



11-1-2018

The Biosimilar Patent Dance- If You Don't Dance You're No Friend of Mine

Ladonnikov, Alexej

Follow this and additional works at: <https://digitalcommons.law.scu.edu/chtlj>

 Part of the [Intellectual Property Law Commons](#), and the [Science and Technology Law Commons](#)

Recommended Citation

Ladonnikov, Alexej, *The Biosimilar Patent Dance- If You Don't Dance You're No Friend of Mine*, 35 SANTA CLARA HIGH TECH. L.J. 135 (2018).

Available at: <https://digitalcommons.law.scu.edu/chtlj/vol35/iss1/4>

This Comment is brought to you for free and open access by the Journals at Santa Clara Law Digital Commons. It has been accepted for inclusion in Santa Clara High Technology Law Journal by an authorized editor of Santa Clara Law Digital Commons. For more information, please contact sculawlibrarian@gmail.com, pamjadi@scu.edu.

THE BIOSIMILAR PATENT DANCE – IF YOU DON’T DANCE, YOU’RE NO FRIEND OF MINE

By Alexej Ladonnikov¹

In response to political pressure, Congress has been seeking solutions to control drug prices and make it easier for consumers to afford pharmaceuticals. The legislative response to this concern was the Biosimilar, Price, Competition, and Innovation ACT (“BCPIA”). This act allows the Food and Drug Administration (“FDA”) to accelerate the approval pathway for biosimilar drugs that effectively act as generic drugs (“generics”). This note analyzes how courts have handled the following three outstanding issues with the BCPIA: (1) whether compliance with the BCPIA is required or optional; (2) whether an applicant needs to wait until after the FDA approves a drug to notify the creator of the patented product of their intent to market the biologic; and (3) whether the applicant needs to participate in the entire process.

CONTENTS

INTRODUCTION.....	136
I. BACKGROUND	137
A. <i>What are Biosimilars and why is the BPCIA needed?</i>	137
B. <i>BPCIA—abbreviated approval pathway</i>	140
C. <i>The Patent Dance</i>	141
II. ANALYSIS	142
A. <i>Amgen v. Sandoz – is the patent dance required, and when are NCMs filed?</i>	143
1. Background	143
2. Issues	144
3. Supreme Court Decision	144
a. aBLA Disclosure	144
b. aBLA Disclosure Analysis	145
c. NCM prior to FDA Approval.....	147
d. NCM Analysis.....	148

¹ JD/MBA Candidate, Expected Graduation May 2020, Santa Clara University

e. Can companies engage in the patent dance only part-way?	148
.....	148
B. <i>Janssen v. Celltrion</i>	148
1. Background	148
2. District Court Decision.....	149
3. Analysis.....	150
C. <i>Amgen v. Hospira</i>	150
1. Background	150
2. Circuit Court Decisions.....	151
3. Analysis.....	152
IV OVERALL CONSIDERATIONS	153
CONCLUSION	153

INTRODUCTION

Ever since the financial collapse of 2008, American consumer budgets have been increasingly squeezed.² This led to increased political pressure to rein in drug prices.³ In 2009, Congress enacted the BPCIA in an effort to control drug prices.⁴ The BPCIA provided an accelerated FDA approval pathway for “biosimilars,” which are biologics with similar pharmacological features to ones already on the market. Those features are similar enough that biosimilars effectively act as generics.⁵ Biologics are a class of large molecules, usually derived via recombinant DNA techniques in specialized tissues cultures, producing drugs as complex as monoclonal antibodies and immunoglobins.⁶

Biologics are one of the fastest growing segments of the pharmaceutical industry, with the top 10 products accounting for \$73 billion in global sales as of 2017.⁷ Unfortunately, intellectual property rights relating to biosimilars, when marketed as generics, are too complex to effectively regulate under the pre-BPCIA framework

²*Household Expenditures and Income*, Pew Charitable Trusts (Mar 2016), http://www.pewtrusts.org/-/media/assets/2016/03/household_expenditures_and_income.pdf.

³Shamane Mills, *States Try To Rein In Prescription Drug Prices*, WPR (April 27, 2017, 3:15pm), <https://www.wpr.org/states-try-rein-prescription-drug-prices>.

⁴42 U.S.C. § 262.

⁵*Generic Drugs: Questions & Answers*, FDA INFORMATION FOR CONSUMERS (DRUGS) (Jan. 04 2018), <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/QuestionsAnswers/ucm100100.htm>.

⁶*How do Drugs and Biologics Differ?*, BIOTECHNOLOGY INNOVATION ORGANIZATION, <https://www.bio.org/articles/how-do-drugs-and-biologics-differ>.

⁷Kathlyn Stone, *Top 10 Biologic Drugs in the United States*, THE BALANCE (Oct. 12, 2017), <https://www.thebalance.com/top-biologic-drugs-2663233>.

established by the Hatch-Waxman Act.⁸ The BPCIA established such a framework for handling patent infringement disputes by a mechanism that has come to be known as “the patent dance.”⁹ This dance involves several rounds of information exchange and negotiation to clearly delineate any infringement claims, and is meant to cut down on the time and expense of discovery and litigation.¹⁰

This article outlines the current jurisprudence on some of the major unresolved issues relating to the BPCIA. This article first summarizes the salient elements of the BPCIA and the patent dance, then addresses three major issues that the courts are currently reviewing or have recently reviewed. First, this article assesses whether compliance with the BPCIA patent dance is a required or an optional procedure. This issue will determine how much “bite” the BPCIA legislation has on parties that wish to use the abbreviated approval pathway, but spurn open exchanges of information, and consequently impact how many millions of dollars worth of litigation will play out. Second, and in conjunction with the first issue, the question arises of whether an applicant must wait until after FDA approval to notify a reference product sponsor (“RPS”), the creator of the patented product, of their intent to market their product. The answer will dictate whether patent holders (“innovators”) will be given an extra 180 days of patent exclusivity on top of their existing 12 years. Lastly, this article looks at whether innovators or generic manufacturers must engage with the entire sequence of steps, or may engage more selectively, thereby influencing expensive litigation while still gaining some benefit from the legislation. Each of these three issues are raised in current and pending court actions at varying levels. The analysis of this article is informed by the discussion of these issues in such court cases alongside the legislative history of the BPCIA.

