data, and therefore manufacturers will have to invest greater amounts of resources to achieve interchangeable status. This is a significantly higher hurdle to jump than simply filing as a biosimilar product. Even after a manufacturer conducts the additional clinical trials in an attempt to gain interchangeable status, the FDA may still reject the application if it is not satisfied with the results.

The BPCIA however, provides an incentive to manufacturers who take on this greater risk and investment. The first follow-on biologic to be awarded interchangeable status is provided a one-year period of market exclusivity in which no other follow-on biologic may be deemed interchangeable.<sup>64</sup> It is important to distinguish between the

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<sup>59</sup> See *Background Information: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations (Purple Book)*, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TheTherapeuticBiologicApplications/Biosimilars/ucm411424.htm> (last updated Mar. 5, 2015); see also U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY REFERENCE PRODUCT EXCLUSIVITY FOR BIOLOGICAL PRODUCTS FILED UNDER SECTION 351(A) OF THE PHS ACT 2 (2014).

<sup>60</sup> 42 U.S.C. § 262(k)(7)(B).

<sup>61</sup> 42 U.S.C. § 262(k)(7)(A).

<sup>62</sup> 42 U.S.C. § 262(k)(4) (effective Jan. 7, 2011).

<sup>63</sup> FDA, *Info for Industry*, *supra* note 55. Additionally, if the biologic drug is administered "more than once to an individual," the application must include "information to demonstrate that the risk in terms of safety or diminished efficacy of alternating or switching between use of the proposed interchangeable product and the reference product is not greater than the risk of using the reference product without such alternating or switching." *Id.*

<sup>64</sup> 42 U.S.C. § 262(k)(6) (effective Jan. 7, 2011).

period of exclusivity afforded to interchangeable follow-on biologics and that afforded to the first successful paragraph IV challenger under the Hatch-Waxman Act. Unlike the Hatch-Waxman Act's 180-day period of exclusivity, the BPCIA provides no complete period of exclusivity for a follow-on biologic. The period of exclusivity under the BPCIA only relates to the interchangeable status itself.<sup>65</sup> Therefore, the FDA may approve a follow-on biologic as interchangeable irrespective of whether other biosimilars for the same reference product are already on the market. Additionally, the approval of an interchangeable follow-on biologic does not preclude the FDA from approving other follow-on biologics as biosimilar during the one-year period of exclusivity.

The BPCIA and the Hatch-Waxman Act also differ with respect to their patent provisions. Unlike the Hatch-Waxman Act, which requires brand-name manufacturers to list their relevant patents in an official compendium, the BPCIA has no comparable provision.<sup>66</sup> Rather, section 351(l) of the BPCIA provides a mechanism for the brand-manufacturer and the follow-on biologic manufacturer to exchange information relating to any relevant patents.<sup>67</sup> This exchange has come to be known as the "patent dance."<sup>68</sup> Similar to filing of an ANDA application, when a follow-on biologic manufacturer files an aBLA, it constitutes an act of patent infringement likely triggering litigation.<sup>69</sup>

Unlike the Hatch-Waxman settlements, which are required to be reported to FTC under the MMA, BPCIA settlements do not have the same requirement.<sup>70</sup> BPCIA settlements however, are unlikely to slip past the FTC's watchful eye. This is because the institution of infringement litigation involving biologics is required to be reported to the FDA, which then publishes notice in the Federal Register.<sup>71</sup>

#### IV. REVERSE PAYMENT SETTLEMENTS AND FTC V. ACTAVIS

This section first outlines the conditions that developed over the course of the decade prior to the *Actavis* decision. It then analyzes the Supreme Courts reasoning in *Actavis*, followed by a discussion of the relevant post-*Actavis* developments.

##### A. Reverse Payment Settlements Prior to *Actavis*

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<sup>65</sup> 42 U.S.C. § 262(k)(6)(A).

<sup>66</sup> The Patient Protection and Affordable Care Act, Pub. L. No. 111-148, Stat. 119, §§7001 – 7003 (2010).

<sup>67</sup> See generally 42 U.S.C. § 262(l).

<sup>68</sup> Carl J. Minniti III, *Biosimilar Litigation: The Tussle Over How to Resolve Biologic Patents*, 2015 A.B.A. SCITECH LAW. 16, 17.

<sup>69</sup> See generally 42 U.S.C. § 262(l).

<sup>70</sup> The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066. *c.f.*, The Patient Protection and Affordable Care Act, Pub. L. No. 111-148, Stat. 119, §§7001 – 7003 (2010).

<sup>71</sup> Darren S. Tucker & Gregory F. Wells, *Emerging Competition Issues Involving Follow-on Biologics*, 2014 A.B.A. ANTITRUST 100, 101.

Prior to *Actavis*, the lower courts had a history of allowing reverse payment settlements in ANDA litigation.<sup>72</sup> In the decade immediately preceding *Actavis*, “nearly all the appellate courts that had examined [reverse] payment settlements concluded that they did not present antitrust concern because they fell within the exclusory scope of the patent.”<sup>73</sup> These courts “relied on the mere existence of a patent—even one that was invalid or not infringed—to justify any payment.”<sup>74</sup> By 2012, despite the Federal, Second, and Eleventh Circuits’ upholding of these agreements,<sup>75</sup> the “Supreme Court show[ed] no interest in wading into the area.”<sup>76</sup> In July of 2012 however, the Third Circuit strayed from its sister circuit’s reasoning and found that reverse payment settlements are “prima facie evidence of an unreasonable restraint of trade.”<sup>77</sup> Additionally, although the Sixth and D.C. Circuits did not explicitly accept or reject the legality of reverse payment settlements, they recognized the potential anticompetitive effects of the arrangements.<sup>78</sup>

In December of 2012, the Court granted the petition for writ of certiorari in *FTC v. Watson Pharmaceuticals*, a case on appeal from the Eleventh Circuit, and finally agreed to address the issue and resolve the circuit split.<sup>79</sup> In this case, the FTC filed suit alleging that the defendant generic drug manufacturers violated section five of the Federal Trade Commission Act by entering into reverse payment settlement agreements.<sup>80</sup> The District Court dismissed the complaint.<sup>81</sup> On appeal, the Eleventh Circuit affirmed the dismissal of the complaint reasoning that as long as the agreements anticompetitive effects fall within the scope of the patent’s exclusory potential, the

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<sup>72</sup> Carrier, *supra* note 4, at 114 (citing *In re Ciprofloxacin Hydrochloride Antitrust Litig.*, 544 F.3d 1323, 1336 (Fed. Cir. 2008); *In re Tamoxifen Citrate Antitrust Litig.*, 466 F.3d 187, 213 (2d Cir. 2006); *Schering-Plough Corp. v. FTC*, 402 F.3d 1056, 1072 (11th Cir. 2005)).

<sup>73</sup> *Id.* Generally, the “scope of the patent” test immunized reverse payment settlements from antitrust attack so long as the anticipative effects of the agreement fall within the exclusory potential of the patent. *Actavis*, 133 S. Ct. 2223, 2230.

<sup>74</sup> Carrier, *supra* note 4, at 114. “The courts only carved out exceptions for fraud before the Patent Office or sham litigation.” *Id.* at 114 n.9 (citing *In re Ciprofloxacin Hydrochloride Antitrust Litig.*, 544 F.3d 1323, 1336 (Fed. Cir. 2008); *FTC v. Watson Pharms., Inc.*, 677 F.3d 1298, 1312 (11th Cir. 2012)).

<sup>75</sup> Carrier, *supra* note 4, at 114.

<sup>76</sup> Michael A Carrier, *Reverse Payment Home Run for Pharma Antitrust Enforcement*, IPWATCHDOG (July 16, 2012), <http://www.ipwatchdog.com/2012/07/16/reverse-payment-home-run-for-pharma-antitrust-enforcement/id=26491>; see also *In re Tamoxifen Citrate Antitrust Litig.*, 466 F.3d 187 (2d Cir. 2006); *Schering- Plough Corp. v. FTC*, 402 F.3d 1056 (11th Cir. 2005).