I. BACKGROUND

A. *What are Biosimilars and why is the BPCIA needed?*

In 1984, the Drug Price Competition and Patent Term Restoration Act (informally known as the Hatch-Waxman Act) was enacted.¹¹ Hatch-Waxman encouraged more companies to make use of the

⁸ Dennis Crouch, *BPCIA: Patent Dance Steps Becoming a Bit Clearer*, PATENTLYO (Aug. 16, 2017), <https://patentlyo.com/patent/2017/08/patent-becoming-clearer.html>.

⁹ *Id.*

¹⁰ 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, 775 (2010).

¹¹ 21 U.S.C. § 355.

Abbreviated New Drug Application (“ANDA”) for generic drugs.¹² While generic drug manufacturers were already allowed to use this approval “fast-lane,” Hatch-Waxman gave innovators and generic manufacturers protections and incentives designed to get generics to market sooner while also protecting innovators.¹³ This led to a boom in the generic drug industry, which helped drive drug prices down over time.¹⁴

Up until the 1990s, the pharmaceutical industry was working overwhelmingly on “small molecule” drugs.¹⁵ Drugs of this type are created by chemists going through discrete chemical addition steps to form the structure of the final molecule.¹⁶ Since then, the advent and refinement of recombinant DNA technology has opened up an entirely new type of product – large molecule drugs, also known as biologics or biopharmaceuticals. These “large molecules” offer orders of magnitude more complexity and clinical applications. The BPCIA defines a biologic as a “virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product”¹⁷

For the purposes of this article, the focus will be on therapeutic proteins. Humira is an excellent example of a therapeutic protein, as it illustrates the structural and manufacturing complexity of biologics, as well as both their economic and medical value. It is the leading treatment for rheumatoid arthritis and has garnered 16 billion dollars in sales as of 2016.¹⁸ In context of technical complexity, the active molecule in Humira has a molecular weight of 144,190.3 g/mol, while

¹² Allen M. Sokal & Bart A. Gerstenblith, *The Hatch-Waxman Act: Encouraging Innovation and Generic Drug Competition*, FINNEGAN: CURRENT TOPICS IN MEDICINAL CHEMISTRY (2010), <https://www.finnegan.com/en/insights/the-hatch-waxman-act-encouraging-innovation-and-generic-drug.html>.

¹³ Donald Chisum, *Chisum on Patents 161* (Matthew Bender & Company, Inc. 2017).

¹⁴ Ralph A. Lewis, *The Emerging Effects of the Drug Price Competition and Patent Term Restoration Act of 1984*, 8 J. CONTEMP HEALTH L. & POL’Y 361, 361-78 (1992); Luke M. Olson & Brett W. Wendling, *The Effect of Generic Drug Competition on Generic Drug Prices During the Hatch-Waxman 180-Day Exclusivity Period*, FTC BUREAU OF ECONOMICS (Apr. 2013), <https://www.ftc.gov/sites/default/files/documents/reports/estimating-effect-entry-generic-drug-prices-using-hatch-waxman-exclusivity/wp317.pdf>.

¹⁵ *Orphan Drugs Lead 2015 Approvals*, BIOTECHPRIMER (Jan. 7 2016), <https://weekly.biotechprimer.com/orphan-drugs-drive-fda-approval-record-for-2015/>.

¹⁶ *How do Drugs and Biologics Differ?*, BIOTECHNOLOGY INNOVATION ORGANIZATION, <https://www.bio.org/articles/how-do-drugs-and-biologics-differ>.

¹⁷ 42 U.S.C § 262(i)(1).

¹⁸ Alex Philippidis, *The Top 15 Best-Selling Drugs of 2016*, GENETIC ENGINEERING & BIOTECH NEWS (Mar. 6, 2017), <https://www.genengnews.com/the-lists/the-top-15-best-selling-drugs-of-2016/77900868>.

another recent blockbuster drug named Sovaldi (which treats Hepatitis C) has a molecular weight of 529.5 g/mol, which is typical of small molecules.¹⁹ This 1000 factor difference is salient because it underscores the critical value of manufacturing techniques for large molecule drugs.²⁰ A talented chemist can look at a small molecule compound and work backwards from the structure to form a synthesis pathway of discrete steps that is different from that of the innovator's steps.²¹ In contrast, large molecules can only be assembled by biological processes by living cells, usually by genetically engineering bacteria and optimizing their environment in highly selective ways.²² Recombinant DNA technology has been used to engineer various kinds of specialized tissues to produce the required drugs en masse.²³ This results in a situation where a generic manufacturer is far more likely to infringe on an innovator's patented manufacturing techniques when producing a biologic than a small molecule.

Because of how much more complicated both structures and production techniques are in biologics, the regulatory mechanisms meant to stimulate generic manufacturing under the Hatch-Waxman Act are inadequate.²⁴ The cost of developing a biologic is currently estimated to be \$2.5 billion (doubling in the last ten years alone)²⁵, whereas generic manufacture is estimated to only cost \$100-250 million.²⁶ This cost differential results in both parties willing to engage in costly and exceptionally time consuming patent suits, resulting in drugs getting to market far more slowly than they otherwise would. Thus, it became necessary to pass legislation aimed specifically at the increased complexity found in biologics, resulting in the BPCIA.

¹⁹ See Christopher A. Lipinski, *Lead- and drug-like compounds: the rule-of-five revolution*, 1 DRUG DISCOVERY TODAY: TECHNOLOGIES, 337-341 (2004).

²⁰ *Small Molecule Versus Biological Drugs*, GENETICS AND BIOSIMILARS INITIATIVE (Jun. 29, 2012), <http://www.gabionline.net/Biosimilars/Research/Small-molecule-versus-biological-drugs>.

²¹ See generally Brown et. al, *Organic Chemistry* (4th ed. 2005).

²² Thomas Morrow & Linda Hull Felcone, *Defining the Difference: What Makes Biologics Unique*, NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION (Sep. 4, 2004), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3564302/>.

²³ *Id.*

²⁴ Martha M. Rumore, *The Hatch-Waxman Act - 25 Years Later: Keeping the Pharmaceutical Scales Balanced*, PHARMACY TIMES (Aug. 15, 2009), <http://www.pharmacytimes.com/publications/supplement/2009/genericsupplement0809/generic-hatchwaxman-0809>.

²⁵ Rick Mullin, *Cost to Develop New Pharmaceutical Drug Now Exceeds \$2.5B*, SCIENTIFIC AMERICAN (Nov. 24, 2014), <https://www.scientificamerican.com/article/cost-to-develop-new-pharmaceutical-drug-now-exceeds-2-5b/>.

²⁶ Erwin Blackstone & Joseph Fuhr Jr., *The Economics of Biosimilars*, NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION (Sep. 2013), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4031732/>.

B. BPCIA—abbreviated approval pathway

Much like the Hatch-Waxman Act, the BPCIA offers an abbreviated approval pathway for biologics that are meant to act as cheaper replacements for biologics already on the market. For small molecules, generic products contain the identical chemical element as the drug innovator's product. In biologics, the active element must be relatively similar to the original product but does not have to have *identical* physical properties. The BPCIA categorizes biologics into two classes: biosimilar and interchangeable.²⁷

To receive biosimilar status, a manufacturer must prove that the compound in question is “highly similar to the reference product notwithstanding minor differences in clinically inactive components . . .”²⁸ and that there is “no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.”²⁹ To achieve this, data must be derived from analytical studies of the material itself as well as clinical studies, which include immunogenicity, pharmacokinetics, and pharmacodynamics.³⁰ These clinical studies must sufficiently show “safety, purity, and potency in 1 or more appropriate conditions of use for which the reference product is licensed and intended to be used and for which licensure is sought for the biological product”³¹ Essentially, a generic manufacturer must prove chemical and clinical similarity so as to show no meaningful difference when compared to the reference material. Additionally, the mechanism of action must be the same if that mechanism is known, the route and dosage must be the same, and the production facilities must meet safety standards.³²

Once these requirements have been met, a drug is given biosimilar status. This means that it may be marketed as an equivalent treatment as the reference product, but a patient's health care provider must take action to switch a patient onto the newly marketed generic.³³ This leads to the second tier of similarity, codified in the BPCIA as “interchangeable.”³⁴ Once a drug has satisfied the requirements to be interchangeable with its reference product, it may be switched with the

²⁷ 42 U.S.C. § 262(i)(2).

²⁸ 42 U.S.C. § 262(i)(2)(A).

²⁹ 42 U.S.C. § 262(i)(2)(B).

³⁰ 42 U.S.C. § 262(k)(2)(A)(i)(I).

³¹ DONALD O. BEERS & KURT R. KARST, *GENERIC AND INNOVATOR DRUGS: A GUIDE TO FDA APPROVAL REQUIREMENTS* 21-1 (8th ed. 2017)

³² 42 U.S.C. § 262(k)(2)(A)(i)(II); 42 U.S.C. § 262(k)(2)(A)(i)(III); 42 U.S.C. § 262(k)(2)(A)(i)(IV); 42 U.S.C. § 262(k)(2)(A)(i)(V).

³³ 42 U.S.C. § 262(i)(3).

³⁴ *Id.*

reference product without any action by the prescribing health care provider, making it more akin to a small molecule generic.³⁵

To be given interchangeable status, a product must first satisfy all of the biosimilarity requirements outlined above.³⁶ After this, an applicant must show that if a “product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product.”³⁷ Essentially, the risks associated with switching from original to generic must be no greater than the risks of the original drug alone. This criterion is critical for drugs that require long term administration as opposed to single dose drugs used to treat acute conditions.

C. *The Patent Dance*

The BPCIA laid out a mechanism by which the RPS and biosimilar applicants could resolve patent disputes. This mechanism, dubbed the “patent dance,” consists of a series of steps between the RPS, which is the party that owns the drug being used as a reference material for a biosimilar, and the abbreviated Biologic License Application (“aBLA”) applicant going through several rounds of information exchange. This dance is aimed at narrowing the scope of the eventual patent litigation, preemptively cutting down on costly and time consuming discovery and helping deliver drugs to patients more quickly and at a lower cost.³⁸

The patent dance involves two stages, the first having seven major steps:

Stage 1:

1. Applicant files aBLA with FDA, creating an “artificial” infringement.
2. Within 20 days of the FDA accepting their drug for review, a new drug applicant notifies the RPS of their plans to release a biosimilar, confidentially discloses their FDA application for the drug, and confidentially discloses their manufacturing information.
3. Within 60 days of (1), RPS then identifies patents it could

³⁵ *Id.*

³⁶ 42 U.S.C. § 262(k)(4)(A).