<sup>77</sup> *In re K-Dur Antitrust Litig.*, 686 F.3d 197, 218 (3d Cir. 2012), *vacated by* *Merck & Co. v. Louisiana Wholesale Drug Co.*, 133 S. Ct. 2849 (2013), *vacated by* *Upsher-Smith Labs., Inc. v. Louisiana Wholesale Drug Co.*, 133 S. Ct. 2849 (2013) and reinstatement granted, No. 10-2077, 2013 WL 5180857 (3d Cir. Sept. 9, 2013). “As a practical matter, the scope of the patent test does not subject reverse payment agreements to any antitrust scrutiny.” *Id.*

<sup>78</sup> Sheila Lynch-Afryl, *Supreme Court Agrees to Hear “Pay for Delay” Cases on Generic Drugs* (Dec. 10, 2012), [http://www.dailyreportingsuite.com/health/news/supreme\\_court\\_agrees\\_to\\_hear\\_pay\\_for\\_delay\\_cases\\_on\\_generic\\_drugs](http://www.dailyreportingsuite.com/health/news/supreme_court_agrees_to_hear_pay_for_delay_cases_on_generic_drugs).

<sup>79</sup> *Id.*; *FTC v. Watson Pharmaceuticals, Inc.*, 677 F.3d 1298 (2012).

<sup>80</sup> *Actavis*, 133 S. Ct. at 2227, 2230.

<sup>81</sup> *Id.* at 2230.

settlement is immune from antitrust attack.<sup>82</sup> The court also reasoned that because of the public policy favoring settlements, courts could not require the parties to continue to litigate in order to avoid antitrust liability. The Supreme Court's grant of certiorari attracted significant attention and thirty-one states filed amicus briefs with the Supreme Court supporting the FTC's position on the issue.<sup>83</sup>

## B. The *Actavis* Decision

In *Actavis*, the Supreme Court finally resolved the circuit split, and found that reverse payment settlements carry with them “the risk of significant anticompetitive effects.”<sup>84</sup> The Court held that reverse payment settlements, “where large and unjustified”, should not be shielded from antitrust attack simply because the agreement falls within the exclusory scope of a patent.<sup>85</sup> In doing so, the Court rejected the FTC's position that these arrangements should be deemed presumptively unlawful and analyzed under antitrust law's truncated “quick look” rule.<sup>86</sup> Rather, the Court held that these arrangements should be reviewed under the rule of reason.<sup>87</sup> The Court's conclusion was supported by five considerations, which when taken together support a finding that these types of agreements should be subjected to antitrust scrutiny via the rule of reason.<sup>88</sup>

For the Court's first consideration, it stated that reverse payment settlements have the “potential for genuine adverse effects on competition.”<sup>89</sup> The Court reasoned that a reverse payment settlement amounted to a “purchase by the patentee of the exclusive right to sell its product, a right it already claims but would lose if the patent litigation were to continue and the patent were held invalid or not infringed by the generic product.”<sup>90</sup> Through the use of these settlements agreements, the brand-manufacturer is able to entice a generic manufacturer to stay out of the market, keeping the drug at the patentee-set price, in return for splitting the monopoly generated profits.<sup>91</sup> In doing so, “[t]he patentee and the challenger gain; the consumer loses.”<sup>92</sup>

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<sup>82</sup> *Id.*

<sup>83</sup> *Id.*

<sup>84</sup> *Id.* at 2237.

<sup>85</sup> *Id.* at 2227.

<sup>86</sup> *Actavis*, 133 S. Ct. at 2237-38.

<sup>87</sup> *Id.*

<sup>88</sup> *Id.* at 2234-37.

<sup>89</sup> *Id.* at 2234 (citing *Cal. Dental Ass'n. v. Fed. Trade Comm'n.*, 526 U.S. 756, 768-87 (1999)).

<sup>90</sup> *Id.* at 2235.

<sup>91</sup> *Actavis*, 133 S. Ct. at 2334. By way of example, “Suppose . . . that the exclusive right to sell [the drug] produces \$50 million in supracompetitive profits per year for the patentee . . . [and] that the patent has 10 more years to run.” *Id.* If litigation results in patent invalidation or a finding of non-infringement, the patentee would stand to lose \$500 million in revenues, “a sum that then would flow in large part to consumers in the form of lower prices.” *Id.* A payment from the brand-manufacturer to the generic manufacture in exchange for staying out of the market allows prices to remain at the patentee-set monopoly price, potentially generating the full \$500 million dollars while dividing the proceeds amongst the two parties. *Id.*

The Court explained that this type of practice was made possible by the Hatch-Waxman Act's statutory scheme. While one would imagine that a large reverse payment might signal to other generic competitors that the brand-name patent is weak, therefore enticing others to challenge the patent, this is not the case. The Hatch-Waxman Act only affords the first paragraph IV challenger the valuable 180-day period of exclusivity.<sup>93</sup> Therefore, a settlement with the first challenger significantly reduces the incentives for subsequent challengers because it takes the 180-day period of exclusivity off the table.<sup>94</sup> If a subsequent challenger were to successfully challenge the brand-name patent, its investment in litigating the patents validity "will free not just the challenger to compete, but all other potential competitors too."<sup>95</sup> Even if a subsequent challenger wanted to enter the market, it would still have to wait out the thirty-month stay period before the FDA could approve its application.<sup>96</sup> Therefore, these two provisions taken together "removes from consideration the most motivated challenger, and the one closest to introducing completion."<sup>97</sup>

The second consideration was that the "anticompetitive consequences [resulting from the reverse payment settlement] will at least sometimes prove unjustified."<sup>98</sup> The Court acknowledged that the payments may sometimes "amount to no more than a rough approximation of the litigation expenses" or a payment for other services performed by the generic manufacturer.<sup>99</sup> However, that possibility failed to justify the dismissal of the FTC's complaint because, without inquiry it is difficult to determine whether the reverse payment settlement is justified under antitrust law. Accordingly, the antitrust defendant in an antitrust proceeding has the opportunity to demonstrate that the agreement is lawful under the rule of reason.<sup>100</sup>

The third consideration was that, "where a reverse payment threatens to work unjustified anticompetitive harm, the patentee [brand-manufacturer] likely possesses the power to bring that harm about in practice."<sup>101</sup> Essentially, the Court recognized that a large payment itself might be a strong indicator of the power to charge higher than competitive prices. In turn, this ability to make large payments to keep competitors off the market may be a "strong indication of market power."<sup>102</sup>

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<sup>92</sup> *Id.*

<sup>93</sup> *Actavis*, 133 S. Ct. at 2235.

<sup>94</sup> *Id.*

<sup>95</sup> *Id.*

<sup>96</sup> *Id.* (citing *California Dental Ass'n. v. FTC*, 526 U.S. 756, 786-87 (1999)).

<sup>97</sup> *Id.* (citations and quotations omitted).

<sup>98</sup> *Id.* at 2236 (citations omitted).

<sup>99</sup> *Actavis*, 133 S. Ct. at 2236. Examples of other services may include distribution of the patented drug or helping to develop the products market.

<sup>100</sup> *Id.* (citations omitted).

<sup>101</sup> *Id.* (citations omitted).

<sup>102</sup> *Id.*

The fourth consideration specifically addressed the Eleventh Circuit’s concern that allowing antitrust scrutiny of these settlements would require the parties to litigate the underlying patent dispute to determine patent validity.<sup>103</sup> The Court however reasoned that it would not be necessary to litigate patent validity to answer the antitrust question because a large unexplained reverse payment could provide a “workable surrogate for a patent’s weakness” and “suggest that the patentee has serious doubts about the patent’s survival.”<sup>104</sup>

For the Fifth and final consideration, the court stated “the fact that a large, unjustified reverse payment risks antitrust liability does not prevent litigating parties from settling their lawsuit.”<sup>105</sup> In short, pharmaceutical patent litigation maybe settled in other ways that do not implicate antitrust concerns. For example, the agreement could allow for the generic market entry prior to the patent’s expiration.<sup>106</sup> The Court stated that while “parties may have reasons to prefer . . . reverse payments, the relevant antitrust question is: What are those reasons?”<sup>107</sup> If the only reason is the desire to maintain monopoly pricing and share in those profits, then antitrust laws likely prohibit the arrangement.<sup>108</sup>

Taking these five considerations together, the Court reasoned that they justify applying antitrust scrutiny to reverse payment settlements and therefore should be analyzed under the rule of reason.<sup>109</sup>

### C. Reverse Payment Settlements Post-*Actavis*

Plaintiffs champing at the *Actavis*-bit, have hit the ground running filing antitrust lawsuits in what is sure to be the backstretch on a long course towards antitrust scrutiny.<sup>110</sup> While the Court’s decision was aimed at “ensur[ing] a robust role

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<sup>103</sup> *Id.*

<sup>104</sup> *Id.* at 2236-37

(An unexplained large reverse payment itself would normally suggest that the patentee has serious doubts about the patent’s survival. And that fact, in turn, suggests that the payment’s objective is to maintain supracompetitive prices to be shared among the patentee and the challenger rather than face what might have been a competitive market—the very anticompetitive consequence that underlies the claim of antitrust unlawfulness).