³⁷ 42 U.S.C. § 262(k)(4)(B).

³⁸ Joanna Brougher, *The Biosimilars Act: Promoting or Discouraging the Development of Generic Biologics?*, NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION (2010), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3008392/>.

reasonably assert against the applicant (based on applicant's disclosures), as well as RPS' own willingness to license those patents.

4. Within 60 days of (2), applicant responds with explanations of why their product does not infringe upon identified patents, why RPS' claims are invalid, or why they are unenforceable. Alternatively, applicant may state that it will not begin commercial marketing until the listed patents expire.
5. Within 60 days of (3), RPS provides a rebuttal to applicant's claims of non-infringement, invalidity, or unenforceability. After applicant's receipt of the rebuttal, the parties have a period of 15 days to negotiate in good faith as to which patents should be the subject of an infringement suit.
6. If the parties agree on which patents to litigate over, RPS files suit over those patents within 30 days of the agreement. But if parties fail to agree within 15 days of starting negotiations, then they simultaneously exchange a list of patents that each party believes should be the subject of the infringement suit.
 - a. After negotiations fail but before the actual exchange of lists of patents, the applicant has to inform RPS of the number of patents it intends to list. RPS's list of patents cannot exceed this number, unless applicant lists no patents, in which case RPS may list one.
7. If the parties simultaneously exchange lists, then RPS has 30 days to file infringement claims on each of the patents on the exchanged lists. Applicant then notifies FDA of the suit within 30 days of service and provides a copy of the complaint.

Stage 2:

1. Applicant provides RPS a notice of commercial marketing ("NCM") no later than 180 days before the date it seeks to market their biosimilar.³⁹

II. ANALYSIS

Unsurprisingly, a contingent of biotech companies have taken each other to court over their respective engagements with the process outlined above. The following analysis looks first at outstanding issues

³⁹ 42 U.S.C. § 262(l).

that still need resolution, and second, at issues that have been resolved without addressing secondary problems.

The first major issue, recently decided by the Supreme Court, is whether parties are obligated to engage with the patent dance at all.⁴⁰ Dependent on this initial engagement issue, is the additional issue of whether an applicant can send its NCM to the RPS prior to FDA approval.⁴¹ Finally, the issue of whether parties have to engage in the patent dance to its completion or may engage in selective steps is addressed.⁴²

A. *Amgen v. Sandoz* – is the patent dance required, and when are NCMs filed?

Of the numerous legal strategies that have arisen since the passage of the BPCIA, one of the most adventurous has been the idea that the patent dance is merely one legal avenue that a party may pursue, but is not required. This strategy has been put into play by several companies, spurring varied judicial responses. Of this group, *Amgen Inc. v Sandoz Inc.* has made its way to final judgment at the Supreme Court of the United States, with the decision being rendered in June 2017.⁴³

1. Background

Amgen has been on the forefront of BPCIA litigation on a variety of issues, but some of the most pivotal decisions have come from Amgen's dispute with Sandoz over Sandoz's proposed usage of the BPCIA to gain streamlined FDA approval for a generic version of Amgen's Filgrastim.⁴⁴ This widely profitable drug is used to treat chemotherapy side effects and has been on the market since 1991.⁴⁵ In October 2014, Amgen filed a complaint, alleging that Sandoz had filed an aBLA with the FDA to take advantage of the shorter approval pathway, but had refused to provide Amgen with a copy.⁴⁶ Additionally, the complaint stated that Sandoz had sent Amgen an NCM prior to FDA approval of the application.⁴⁷ Amgen sought injunctive relief to force Sandoz to comply with the parameters of the

⁴⁰ Complaint at 2, *Amgen Inc. v. Sandoz Inc. et al*, No. 14-CV-04741 (9th Cir. Mar. 23, 2015).

⁴¹ *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1667-8 (2017).

⁴² *Janssen Biotech, Inc. v. Celltrion Healthcare Co.*, 239 F. Supp. 3d 328, 332 (2017).

⁴³ *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1668-9 (2017).

⁴⁴ *Filgrastim, Tbo-filgrastim*, DRUGS (Nov. 11, 2016), <https://www.drugs.com/monograph/filgrastim-tbo-filgrastim.html>.

⁴⁵ *Id.*

⁴⁶ Complaint at 2, *Amgen Inc. v. Sandoz Inc. et al*, No. 14-CV-04741 (9th Cir. Mar. 23, 2015).

⁴⁷ *Id.*

BPCIA.⁴⁸ Amgen initially filed suit and lost in the Northern District of California, then appealed the ruling in the United States Court of Appeals for the Federal Circuit, which made its way to the Supreme Court shortly thereafter.