<sup>105</sup> *Actavis*, 133 S. Ct. at 2237.

<sup>106</sup> *Id.*

<sup>107</sup> *Id.* at 2237.

<sup>108</sup> *Id.* at 2237.

<sup>109</sup> *Id.* at 2237-38.

<sup>110</sup> Post-*Actavis* reverse payment settlement cases collected as of as of March 15, 2016. *See generally* *In re Loestrin 24 Fe Antitrust Litig.*, No. 14-2071, 2016 WL 698077 (1st Cir. Feb. 22, 2016); *In re Loestrin 24 Fe Antitrust Litig.*, No. 1:13-md-2472-S-PAS, 2014 WL 4368924 (D.R.I. Sept. 4, 2014); *In re Solodyn (Minocycline Hydrochloride) Antitrust Litig.*, No. 14-mn-02503, 2015 WL 5458570 (D. Mass. Sept. 16, 2015); *In re Solodyn (Minocycline Hydrochloride) Antitrust Litig.*, No. 14-mn-02503, 2015 WL 5458570 (D. Mass. Sept. 16, 2015); *In re ACTOS End Payor Antitrust Litig.*, No. 1:13-cv-09244, 2015 WL 5610752 (S.D.N.Y. Sept. 22, 2015); *King Drug Co. of Florence, Inc. v. Smithkline Beecham Corp.*, No. 14-1243, 2015

for antitrust analysis” by “articulat[ing] a blueprint for future analysis based on antitrust law’s ‘rule of reason,’”<sup>111</sup> the first courts to tackle reverse payment settlement cases post-*Actavis* veered slightly off course. Specifically, the five *Actavis* considerations appeared to have become a red herring of sorts.<sup>112</sup> These courts interpreted the five considerations to be a modified restatement of the rule of reason.<sup>113</sup>

Only two Appellate courts since *Actavis* have confronted the issue of reverse payment settlements and both of these courts reversed lower court decisions that used the five considerations as a rule of reason analysis.<sup>114</sup> These courts found that the Supreme Court did not intend for the considerations to supplant the “rule-of-reason” analysis.<sup>115</sup> Rather, the *Actavis* Court provided these five considerations merely as justification for concluding that the reverse payment settlements at issue should no longer be afforded blanket antitrust immunity and should be subject to the rule of reason.<sup>116</sup>

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WL 3967112 (3d Cir. June 26, 2015); *In re Effexor XR Antitrust Litig.*, No. 11-5479 (PGS)(LHG), 2014 WL 4988410 (D.N.J. Oct. 6, 2014); *In re Lipitor Antitrust Litig.*, No. 3:12-cv-02389 (PGS), 2014 WL 4543502 (D.N.J. Sept. 12, 2014); *In re Lamictal Direct Purchaser Antitrust Litig.*, No. 12-cv-995 (WHW), 2014 WL 282755 (D.N.J. Jan. 24, 2014); *In re Lipitor Antitrust Litig.*, No. 3:12-cv-2389 (PGS), 2013 WL 4780496 (D.N.J. Sept. 5, 2013); *King Drug Co. of Florence, Inc. v. Cephalon, Inc.*, No. 2:06-cv-01797 (E.D. Pa. Dec. 14, 2015); *In re Wellbutrin XL Antitrust Litigation*, No. 2:08-cv-02431, 2015 WL 5582289 (E.D. Pa. Sept. 23, 2015); *FTC v. AbbVie, Inc.*, No. 14-5151, 2015 WL 2114380 (E.D. Pa. May 6, 2015), motion to reconsider denied in *FTC v. AbbVie, Inc.*, 2015 WL 5025438, No. 14-5151 (E.D. Pa. Aug. 25, 2015); *FTC v. Cephalon Inc.*, No. 2:08-cv-2141 (E.D. Pa. Jan. 27, 2015); *Time Ins. Co. v. AstraZeneca*, No. 2014 WL 4933025 (E.D. Pa. Oct. 1, 2014); *In re Niaspan Antitrust Litig.*, No. 13-MD-2460, 2014 WL 4403848 (E.D. Pa. Sept. 5, 2014); *United Food and Commercial Workers Local 1776 v. Teikoku Pharma USA, Inc.*, No. 14-md-02521-WHO (N.D. Cal. Nov. 17, 2014).

<sup>111</sup> Carrier, *supra* note 4, at 114. “The Lamictal and Loestrin courts purported to apply an analysis based on the rule of reason. But they diverged from the Supreme Court in centering their analysis on five factors discussed in *Actavis*.” *Id.* at 115. See generally *In re Loestrin 24 Fe Antitrust Litig.*, 45 F. Supp. 3d 180 (D.R.I. 2014); *In re Lamictal Direct Purchaser Antitrust Litig.*, 18 F. Supp. 3d 560 (D.N.J. 2014) vacated and remanded sub nom. *King Drug Co. of Florence v. SmithKline Beecham Corp.*, 791 F.3d 388 (3d Cir. 2015).

<sup>112</sup> The court in, *In re Lamictal Direct Purchaser Antitrust Litigation*, “used the five factors that the *Actavis* Court had employed to justify more aggressive antitrust scrutiny to instead excuse its decision to employ less vigorous scrutiny.” Carrier, *supra* note 4, at 113. Also, in *In re Loestrin 24 FE Antitrust Litigation*, the court relied on the Lamictal decision to also dismiss a plaintiff’s challenge to the reverse payment settlement. *Id.*

<sup>113</sup> These courts read the *Actavis* decision to mean that the five factors are to be applied to the facts of a case in order to determine whether a reverse payment settlement satisfies the antitrust “rule of reason.” Carrier, *supra* note 4, at 115.

<sup>114</sup> See *In re Loestrin 24 Fe Antitrust Litig.*, No. 14-2071, 2016 WL 698077 (1st Cir. Feb. 22, 2016); *King Drug Co. of Florence v. Smithkline Beecham Corp.*, 791 F.3d 388 (3d Cir. 2015), *cert. denied*, 137 S. Ct. 446 (2016).

<sup>115</sup> See *In re Loestrin 24*, 2016 WL 698077; *King Drug Co. of Florence*, 791 F.3d 388.

<sup>116</sup> Carrier, *supra* note 4, at 113. The *Actavis* Court “did not [] introduce the five factors as the foundation of a new and unique rule-of-reason analysis.” *Id.* at 116. Rather, “the Court employed the five factors . . . to show why the ‘general legal policy favoring the settlement of disputes’ did not displace ordinary antitrust analysis.” *Id.*

Another key issue addressed post-*Actavis* was whether the *Actavis* decision applied to non-cash settlement payments. These payments included non-authorized generic agreements or other ancillary services.<sup>117</sup> The only two circuits to address this issue, the First and the Third, have held that the *Actavis* decision applies to both cash and non-cash payments.<sup>118</sup> Additionally two district courts have also reached the same conclusion to date.<sup>119</sup>

## V. SIMILAR CONSIDERATIONS: BPCIA REVERSE PAYMENT SETTLEMENTS

With the rise of follow-on biologics in the United States<sup>120</sup> – and their potential to transfer at least \$110 billion<sup>121</sup> of value from reference biologic manufacturers to follow-on biologic manufactures over the next decade – zealous patent litigation is sure to ensue. It is estimated that the potential savings from just eleven follow-on biologics anticipated to enter the U.S. market from 2014 to 2024 could amount to \$250 billion.<sup>122</sup> This would result in significant cost savings for consumers and the healthcare industry as a whole.

As the Supreme Court has previously recognized, an “antitrust analysis must sensitively recognize and reflect the distinctive economic and legal setting of the regulated industry to which it applies.”<sup>123</sup> In following this directive, this section will argue that the *Actavis* decision should apply to reverse payment settlements under the BPCIA for three reasons. First, immunizing reverse payment settlements from antitrust scrutiny would contravene congressional intent underlying the BPCIA. Second, the five considerations addressed by the *Actavis* Court not only justify the application of antitrust scrutiny to Hatch-Waxman litigation settlements, but also to BPCIA litigation settlements. Third, public policy favors the application of antitrust scrutiny to these types of agreements.

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<sup>117</sup> Michael A. Carrier, *Payment After Actavis*, 100 IOWA L. REV. 7, 9 (2014).

<sup>118</sup> See *In re Loestrin 24*, 814 F.3d 538 (1st Cir. 2016); see also *King Drug Co. of Florence*, 791 F.3d 388 (3d Cir. 2015).

<sup>119</sup> See *United Food & Commercial Workers Local 1776 v. Teikoku Pharma USA, Inc.*, 74 F. Supp. 3d 1052, (N.D. Cal. 2014); see also *In re ACTOS End Payor Antitrust Litig.*, 2015 WL 5610752, 19 (S.D.N.Y. Sept. 22, 2015).

<sup>120</sup> Jeff Overley, *Amgen Patent Suit Targets Sandoz's Enbrel Biosimilar*, LAW360 (Feb. 29, 2016, 4:27 PM), <http://www.law360.com/articles/765014/amgen-patent-suit-targets-sandoz-s-enbrel-biosimilar> (“Amgen launched a patent suit against Sandoz on Friday in New Jersey federal court to delay a biosimilar version of its blockbuster immunosuppressant Enbrel, teeing up a fight with multibillion-dollar stakes.”).

<sup>121</sup> Ben Hirschler, *Biosimilar drugs could save up to \$110 billion by 2020: IMS* (Mar. 29, 2016), <http://www.reuters.com/article/us-biotech-biosimilars-idUSKCN0WV07Q>.

<sup>122</sup> Joseph P. Fuhr Jr., *Biosimilars Can Save Lives and Cost Less* (Aug. 8, 2014), <http://www.forbes.com/sites/realspin/2014/08/08/biosimilars-can-save-lives-and-cost-less/#3fof4f883b2f>.

<sup>123</sup> *Verizon Commc'ns Inc. v. Law Offices of Curtis V. Trinko, LLP*, 540 U.S. 398, 411 (quoting *Concord v. Boston Edison Co.*, 915 F.2d 17, 22 (C.A.1 1990)).



## A. BPCIA Reverse Payment Settlements Contravene Congressional Intent

While, it is true that a significant portion of the Supreme Court’s reasoning in *Actavis* was rooted in the Hatch-Waxman Act’s unique features, rather than reading the decision narrowly and limiting its holding to the Hatch-Waxman context, the decision can be read more broadly and be characterized as the Court deferring to a statutory scheme. Congress, in drafting the Hatch-Waxman Act, addressed the balancing of private and public interests by providing a tradeoff – “extending patent terms based on regulatory delay in exchange for earlier entry of generic competition.”<sup>124</sup> The *Actavis* Court in acknowledging the Congressional intent behind the act reasoned that its “general procompetitive thrust ” and “specific provisions facilitating challenges to a patent’s validity” support the notion that courts should allow for antitrust scrutiny of reverse payment settlements in the ANDA context.<sup>125</sup>

The BPCIA also has a “general procompetitive thrust.” In drafting the BPCIA, Congress was mindful of patent policy and the importance of incentivizing innovation. This notion is supported by the extensive legislative history of the BPCIA, and the lengthy debate over the act’s exclusivity provisions. The appropriate length of market exclusivity was one of the most hotly contested issues during drafting<sup>126</sup> and several hearings in both the House and Senate were held at which this issue was addressed.<sup>127</sup>

During these hearings the biologic pharmaceutical industry proffered a number of reasons as to why a new biologic should be afforded a period of market exclusivity.<sup>128</sup> First, it argued that because a follow-on biologic would “only have to be ‘highly similar’ to rather than the ‘same as’ the innovator product,” there exists a “very real potential that the manufacturer of a [follow-on biologic] may be able to secure abbreviated regulatory approval based at least in part on the innovator’s prior approval, and, at the same time, avoid infringing patents that protect the innovator’s biotech product.”<sup>129</sup> Second, it was argued that “because of the nature of biologic products - produced by

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<sup>124</sup> Rudolph J.R. Peritz, *The Competition Question Unasked in Actavis: What is the Scope of the Patent Right to Exclude?*, 28 ANTITRUST 45, 48 (2013), <http://awa2014.concurrences.com/IMG/pdf/fall13-peritzc.pdf>.

<sup>125</sup> *FTC v. Actavis*, 133 S. Ct. 2223, 2236 (2013).

<sup>126</sup> See generally Krista Hessler Carver et al., *An Unofficial Legislative History of the Biologics Price Competition and Innovation Act of 2009*, 65 FOOD & DRUG L. J. 671 (2010).

<sup>127</sup> *Id.* at 727-28.

<sup>128</sup> The Biologic Industry was represented at these hearings by Biotechnology Innovation Organization (BIO). “BIO is the world’s largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products.” Biotechnology Innovation Org., *About BIO*, <https://www.bio.org/articles/about-bio>.

<sup>129</sup> See Carver et al., *supra* note 126, at 727.

living cells and organisms - patent protection is different from and may be weaker than that afforded to small [ ] molecule[ ] drugs.”<sup>130</sup>

Third, it was argued that, “as a result of current limitations of patentability of naturally occurring substances, many biologics are protected only by process patents that may be easier to design around.”<sup>131</sup> For these three reasons, the biologics industry concluded that a period of exclusivity for new biologic drugs would provide an “‘insurance policy’ for ‘instances where the [follow-on biologic] manufacturer is able to work around the patents held by the innovator but still gain approval of its [follow-on biologic]’”.<sup>132</sup> With these considerations in mind, the biologics industry advocated for a period of market exclusivity somewhere in the range of twelve to fourteen years.<sup>133</sup>

In Contrast to the industry position, a 2009 FTC study found that twelve years of exclusivity is “unnecessary” to promote innovation and to convince companies to invest in biologics.<sup>134</sup> Notably, every administration budget proposal since this 2009 study has called for a reduction in the period of exclusivity from twelve years to seven years to “foster greater [follow-on] biologic competition and reduce the cost burden on patients and payers associated with these drugs.”<sup>135</sup> The FTC report’s findings were based on five assumptions. First, the development costs for a follow-on biologic are likely to be “much higher than the costs of developing a [small molecule generic] drug due to the ‘substantial costs to obtain FDA approval’” and the significant costs associated with manufacturing.<sup>136</sup> Second, most follow-on biologics will not be deemed interchangeable with the reference product and therefore follow-on biologic manufacturers will be required to market their products adding to development costs.<sup>137</sup>

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<sup>130</sup> *Id.* (noting that “several requirements for obtaining a patent are interpreted more stringently for biotechnology inventions than for most other technologies.”).

<sup>131</sup> *Id.*

<sup>132</sup> *Id.* Essentially, the patents on biologic products were considered by the industry to reward innovation at the earlier research and design phase of a drugs life cycle. *Id.* at 735. While the data and market exclusivity provisions reward the manufacturer for its investment of time and resources in bringing the product to market. *Id.*

<sup>133</sup> See Carver et al., *supra* note 117, at 735. Although brand-name small molecule drugs on average are on the market with out generic competition for 12.2 to 13.7 years, it is important to distinguish between the Hatch-Waxman and BCPIA here. Henry Grabowski et al., *Brief Report: Recent Trends in Brand-name and Generic Drug Competition*, 2013 J. MED. ECON. 1, <http://fds.duke.edu/db/attachment/2575>. The 12.2 to 13.7 years a generic drug is on the market without competition is *respective* of patent life, where as the BPCIA’s twelve-year data exclusivity period is *irrespective* and potentially in addition to patent life. *Id.*

<sup>134</sup> Burcu Kilic & Courtney Pine, *Inside Views: Decision Time on Biologics Exclusivity: Eight Years is No Compromise* (July 27, 2015), <http://www.ip-watch.org/2015/07/27/decision-time-on-biologics-exclusivity-eight-years-is-no-compromise/#page=8>.

<sup>135</sup> *Id.* (Additionally, the President’s 2016 budget proposes “prohibiting additional periods of exclusivity for brand biologics due to minor changes in product formulations”).