2. Issues

The issues raised by Amgen's complaint are two-fold. The first issue is that by refusing to provide Amgen with a copy of the aBLA sent to the FDA, Sandoz was refusing to engage in the patent dance, and it was Amgen's position that such engagement was mandatory and could be enforced via injunctive relief.⁴⁹ The second issue was whether an NCM could be issued prior to FDA approval of an application, as this would cut short the otherwise required 180-day continued exclusivity period that a patent holder keeps between generic approval and first commercial marketing.⁵⁰

3. Supreme Court Decision

The Court held that federal injunctive relief was unavailable as a means of enforcing the patent dance, but remanded the case back to the circuit court to determine if state injunctive relief is a valid alternative.⁵¹ Furthermore, the Court held that an applicant did not have to wait for FDA approval to send an RPS the required NCM.⁵²

a. aBLA Disclosure

21 U.S.C. §262(l)(2)(A) states that an applicant "shall provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k)"⁵³ The circuit court held that the list of remedies available for artificial infringement found in §271(e)(4) (which does not contain injunctive relief) was the exhaustive list.⁵⁴ While this led to the correct conclusion, the Supreme Court found this to be the incorrect reasoning. It explained §271(e)(4) only applies to artificial infringement, and that the positive act of handing over the aBLA was what created that artificial infringement.

⁴⁸ *Id.* at 23.

⁴⁹ *Id.* at 2.

⁵⁰ *Id.* at 23.

⁵¹ *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1668-9 (2017).

⁵² *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1680 (2017).

⁵³ 21 U.S.C. §262(l)(2)(A).

⁵⁴ *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347, 1352 (2015).

The failure to give the aBLA meant no artificial infringement occurred, making §271(e)(4) inapplicable.⁵⁵

The Court also held that aBLA handover is not enforceable by federal injunction because of the text found in §262(l)(9)(C), which states that if an applicant fails to provide the aBLA to the RPS, then the RPS has a cause of action under 28 U.S.C. §2201 for declaration of infringement, validity, or enforceability for the patents involved in the biologic or its manufacture.⁵⁶ What this means is that an RPS can file a declaratory judgment action against an applicant for artificial infringement. This gives the RPS control over the scope and timing of litigation that the applicant would otherwise possess, but more importantly, it deprives the applicant of the power to be sure of its legal rights *prior* to marketing. Consequently, this position puts the applicant at risk of spending money on moving forward with commercial marketing ventures without the assurance that such marketing will be found legal in later litigation.

The Court continued to explain that the lack of any other textually specified remedy for failure to hand over the aBLA indicates that Congress intended this remedy to be the only federally available one, to the exclusion of federal injunctive relief.⁵⁷ Despite this, Amgen's original causes of actions included both BPCIA claims and state claims, such as unfair competition under California Business & Professions Code § 17200.⁵⁸ The case was remanded to the circuit court to decide whether Sandoz conduct was unlawful under state law, and whether such state law remedies are pre-empted by the BPCIA.⁵⁹ Upon review, the circuit court found that any injunctive relief provided by state law would exhibit both field and conflict preemption by the careful framework of the BPCIA erected by Congress.⁶⁰

b. aBLA Disclosure Analysis

The final result of the Supreme Court's decision poses a choice to biosimilars applicants: engage in the patent dance, or cede some control of when and what patents are litigated to the RPS. For now, this will result in a cost benefit analysis for manufacturers, which will be driven largely by business decisions.

⁵⁵ Sandoz Inc. v. Amgen Inc., 137 S. Ct. 1664, 1668-9 (2017).

⁵⁶ *Id.*; 21 U.S.C. § 262(l)(9)(C).

⁵⁷ Sandoz Inc. v. Amgen Inc., 137 S. Ct. 1664, 1677 (2017).

⁵⁸ Complaint at 2-3, Amgen Inc. v. Sandoz Inc. et al, No. 14-CV-04741 (9th Cir. Mar. 23, 2015).

⁵⁹ Sandoz Inc. v. Amgen Inc., 137 S. Ct. 1664, 1682 (2017).

⁶⁰ Amgen Inc. v. Sandoz Inc., 877 F.3d 1315, 1326 (2017).

It is worth noting an important difference in the questions that Amgen posed at the trial level and the answers that the Supreme Court supplied. Amgen's disclosure claim was functionally comprised by two questions: (1) is aBLA disclosure "required," and (2) is injunctive relief available for violation of that requirement? Yet, the Court's response was to the question "is injunctive relief available for violations of the required aBLA disclosure?" The Court deftly avoided answering the direct question of whether aBLA disclosure is "required" in the sense that it is unlawful to refuse to do so, or whether it is simply a "condition precedent."⁶¹ The Court stated: "[w]e decline to resolve this particular dispute definitively because it does not present a question of federal law."⁶² It continued on to explain that a federal court's job in this situation was to determine whether the aBLA had been supplied to the RPS, and if not, to allow the RPS to file a declaratory judgment action, per §262(1)(9)(C).⁶³ A ruling on whether the aBLA disclosure is mandatory or conditional would only matter in the context of designating it as "unlawful" conduct for the purposes of other laws where specifically "unlawful" conduct is penalized.⁶⁴ (One such example is California Business & Professions Code § 17200.)

The Court then remanded the case to the circuit court to specifically decide if California law would treat noncompliance with the requirement as "unlawful," which would potentially open the door to state law remedies.⁶⁵ Despite this, the circuit court's opinion in the remanded case also manages to artfully avoid answering the direct question of whether noncompliance is "unlawful." Instead, the circuit court goes directly to the question of whether federal law in this arena pre-empts any state law, which the court affirms.⁶⁶ By deciding that no possible state remedy would be applicable due to preemption, the circuit court avoided having to answer the Supreme Court's question of the "unlawful" nature of the behavior for purposes of state law.

This result is yet another parallel with the Hatch-Waxman provisions: a company harmed by another company's actions under Hatch-Waxman cannot obtain a court order for compliance. Despite closing the door, the Court left the proverbial window open: in a footnote, the Court commented that it's holding "express[ed] no view on whether a district court could take into account an applicant's

⁶¹ *Id.* at 1678.

⁶² *Id.* at 1679.

⁶³ *Id.* at 1680.

⁶⁴ *Id.* at 1679.

⁶⁵ *Id.*

⁶⁶ *Amgen Inc. v. Sandoz Inc.*, 877 F.3d 1315, 1326-28 (2017).

violation of §262(l)(2)(A) (or any other BPCIA procedural requirement) in deciding whether to grant a preliminary injunction . . . against marketing the biosimilars.”⁶⁷ It appears that the Court left open the possibility that a district court could consider a company’s violation of aBLA disclosure as a factor in deciding to give injunctive relief during a patent infringement trial.⁶⁸ Given the quality and quantity of BPCIA litigation that has occurred, it is likely that this point will come up in future cases.

In addition to the existing legal wrangling over BPCIA requirements, one notable provision has thus far not been given a great deal of attention. §252(f) states that any person that violates the provisions of the section can be fined or imprisoned up to one year.⁶⁹ This leaves open the possibility of federal criminal charges for violations of BPCIA, as well as giving the FDA a lever upon which to rely if it decides to compel companies to comply with the statute.

c. NCM prior to FDA Approval

§262(l)(8)(A) states that an aBLA applicant will “provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product is licensed. . . .”⁷⁰ While the circuit court interpreted this language to mean that the applicant had to receive FDA licensure prior to NCM issuance, the Supreme Court disagreed.⁷¹

The Court applied a grammatical analysis to the text, holding that “‘biological product licensed under subsection (k)’ modifies ‘commercial marketing’ rather than ‘notice,’ ‘commercial marketing’ is the point in time by which the biosimilar must be ‘licensed.’”⁷² This gives the applicant full freedom on whether to submit the NCM before or after FDA approval. The Court disagreed with the circuit court’s ruling that the provision implied two separate time requirements for provision of the NCM – after FDA approval and at least 180 days before commercial sale.⁷³ “Had Congress intended to impose two timing requirements in §262(l)(8)(A), ‘it presumably would have done so expressly as it did in the immediately following’ subparagraph.”⁷⁴

⁶⁷ Sandoz Inc. v. Amgen Inc., 137 S. Ct. 1664, 1677 n.2 (2017).

⁶⁸ *Id.*

⁶⁹ 42 U.S.C. § 262(f).

⁷⁰ 42 U.S.C. §262(l)(8)(A).

⁷¹ Sandoz Inc. v. Amgen Inc., 137 S. Ct. 1664, 1680 (2017).

⁷² *Id.* at 1668.

⁷³ *Id.* at 1680.

⁷⁴ *Id.*

d. NCM Analysis

While Supreme Court's ruling on the NCM issue was based largely on grammatical analysis, the conclusion was well supported by arguments concerning Congressional intent. Specifically, whether NCM issuance was required to occur at least 180 days after FDA licensure. It is understood that FDA licensure will only occur after the end of a patent holder's exclusivity period. If the Court had decided in Amgen's favor, this would have resulted in exclusivity periods effectively becoming 12.5 years instead of 12 years. Such a change in policy is not something specifically intended by Congress, and thus supports the position that Congress did not plan for the statute to be interpreted as such.⁷⁵

e. Can companies engage in the patent dance only part-way?

While *Amgen v. Sandoz* addressed refusal to follow the BPCIA litigation pathway, other companies have attempted to hedge their bets by engaging in the patent dance, but only to the degree maximally advantageous to them. This has been the strategy adopted in numerous cases, resulting in similarly legion quantities of litigation. Unfortunately, none of these cases have been granted certiorari by the Supreme Court, so we have only district and appellate opinions upon which to rely. The two cases outlined below are instructive as to both current litigation strategies and judicial responses.

B. Janssen v. Celltrion

1. Background

In 2015, Janssen Biotech Inc. filed suit against Celltrion Inc. for, amongst other things, failure to disclose manufacturing information.⁷⁶ Celltrion handed over its aBLA application to Janssen as specified by the BPCIA, but failed to hand over the manufacturing information that is also specified in the BPCIA.⁷⁷ While the parties moved forward part way through the information exchange process, Janssen repeatedly requested the manufacturing information, and was rebuffed each time.⁷⁸ Celltrion also acquiesced to Janssen's first round list of patents to litigate, and refused to continue any further in the patent dance on

⁷⁵ *Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1680 (2017).

⁷⁶ Complaint at 2, *Janssen Biotech, Inc. v. Celltrion Healthcare Co.*, 2017 U.S. Dist. LEXIS 16303 (No. 15-CV-10698).

⁷⁷ *Id.* at 3.

⁷⁸ *Id.* at 21-23.

the theory that acquiescence to the list renders the remaining steps moot.⁷⁹

Celltrion also claimed that Janssen was required to file suit within 30 days of receiving Celltrion's acquiescence to litigate over the patents sent to them in the first round of the patent dance, with failure to do so resulting in only reasonable royalties as an available remedy.⁸⁰ Celltrion's position relied on 35 U.S.C. § 271(e)(6), which states that infringement damages under 42 U.S.C. §§ 262(l)(4) and (5)(B) are limited to reasonable royalty if the suit is filed more than 30 days after the patent dance.⁸¹ Janssen's position was that the 30-day filing requirement only applied to patents that were a result of a full patent dance, and that failure to follow the required steps meant that the 30-day requirement was not applicable, meaning Janssen could seek lost profits.⁸²

It appears that Celltrion's strategy was to set the tempo of litigation by not handing over manufacturing patents related to the aBLA, thereby limiting Janssen's "menu" of patents upon which it could dispute. When Janssen picked out a set of relevant product patents for the first round of information exchange, Celltrion simply acquiesced to Janssen's chosen patents. Because Janssen believed it had to pick patents that it had information on, and because the manufacturing information was withheld, Celltrion adroitly limited Janssen's ability to sue for the full suite of appropriate patents (or so it thought).