<sup>136</sup> See Carver et al., *supra* note 126, at 787.

<sup>137</sup> *Id.*

Third, “physicians may be reluctant to switch patients to [follow-on biologics] based on concerns that patients may react differently.”<sup>138</sup> Fourth, healthcare providers may need to be retrained upon switching to a follow-on biologic, because “biologics are ‘combined with ancillary medical services and products that require specialty training for proper handling and administration.’”<sup>139</sup> And fifth, biologics are often reimbursed through medical benefits rather than pharmacy benefits therefore removing the “traditional incentives for using lower priced drugs -such as co-pays and tiered formularies.”<sup>140</sup> Despite the FTC report, ultimately the biologics industry prevailed and the BPCIA included a twelve-year period of exclusivity. This demonstrates that Congress agreed with – or at least catered to – the biologic industry’s position that patents for these products are likely weaker or prone to work around. By allowing for a twelve-year period of exclusivity that is irrespective of patent life, or even patentability, Congress provided the reference biologic manufacturers with the “insurance policy” they requested.

If courts were to find that the *Actavis* decision does not apply to BPCIA litigation, the biologics industry will essentially be given two bites of the proverbial apple. On the one hand, during drafting, the biologics industry argued that biologic manufacturers require an exclusivity period because biologic patents are weak or may be susceptible to design around.<sup>141</sup> In other words, biologic patents possess limited exclusory potential. On the other hand, biologic manufacturers, in asking courts to refrain from scrutinizing BPCIA reverse payment settlements under antitrust principles, the manufacturers would have to argue that the right to prevent competitors from entering the market falls squarely within the scope of their patents’ exclusory potential – the same patents that were presumed to have limited exclusory potential. Patents that Congress recognized may be potentially weak or susceptible to work around.

The BPCIA, in considering industry experience with the Hatch-Waxman Act, “import[ed] a familiar and successful compromise between biologics manufacturers’ desire for a limited monopoly to incentivize innovation and consumers’ need for broad access to biotherapies.”<sup>142</sup> The Act provides reference biologic manufacturers a “lengthy exclusivity period,” while at the same time encouraging potential follow-on biologic manufacturers to create similar drugs through a faster approval process and the promise of substitutability for interchangeable biologics.<sup>143</sup> In effect, Congress justified a limited overriding of the patent system in the name of innovation. The trade-off was market exclusivity for the reference product in exchange for allowing follow-on competitors to rely on their data by way of an abbreviated approval pathway. Accordingly, a court faced with a reverse payment settlement under the BPCIA should follow the *Actavis*

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<sup>138</sup> *Id.*

<sup>139</sup> *Id.*

<sup>140</sup> *Id.*

<sup>141</sup> See Carver et al., *supra* note 126, at 727.

<sup>142</sup> Joanna M. Shepherd, *Biologic Drugs, Biosimilars, and Barriers to Entry*, 25 HEALTH MATRIX 139, 161 (2015), <http://scholarlycommons.law.case.edu/healthmatrix/vol25/iss1/8>.

<sup>143</sup> *Id.*

Court's guidance and look to the congressional intent behind the BPCIA and the act's own "procompetitive thrust" to reach the same result.<sup>144</sup>

## B. The BPCIA and the Five *Actavis* Considerations

We now turn briefly to the five considerations addressed in *Actavis* and their applicability to settlements under the BPCIA. By way of disclaimer, this is by no means an endorsement of the analysis undertaken by the early post-*Actavis* courts in which the five considerations were used as a modified rule of reason analysis.<sup>145</sup> Rather, this analysis is to demonstrate that the five considerations that guided the *Actavis* Court to conclude that reverse payment settlements arising from Hatch-Waxman litigation should be subject to antitrust scrutiny, are also applicable to settlements arising from BPCIA litigation.

The first consideration addressed by the *Actavis* Court noted that reverse payments have the potential for genuine adverse effects on competition.<sup>146</sup> The Court found that the brand-manufacturer's ability to purchase the exclusive rights to sell its product was indicative of an adverse effect on competition.<sup>147</sup> This brand-manufacturer purchase of the exclusive right to sell its product was made possible by several key provisions of the Hatch-Waxman Act.<sup>148</sup> Although these key provisions differ in important part, or are absent entirely from the BPCIA, I will demonstrate how the same potential exists for the reference manufacturer to purchase the exclusive right to sell its product.

Unlike in the Hatch-Waxman context, a reverse payment under the BPCIA, theoretically, will not always amount to a purchase by the reference manufacturer, of an exclusive right to sell its product. This is due to the differences in exclusivity periods and the stay provision found in the Hatch-Waxman Act as compared to the BPCIA.<sup>149</sup> Unlike the Hatch-Waxman Act, which provides a 180-day period of exclusivity to the first successful paragraph IV challenger, the BPCIA only provides a period of exclusivity for interchangeable follow-on biologic products.<sup>150</sup> Also, unlike the Hatch-Waxman Act, the BPCIA contains no thirty-month stay provision.<sup>151</sup>

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<sup>144</sup> See *FTC v. Actavis*, 133 S. Ct. 2223, 2236 (2013).

<sup>145</sup> *In re Loestrin 24 Fe Antitrust Litig.*, 45 F. Supp. 3d 180 (D.R.I. 2014); *In re Lamictal Direct Purchaser Antitrust Litig.*, 18 F. Supp. 3d 560 (D.N.J. 2014), *vacated and remanded sub nom. King Drug Co. of Florence*, 791 F.3d 388 (3d Cir. 2015).

<sup>146</sup> *Actavis, Inc.*, 133 S. Ct. at 2235-36.

<sup>147</sup> *Id.*

<sup>148</sup> See generally, *id.*

<sup>149</sup> See generally, The Patient Protection and Affordable Care Act, Pub. L. No. 111-148, §§7001 - 7003 (2010).

<sup>150</sup> *Id.*

<sup>151</sup> *Id.*

The period of exclusivity afforded to an interchangeable biologic only relates to the interchangeable status itself and only prevents the FDA from approving another product as interchangeable for a year.<sup>152</sup> Therefore, the FDA may still approve other products as biosimilar biologics. Despite the possibility of biosimilar biologic competition, if a follow-on biologic manufacturer were to gain approval as an interchangeable product, it may still create a situation ripe for a reverse payment settlement. Interchangeable products may be more likely to have greater market penetration as compared to biosimilar biologics that will likely gain minimal market share.<sup>153</sup>

However, for the foreseeable future, the approval pathway for interchangeable products may not be an ideal pathway for manufactures as it comes with inherent risks. The FDA finally released draft guidance related to the interchangeability pathway in January 2017, which provides a flexible and “case-by-case” approach for the approval of interchangeable biologics.<sup>154</sup> The FDA’s general lack of experience with the approval of interchangeable biologics and the inherent uncertainty of a “case-by-case” approach may deter follow-on biologic manufacturers from initially pursuing this pathway.<sup>155</sup> Also, this route may be too costly for manufacturers because it requires additional clinical testing.<sup>156</sup> Even after a manufacturer conducts the extra clinical trials, if the FDA finds the results insufficient, it may reject the application for interchangeable status. This level of risk and uncertainty may shift the majority of the filings into the biosimilar pathway, rather than the interchangeable pathway, which provides no period of exclusivity.

Accordingly, the pertinent question is then – if a follow-on biologic manufacturer files under the biosimilar pathway, which provides no period of exclusivity and no stay of FDA approval, how can a reference biologic manufacturer’s reverse payment settlement ever amount to the purchase of the exclusive right to sell its product? While the BPCIA permits multiple follow-on manufactures to enter the market at the same time, this may prove unlikely in practice.

Unlike generic small molecule drugs, developing a follow-on biologic requires clinical research and marketing. Therefore, few or potentially just a single manufacture may be all that is ready to enter the market at a time.<sup>157</sup> Notably, despite the approval of

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<sup>152</sup> See 42 U.S.C. § 262(k)(6)(A).

<sup>153</sup> See generally Erwin A. Blackstone & P. Fuhr Joseph, Jr., *The Economics of Biosimilars*, 6 AM. HEALTH & DRUG BENEFITS 469 (2013).

<sup>154</sup> CONSIDERATIONS IN DEMONSTRATING INTERCHANGEABILITY WITH A REFERENCE PRODUCT: GUIDANCE FOR INDUSTRY (Jan. 12, 2017), <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537135.pdf>.