2. District Court Decision

Judge Wolf of the Massachusetts District Court favored Janssen's position on the issue of lost profits versus reasonable royalties being available. When discussing the reasonable royalty limitation of infringement cases resulting from a full patent dance, the court stated that "[i]t is only the patents that emerge from this negotiation and, if necessary, dispute resolution procedure that are subject to a reasonable royalty damages limitation if the patentee does not sue within 30 days of the end of this process."⁸³ Essentially, the court held that the reasonable royalty limitation only applied to patents that were an end product of the full patent dance.

⁷⁹ *Id.* at 23.

⁸⁰ *Id.*

⁸¹ 35 U.S.C. § 271(e)(6); 42 U.S.C. § 262(l)(4).; 42 U.S.C. § 262(l)(5)(B); Complaint at 23, *Janssen Biotech, Inc. v. Celltrion Healthcare Co.*, 2017 U.S. Dist. LEXIS 16303 (No. 15-CV-10698).

⁸² *Id.* at 30.

⁸³ *Janssen Biotech, Inc. v. Celltrion Healthcare Co.*, 239 F. Supp. 3d 328, 332 (2017).

The court continued on to discuss the word “shall” as used in §262(1)(4) and (5), which states that parties “shall engage in good faith negotiations . . .” and concluded that the language indicated a statutory requirement of following the steps in order to receive the benefit of limiting damages to reasonable royalties.⁸⁴

3. Analysis

This ruling was interesting in its contrast to *Amgen v. Sandoz* in the different amount of “bite” the court construes the BPCIA as having. While *Amgen*’s holding gave an RPS a relatively limited amount of leverage by giving it the power to set the tempo of litigation, this ruling gives an RPS a more specific and sharp ability to pursue far more damages in cases of non-compliance. This ruling appears to punish non-compliance more concretely.

C. *Amgen v. Hospira*

1. Background

In a parallel litigation to *Janssen v. Celltrion*, Amgen filed suit in 2015 against Hospira Inc., claiming that Hospira had failed to provide adequate manufacturing information in conjunction with its aBLA disclosure to Amgen.⁸⁵ It should be noted that Hospira’s response was that the required information was part of its aBLA disclosure.⁸⁶ The parties continued on with the patent dance, resulting in an infringement suit for a set of patents connected to drug production methods. Amgen went on to assert that Hospira’s refusal to hand over information in connection with a cell culture medium used in their production process prevented Amgen from “assess[ing] the reasonableness of asserting claims for infringement” during the required rounds of information exchange.⁸⁷ Amgen sought discovery to remedy the situation, as contemplated and allowed in the Supreme Court reviewed decision of *Amgen v. Sandoz*.⁸⁸ The district court found that Hospira had to produce the required information only insofar as it was relevant to the existing claims of infringement, and not on the much broader basis of BPCIA requirements not tied to specific claims.⁸⁹ Based on this

⁸⁴ *Id.*

⁸⁵ Complaint at 3, *Amgen Inc. v. Hospira, Inc.*, 232 F. Supp. 3d 621 (No. 15-cv-00839-UNA).

⁸⁶ *Amgen Inc. v. Hospira, Inc.*, 866 F.3d 1355, 1357 (2017)

⁸⁷ *Id.* at 1358.

⁸⁸ *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347, 1356 (2015); Discovery Request at 1-2, *Amgen Inc. v. Hospira, Inc.*, 232 F. Supp. 3d 621 (No. 15-cv-00839-RGA).

⁸⁹ Discovery Transcript at 40-41, *Amgen Inc. v. Hospira, Inc.*, 232 F. Supp. 3d 621 (No. 15-cv-00839-RGA).

analysis, the district court ruled against Amgen, stating that the sought information was not relevant to the claimed infringements.⁹⁰

2. Circuit Court Decisions

Unsurprisingly, Amgen appealed this ruling.⁹¹ In a decision handed down after the Supreme Court's ruling in *Amgen v. Sandoz*, the circuit court looked to five possible avenues that Amgen could pursue to compel disclosure of process information related to §262(1)(2)(A).⁹²

- (1) Injunctive relief as a matter of federal law to enforce compliance with the mandates set out in the BPCIA.⁹³
- (2) Injunctive relief as a matter of state law.⁹⁴
- (3) Filing suit for patent infringement on the basis of failure to comply with the disclosures of §262(1)(2)(A).⁹⁵
- (4) Filing suit on patents actually described in §262(1)(3), which are the ones that the RPS believes could reasonably be asserted in the post-patent dance litigation.⁹⁶
- (5) Filing suit on a patent that *could be* identified under §262(1)(3).⁹⁷

Per *Amgen v. Sandoz*, option (1) was explicitly shut down.⁹⁸ Option (2) was also shut down several months later when, on remand, the circuit court found no state remedies available for violations of the BPCIA due to pre-emption.⁹⁹ Option (3) was also non-viable because *Amgen* held that a failure to disclose information was not an act of artificial infringement, therefore allowing for no cause of action in that regard.¹⁰⁰ As to options (4) and (5), Amgen did not list patents connected to cell culture mediums in its information exchanges, nor did it bring suit on those patents as ones that “could be identified” under §262(1)(3)(A).¹⁰¹

⁹⁰ *Id.*

⁹¹ Discovery Appeal Motion at 1, *Amgen Inc. v. Hospira, Inc.*, 232 F. Supp. 3d 621 (No. 15-cv-00839-RGA).

⁹² *Amgen Inc. v. Hospira, Inc.*, 866 F.3d 1355, 1360 (2017).

⁹³ *Id.*

⁹⁴ *Id.*

⁹⁵ *Id.*

⁹⁶ *Id.* at 1361.

⁹⁷ *Id.*

⁹⁸ *Id.* at 1360.

⁹⁹ *Id.*

¹⁰⁰ *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347, 1355 (2015).

¹⁰¹ *Id.* at 1361.

Amgen eschewed the above options in favor of a more novel approach. It filed suit for infringement on the patents positively established by the patent dance, then filed motions for discovery of information in connection with the cell culture medium that Hospira refused to provide manufacturing information for.¹⁰²

In its opinion, the court looked to *Amgen v. Sandoz* to inform its analysis. Starting with the baseline that discovery is ruled by the Federal Rules of Civil Procedure, the court found that discovery for the requested information would be inappropriate because it was not “relevant to any party’s claim or defense.”¹⁰³ The composition of the cell culture media was not connected to infringement on the patents specified in the complaint, nor any defenses raised by Hospira. Amgen argued that withholding such information during the patent dance gives an applicant unilateral power to decide which patents would be litigated by preventing the RPS from identifying ones related to the product that the RPS believes could reasonably be asserted. This is exactly the situation outlined in *Janssen v. Celltrion* above.

The court was not persuaded, pointing out that the BPCIA penalizes applicants who refuse to exchange information by removing the applicant's power to file suit for declaratory judgment, which was one of the central holdings of *Amgen v. Sandoz*. Moreover, the court underscored the Federal Rules of Civil Procedure Rule 11 requirement of filing claims that “will likely have evidentiary support after a reasonable opportunity for further investigation or discovery.”¹⁰⁴ On this basis, “if a sponsor forms a belief based on an inquiry limited by an applicant's withholding of information, the sponsor has still satisfied Rule 11.”¹⁰⁵ The result was that Amgen should have filed all complaints it believed might reasonably be borne out by discovery, instead of limiting its complaints and then using discovery to give grounds for amending the complaints.

3. Analysis

The result of this holding, if upheld, is deeply uncertain. On one hand, it correctly punishes actors that benefit themselves by using the BPCIA’s abbreviated approval pathway but refuse to abide by its litigation curtailing patent dance.

On the other hand, overly zealous RPS actors may see this ruling as a *carte blanche* to engage in the full patent dance, and then

¹⁰² *Amgen Inc. v. Hospira, Inc.*, 866 F.3d 1355, 1359 (2017).

¹⁰³ Fed. R. Civ. P. 26(b)(1); *Amgen Inc. v. Hospira, Inc.*, 866 F.3d 1355, 1362 (2017).

¹⁰⁴ Fed. R. Civ. P. 11(b)(3).

¹⁰⁵ *Amgen Inc. v. Hospira, Inc.*, 866 F.3d 1355, 1362 (2017).

subsequently file suit for additional patents on the grounds of some modicum of belief that discovery will yield new ones worth litigating. Applicants may fear this exact result, driving them further away from a willingness to engage in the patent dance at all, ultimately demeaning its purpose of reducing litigation times to get affordable drugs to patients more quickly.

IV OVERALL CONSIDERATIONS

The results of *Amgen v. Sandoz* and cases citing it may be instructive in the coming years of biosimilar related litigation. Now that the Court has established that the patent dance is optional, applicants are given the power to choose between sharing all required information, or giving the RPS power to file for declaratory judgments or standard patent infringement suits. This leads to less certainty for RPS actors since they will never know what option an applicant will take ahead of time, putting the onus of litigation preparedness on innovators. Furthermore, the BPCIA was meant to curtail endless patent infringement litigation. By de-clawing the BPCIA of federal injunctive relief as an option and allowing patent infringement litigation as a viable alternative, this purpose is at least partially thwarted. The Act itself was the result of 4 years of negotiation, and while maxims of statutory construction cannot be ignored, it seems that the result here upsets an already delicate balance of interests.¹⁰⁶

Moreover, the attitude of “add it to the complaint and hope you can get discovery on it” is contrary to the spirit of the BPCIA, since this runs against the purpose of creating more transparency to reduce litigious gamesmanship. Minimizing one party’s information harms its ability to prepare accordingly and act as a maximally informed rational actor, unnecessarily generating more risk and cost.

CONCLUSION

On the whole, the gamesmanship on display in the above outlined cases ultimately harm the consumer. The BPCIA was designed to reduce the time and cost of litigation, ensuring generic biologics reach market as quickly as possible while protecting patent holder rights, consequently balancing the profit motive of innovators and the downward pressure on costs for consumers. Instead of abiding by the rules, both sides have taken advantage of arguably unclear statutory drafting. This has hurt consumers in both cost and time: the colossal

¹⁰⁶ 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, 816-18 (2010).

legal fees associated with major litigation will no doubt be passed to consumers, and injunctions set by courts with pending cases have slowed the release of generics.

While drug prices have been a major political talking point in recent years, it is unclear whether anyone is willing to spend political capital on legislative action aimed at fixing the statutory language of the BPCIA. Thus far, it seems that balancing interests of innovators and consumers remains within legislative rather than judicial expertise. While maxims of statutory construction are a vital tool of interpretation, it appears that their use has thwarted the original purpose of the text to which they apply, ultimately to the nation's detriment. This is a lesson legislators need to remember as they continue working towards solutions that benefit all the stakeholders in the pharmaceuticals industry.