<sup>155</sup> Simon King, *Can Pharma Learn to Stop Worrying and Love Biosimilars*, FORBES (Feb. 11, 2016), <http://www.forbes.com/sites/simonking/2016/02/11/can-pharma-learn-to-stop-worrying-and-love-biosimilars/#2c04c84b7e15>.

<sup>156</sup> See generally SERTKAYA ET AL., *supra* note 28.

<sup>157</sup> Dan Stanton, *Biosimilars Land in the US as Sandoz Launches Zarxio*, BIOPHARMA REP. (Sept. 3, 2015), <http://www.biopharma-reporter.com/Markets-Regulations/Biosimilars-land-in-the-US-as-Sandoz-launches-Zarxio>.

the first follow-on biologic in the United States, the FDA has yet to provide final guidance for the approval of these drugs.<sup>158</sup> The lack of guidance means that less manufacturers are likely to enter the market.<sup>159</sup> This creates the potential for the reference manufacturer to pay the sole follow-on manufacturer, the one closest to launch, or the one most likely to win at trial, to keep out of the market and essentially purchase the exclusive right to sell its product.

Even in the European Union (EU), which has a defined pathway, there are still a small number of follow-on biologics. Although the EU has an entirely different regulatory scheme for the approval of follow-on biologics, they have allowed for their approval since 2006.<sup>160</sup> Therefore, the EU's experience with these products may prove useful in anticipating trends in the U.S. markets. There are currently twenty approved follow-on biologics in the EU.<sup>161</sup> The twenty approved products relate to eight reference products.<sup>162</sup> Three of the eight reference products have follow-on biologics marketed and produced by a single manufacturer.<sup>163</sup> Although having a single follow-on biologic product competing with a specific reference product is the exception rather than the norm (with respect to this relatively small sample), it demonstrates that in some instances, a reference manufacturer would only need to pay one competitor to stay out of the market to maintain its monopoly. After all, thus far the United States' first follow-on biologic drug is the sole competing product.

While it is true that reverse settlement agreements in BPCIA litigation will not always amount to an actual purchase of the exclusive right to sell its product, each settlement agreement would be subject to a case-by-case antitrust analysis. A case-by-case analysis is exactly what the *Actavis* decision called for when it refused to deem these settlements as presumptively unlawful and subjected each agreement to the full rule of reason analysis.

The Court's second consideration, that the "anticompetitive consequences [of a reverse payment] will at least sometimes prove unjustified,<sup>164</sup> is no different in the BPCIA context than in the Hatch-Waxman context. While it is true that the

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<sup>158</sup> Wayne Winegarden, *Unleashing the Potential of Biosimilars*, FORBES (May 12, 2015), <http://www.forbes.com/sites/econostats/2015/05/12/unleashing-the-potential-ofbiosimilars/2/#55a8de924eea>. The EU has developed guidance and a pathway for approving follow-on biologic drugs, which has resulted in a "more robust [follow-on biologics] market. *Id.* A defined regulatory pathway makes "a large difference in the growth of the [follow-on biologics] market." *Id.* "Compare the 1 approved [follow-on biologic] in the U.S. to the 6 in Japan, 8 in Australia or 20 across Europe." *Id.*

<sup>159</sup> *Id.* "The lack of a certain regulatory pathway means that patients in the U.S. are missing out on the potential benefits from biosimilars that are already deemed safe and effective in other developed countries." *Id.*

<sup>160</sup> *Biosimilars Approved in Europe*, GENERICS AND BIOSIMILARS INITIATIVE, <http://www.gabi-online.net/Biosimilars/General/Biosimilars-approved-in-Europe> (last updated Jan. 14 2016).

<sup>161</sup> *Id.*

<sup>162</sup> *Id.*

<sup>163</sup> *Id.*

<sup>164</sup> *Actavis*, 133 S. Ct. at 2235-36 (citing *California Dental Assn. v. FTC*, 526 U.S. 756, 786-87 (1991) (Breyer, J., concurring in part and dissenting in part)).

“procompetitive effects of a settlement may balance the anticompetitive nature,”<sup>165</sup> much like the settlements in Hatch-Waxman litigation, without inquiry, a court is unable to determine whether or not the settlements violate antitrust principles. While a reverse payment settlement may amount to a rough approximation of “saved litigation costs” or fair market value for other auxiliary services, this should not prevent an antitrust plaintiff from making its case.

For the third consideration, the Court recognized that a large payment might serve as a strong indicator of the brand-manufacturer’s power to charge higher than competitive prices.<sup>166</sup> The *Actavis* court was concerned with the size of the payments, reasoning that a large payment demonstrates market power.<sup>167</sup> In the context of paragraph IV of the Hatch-Waxman Act, the payments to generic manufacturers to stay out of the market had to be large in nature. This is due to the 180-day period of exclusivity in which the generic manufacturer earns the vast majority of profits<sup>168</sup> and “is often worth several hundred million dollars.”<sup>169</sup> These profits are driven by the rapid shift from the brand-name product to the generic product due to automatic substitution laws. The lack of automatic substitution for follow-on biologics will likely reduce the potential profits and therefore smaller payments are likely. Although a large payment is still likely to demonstrate market power, in the context of smaller payments, rather than only relying on size, courts should instead compare the relative size of the payment with the contemplated anticompetitive effects.

The fourth consideration may be more applicable to BPCIA reverse payment settlements than to Hatch-Waxman settlements. The Court reasoned that it would not be necessary to litigate patent validity to answer the antitrust question because a large unexplained reverse payment could provide a “workable surrogate for a patent’s weakness.”<sup>170</sup> As discussed in greater detail above, the relevant patents covering a biologic drug, unlike patents for small molecule drugs, may be weaker or more susceptible to work around. Therefore, there is a greater probability that a large payment signals that the reference biologic manufacturer is threatened by the follow-on biologic product.

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<sup>165</sup> *Id.* at 2236.

<sup>166</sup> *Id.*

<sup>167</sup> *Id.*

<sup>168</sup> *Id.*

<sup>169</sup> Hemphill, *supra* note 43, at 1579.

<sup>170</sup> *Id.* at 2236-37

(An unexplained large reverse payment itself would normally suggest that the patentee has serious doubts about the patent’s survival. And that fact, in turn, suggests that the payment’s objective is to maintain supracompetitive prices to be shared among the patentee and the challenger rather than face what might have been a competitive market—the very anticompetitive consequence that underlies the claim of antitrust unlawfulness).

Lastly, the fifth consideration also holds true in both the BCPIA and Hatch-Waxman context.<sup>171</sup> Parties will always have the option to settle their lawsuit in other ways that do not include reverse payments. Where there is payment to the infringing party, the relevant antitrust question focuses on the reason for that payment.

### C. Public Policy Favors Antitrust Scrutiny of BPCIA Settlements

While not addressed by *Actavis*, *eBay Inc. v. MercExchange*,<sup>172</sup> an earlier Supreme Court patent law decision, may help to shape the analysis of the *Actavis* decision. Notably, *eBay* predated the BPCIA and likely shaped its development.<sup>173</sup> In *eBay*, the Supreme Court held that an injunction should not be automatically issued after a finding of patent infringement of a valid claim.<sup>174</sup> Rather, courts should consider the traditional four-factor test to determine whether a permanent injunction should issue.<sup>175</sup> Prior to this decision, “courts issued permanent injunctions virtually as a matter of course once infringement and validity had been determined.”<sup>176</sup> As the Hatch-Waxman Act predated this decision, it allowed for automatic permanent injunctions, which “presumably reflect[ed] the previous rule as to the availability of injunctive relief” in patent disputes.<sup>177</sup> The BPCIA, however, does not allow for automatic permanent injunctions, which is likely the result of the *eBay* decision being handed down during drafting of the BPCIA.<sup>178</sup>

While facially, *eBay* appears to be a case about patent remedies, its teachings may guide the courts in defining the contours of the *Actavis* decision. As the late Rudolph J.R. Peritz succinctly described,

A patent owner in seeking an injunction asks the court to restrain infringing competitors on the ground that a patent justifies the restraint. Likewise, the defender of a [reverse payment] settlement asks the court to validate the private-agreement equivalent of an injunction. If the issue were framed in these terms, the *eBay* decision would require the branded drug maker (and its generic confederates) to persuade the court that the [settlement] provision satisfies patent law’s test to restrain competitors—that on balance, the benefits and harms, public and private, tip in favor of keeping

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<sup>171</sup> See discussion *supra* Part III.B.

<sup>172</sup> 547 U.S. 388 (2006).

<sup>173</sup> Carver et al., *supra* note 126, at 697 (“[T]he eBay decision effectively meant that there would be no parallel provision in the biosimilar legislation”).

<sup>174</sup> 547 U.S. at 394.

<sup>175</sup> *Id.*

<sup>176</sup> See Carver et al., *supra* note 126, at 697.

<sup>177</sup> *Id.*

<sup>178</sup> *Id.*



generic drug makers off the market. Only then would the settlement fall within the scope of the exclusionary remedy as prescribed by *eBay*. Likewise, only then should a pharmaceutical patent holder be permitted to deploy a settlement agreement to keep a generic competitor off the market.<sup>179</sup>

The Four-factor test for whether a permanent injunction is appropriate requires the plaintiff to show that “(1) it has suffered an irreparable injury; (2) that remedies available at law, such as monetary damages, are inadequate to compensate for that injury; (3) that, considering, the balance of hardships between the plaintiff and defendant, a remedy in equity is warranted; and (4) that the public interest would not be disserved by a permanent injunction.”<sup>180</sup> In applying this standard to a reverse payment settlement, all parties to the settlement agreeing to the injunction equivalent “benefit from the settlement agreement’s injunction-like delay of market entry (and the consequent loss of competition).”<sup>181</sup> A court’s rejection of this type of settlement agreement and the loss of those benefits gained from it “do not cause irreparable private harm . . . because the parties can repair to their patent infringement cases to litigate the claims and seek appropriate remedies.”<sup>182</sup> Therefore, in reverse payment settlement cases, “a strong public interest factor would carry great weight against such weak claims of irreparable private harm.”<sup>183</sup>

The current antitrust definition of public interest would require a court to address the impact on consumers.<sup>184</sup> Therefore, although the Supreme Court has reaffirmed its conclusion that the rule-of-reason analysis should focus on the economic rather than social consequences of the restraint,<sup>185</sup> in light of *eBay*, Courts should consider the impact of reverse settlement agreements on consumers and on paramount public policy interests such as public health and welfare. Specifically, courts must determine whether the public interest factors favor allowing the contemplated restraint on competition.

Three public policy concerns favor the extension of *Actavis*’ holding to settlements under the BPCIA. First, antitrust scrutiny of reverse payment settlements occurring in Hatch-Waxman litigation appears to have increased competition. Second, the cost savings passed on to healthcare consumers have the potential to be much larger with follow-on biologics than with generic drugs. Third, lower priced medication has been demonstrated to increase patient medication adherence, thereby improving patient health and reducing overall healthcare costs.

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<sup>179</sup> Peritz, *supra* note 124, at 48.

<sup>180</sup> *eBay*, 547 U.S. at 391.

<sup>181</sup> Peritz, *supra* note 124, at 48.

<sup>182</sup> *Id.*

<sup>183</sup> *Id.*

<sup>184</sup> *Id.*

<sup>185</sup> Nat’l Soc’y of Prof’l Eng’rs v. U.S., 435 U.S. 679 (1978) (reaffirming court’s view in *Standard Oil*).

## 1. Antitrust Scrutiny of Hatch-Waxman Settlements Has Increased Competition

The initial effect of applying antitrust scrutiny to Hatch-Waxman reverse payment settlements is a positive one with respect to promoting competition. It appears that the *Actavis* decision may have resulted in an initial increase in generic competition despite Chief Justice Roberts prediction. Chief Justice Roberts, in his dissenting opinion quipped:

The irony of all this is that the majority's decision may very well discourage generics from challenging pharmaceutical patents . . . Taking the prospect of settlements off the table . . . puts a damper on the generic's expected value going into litigation, and decreases its incentive to sue in the first place.<sup>186</sup>

Essentially, Chief Justice Roberts reasoned that the *Actavis* decision by its very nature – limiting generic companies' ability to settle Hatch-Waxman litigation – would deter generic competition rather than promote competition undermining the entire purpose of the majority's position. An empirical study that looked at the number of paragraph IV ANDAs filed within the twelve months after *Actavis* noted that there was an increase in the number of filings as compared to the previous four years.<sup>187</sup> These findings indicate that generic competition “appears to have actually accelerated in the wake of the *Actavis* decision.”<sup>188</sup> The study noted that although there has been an increase in the number of Paragraph IV challenges being filed, it is unclear whether this correlates with more generic drugs getting to market.<sup>189</sup> Regardless, this demonstrates that while a reverse payment settlement may be more desirable for a generic manufacturer, limiting these types of settlements will not stop generic manufacturers from innovating. After all, generic manufacturers are in the business of doing exactly that—creating cheaper alternatives to brand-name drugs.

## 2. Cost Savings from Follow-on Biologic Drugs Are Greater than with Generics

Cost savings for consumers, the healthcare industry, and government programs like Medicare and Medicaid with respect to follow-on biologic competition, will likely be more substantial than those realized through generic drug competition. To demonstrate, a look at the pricing for Zarxio, the first follow-on biologic to hit the U.S. markets may be informative.

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<sup>186</sup> *Actavis*, 133 S. Ct. at 2247 (Roberts, C.J., dissenting).

<sup>187</sup> See Krickl & Avery, *supra* note 33, at 538-39.

<sup>188</sup> *Id.*

<sup>189</sup> *Id.* “Nonetheless, the increase in Paragraph IV filings suggests that generics are at least attempting to compete and that their incentive to challenge pioneers' patents has grown.” *Id.* at 539.

A company spokesperson at Sandoz, the manufacturer of Zarxio has explained that their marketing strategy for the product “is much closer to the approach for a branded product than that of generic medicine” and only provides a 15% discount compared to the reference product.<sup>190</sup> This 15% discount compared to the reference product, while on the low end, falls within the industry-estimated range of a 15% to 30% discount for follow-on biologics.<sup>191</sup>

A two-week treatment regimen of Zarxio for an adult male of an average weight costs approximately \$5,706.74 as compared to the reference product Neupogen, which costs approximately \$6,713.<sup>192</sup> The use of Zarxio saves consumers and health insurers approximately \$1,007.11 over the two week period. While this may not seem like a huge saving, Zarxio and Neupogen are relatively inexpensive compared to other biologic products.<sup>193</sup> Further, it is commonly used for short courses of therapy rather than on a long-term basis and therefore, the cost of the treatment is significantly less than that of a product used long term. To better highlight the potential savings to consumers it is easier to compare a small molecule generic drug and a biologic drug that are taken on a long-term basis.

Cymbalta, a small molecule drug used for the treatment of Major Depressive Disorder, at a typical dose costs approximately \$2,646.28 over the course of a year.<sup>194</sup>

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<sup>190</sup> See Stanton, *supra* note 157.

<sup>191</sup> Zachary Brennan, *US CMS Releases New Info Around Biosimilar Pricing, Uptake*, BIOPHARMA REP. (Apr. 2, 2015), <http://www.biopharma-reporter.com/Markets-Regulations/US-CMS-releases-new-info-around-biosimilar-pricing-uptake>.

<sup>192</sup> This calculation is based on a two-week treatment regimen of an individual weighing 195.5 pounds (88.9 kg) at the recommended 5/mcg/kg/day dosing for the prophylaxis of febrile neutropenia in patients with acute myeloid leukemia receiving induction or consolidation chemotherapy. Zarxio, in DRUGDEX [database on the Internet]. Ann Arbor (MI): Truven Health Analytics; 2016 [cited 16 Mar. 2016]. Available from: [www.micromedexsolutions.com](http://www.micromedexsolutions.com). Subscription required to view; CDC.gov, *Body Measurements, National Center for Health Statistics*, <http://www.cdc.gov/nchs/fastats/body-measurements.htm> (The average U.S. adult male weighs 195.5 pounds). For demonstration purposes, all pricing is based on wholesale acquisition cost (WAC) available via RED BOOK, Zarxio, in RED BOOK Online [database on the Internet]. Ann Arbor (MI): Truven Health Analytics; 2016 [cited 16 Mar. 2016]. Available from: [www.micromedexsolutions.com](http://www.micromedexsolutions.com). Subscription required to view (NDC 61314-0312-01, strength 480 mcg/0.8 ml, package size 0.8 ml, WAC \$438.98); Neupogen, in RED BOOK Online [database on the Internet]. Ann Arbor (MI): Truven Health Analytics; 2016 [cited 16 Mar. 2016]. Available from: [www.micromedexsolutions.com](http://www.micromedexsolutions.com). Subscription required to view (NDC 55513-0209-91, strength 480 mcg/0.8 ml, package size 0.8 ml, WAC \$516.45). Package quantity for cost calculations has been rounded up to the nearest whole vial.

<sup>193</sup> See Anna Edney, *Cheaper Biotech Drugs Come to U.S. as Novartis Gets FDA Approval* (Mar. 6, 2015), <https://www.bloomberg.com/news/articles/2015-03-06/novartis-wins-approval-for-first-biosimilar-to-be-sold-in-u-s> (A one month supply of Zarxio’s reference biologic, Neupogen, is estimated to cost about \$3,500); *c.f.* Matthew Herper, *The World's Most Expensive Drugs*, FORBES (Feb. 22, 2010), <https://www.forbes.com/2010/02/19/expensive-drugs-cost-business-healthcare-rare-diseases.html> (The price of a biologic drug for rare diseases could cost over \$100,000 per year).

<sup>194</sup> This calculation is based on a fifty-two-week treatment regimen at the recommended dose of 60 mg/day. Cymbalta, in DRUGDEX [database on the Internet]. Ann Arbor (MI): Truven Health Analytics; 2016 [cited 16 Mar. 2016]. Ann Arbor (MI): Truven Health Analytics; 2016 [cited 16 Mar. 2016], available at [www.micromedexsolutions.com](http://www.micromedexsolutions.com). Subscription required to view (NDC 00002-3270-30, strength 60mg, package size 30s ea, WAC \$218.10).

In comparison, the generic version, Duloxetine costs approximately \$355.87 per year.<sup>195</sup> This roughly equates to an 86% or \$2,290.41 cost savings for switching from the brand to the generic product. While the price discounting of generic small molecule drugs, like the 86% seen here, far exceed the 15%-30% discounts promised by follow-on biologics, the greater cost of biologics makes even a modest 15% discount significant.

For example, Enbrel, a biologic drug used for the treatment of rheumatoid arthritis costs approximately \$48,472.32 over the course of a year.<sup>196</sup> While currently no follow-on biologic version exists,<sup>197</sup> if one were introduced with pricing at 15 to 30% below the cost of the reference product, the cost per year would range from \$33,930.62 to \$41,201.47. This would provide a cost savings ranging from \$7,270.85 to \$14,541.70 per year. Although the discounts here are nowhere near the 86% discount seen with the above mentioned generic small molecule drug, the actual cost savings are roughly three- to six-times greater. Because the cost savings from follow-on biologic competition has the potential to be significantly greater than those from generic competition, settlements delaying entry of follow-on biologics deserve at least the same level of scrutiny applied to Hatch-Waxman settlements.

### 3. Follow-on Biologic Cost Savings Will Improve Public Health & Reduce Overall Healthcare Spending

Cost savings from cheaper follow-on biologics will not only save consumers money, it will also improve patient medication adherence.<sup>198</sup> This is an important consideration because when patients fail to take their medication as directed, it not only results in wasted medication, it also “leads to poor outcomes, which then increase health care service utilization and overall health care costs.”<sup>199</sup> Specifically, nonadherence has been linked to early death, increased emergency room visits, greater rates of hospital admissions, and longer hospital stays—all of which result in greater healthcare costs.<sup>200</sup> An outstanding \$100 to \$300 billion (3% to 10% of total U.S. healthcare costs) of avoidable health care costs has been attributed to medication nonadherence annually.<sup>201</sup>

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This calculation is based on a fifty-two-week treatment regimen at the recommended dose of 60 mg/day. *Duloxetine* (Mar. 16, 2016), <http://www.micromedexsolutions.com>.

<sup>196</sup> This calculation is based on a fifty-two-week treatment regimen at the recommended dose of 40mg/weekly. *Enbrel*, TRUVEN HEALTH ANALYTICS (Mar. 16, 2016), <http://www.micromedexsolutions.com>.

<sup>197</sup> Currently, Novartis AG, the manufacturer of Zarxio, is setting their sights on a follow-on version of Enbrel and is currently engaged in the patent litigation process. Damien Garde, *Novartis Comes for Enbrel in Latest Biosimilar Shot at Amgen* (Oct. 2, 2015), <http://www.fiercebiotech.com/story/novartis-comes-enbrel-latest-biosimilar-shot-amgen/2015-10-02>.

<sup>198</sup> Aurel O. Iuga & Maura J. McGuire, *Adherence and Healthcare Costs*, 7 RISK MGMT & HEALTHCARE POL'Y 35, 35-44 (2014).

<sup>199</sup> *Id.* at 37.

<sup>200</sup> Robert McCarthy, *The Price You Pay for the Drug Not Taken*, 16 BUS. HEALTH 27, 27-28, 30, 32-33 (1998); see generally Dana P. Goldman et al., *Pharmacy Benefits and the Use of Drugs by the Chronically Ill*, 291 [J]AMA 2343 (2004); Lars Osterberg & Terrance Blaschke, *Adherence to Medication*, 353 NEW ENG. J. MED. 487 (2005).

<sup>201</sup> Iuga, *supra* note 198, at 37.

Notably, several studies have shown that patients frequently cite high medication costs as a reason for nonadherence.<sup>202</sup> Therefore, reducing the cost of biologic drugs through follow-on competition has the potential to improve patient medication adherence.

Not only does nonadherence affect direct healthcare spending, it also influences indirect costs such as decreased work productivity and disability costs.<sup>203</sup> It has been estimated that health-related productivity loss costs for employers are 2.3 times higher than the direct health care costs.<sup>204</sup> Therefore, “the benefits of improved medication adherence may be even greater when considered at a societal level.”<sup>205</sup> The greater cost savings associated with follow-on biologics and their potential to impact public health as well as both direct and indirect healthcare spending make this a strong public interest factor that should carry great weight against weak claims of irreparable private harm.

## VI. CONCLUSION

There is much to be seen regarding the development of the follow-on biologics market in the United States and their acceptance by the patients and healthcare professionals. Although it is plausible that we may never see a reverse payment settlement occur in the BPCIA context, if such a settlement should arise, a court tasked with analyzing the agreement should look to the broad teachings of *Actavis* and apply antitrust scrutiny rather than limiting its holding to the Hatch-Waxman context.

Congress, in drafting both the Hatch-Waxman Act and the BPCIA, contemplated the balancing of the need to promote innovation with the public’s interest in a competitive market place. Following the *Actavis* Court’s lead, a court analyzing a settlement under the BPCIA should look to the act’s general “procompetitive thrust” to find grounds for the application of antitrust scrutiny. Because the BPCIA was loosely based on the United States’ experience with the Hatch-Waxman Act, the five considerations addressed in *Actavis* are very much applicable to the BPCIA context. Taking the considerations together, a court should conclude that reverse payment settlements occurring in BPCIA litigation carry with them the potential to inflict anticompetitive harm. Therefore, BPCIA reverse payment settlements should not be immunized from antitrust scrutiny. Additionally, courts should find support in the *eBay* decision to import the consideration of significant public policy issues into the analysis of these agreements.

Should a court fail to extend *Actavis*’ holding to reverse payment settlements under the BPCIA, what standard would the court apply and to what result? The answer would likely be the scope of the patent test – the test used by the majority of courts prior

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<sup>202</sup> In a survey of 10,000 patients, 17% of patients indicated that their medication nonadherence was due to high drug costs. *Id.* at 40. In another survey of 14,464 Medicare beneficiaries, 55.5% of patients who did not fill at least one prescription reported that high medication costs resulted in their nonadherence. *Id.*

<sup>203</sup> *Id.* at 37.

<sup>204</sup> *Id.*

<sup>205</sup> *Id.*

to *Actavis*—a test explicitly repudiated by the Supreme Court. Therefore, the answer to the question of whether *Actavis* applies to settlements occurring in BPCIA litigation is abundantly clear. Reverse payment settlements occurring in BPCIA litigation should not be immunized from antitrust scrutiny and should be subjected to the rule of reason.