The Biologics Price Competition and Innovation Act: "Do You Wanna Dance?"[1]

by Richard A. Catalina Jr.

In 2010, as part of the Patient Protection and Affordable Care Act (commonly referred to as Obamacare), Congress enacted the Biologics Price Competition and Innovation Act of 2009 (BPCIA).[2] Quoting Winston Churchill, the United States Court of Appeals for the Federal Circuit (CAFC) has referred to the BPCIA as "a riddle wrapped in a mystery inside an enigma."[3] Indeed, the BPCIA is a complex statutory regime that established an abbreviated pathway for regulatory approval of follow-on biological products that are either interchangeable (identical) or "highly similar" (*i.e.*, biosimilars) to a previously approved product (reference product).[4] The intent of the statute is to establish "a biosimilar pathway balancing innovation and consumer interests."[5]

While the BPCIA provides a pronounced abbreviated regulatory pathway for interchangeable biologics and biosimilars that is similar in goals and procedures to the Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Act),[6] the statute further provides a unique patent dispute resolution process involving patent-covered biologics. This complex, multi-phased process, which requires mutual cooperation between the parties, is affectionately known as 'the patent dance.'

"The Dance"[7]

In order to obtain a Food and Drug Administration (FDA) license of a pioneer biological product, an applicant must establish that its biologic is "safe, pure, and potent."[8] Similar to obtaining FDA approval for generic drugs under Hatch-Waxman, the BPCIA establishes an "abbreviated biologics licensing application" (aBLA) process for a product sufficiently similar to the reference product without requiring the aBLA applicant to repeat all of the work of the pioneer applicant, referred to in the statute as the "reference product sponsor" (RPS).[9] Under the abbreviated pathway, an aBLA applicant may obtain a license by demonstrating, among other things, that its product is biosimilar to the reference product. In an attempt to "balance innovation and consumer interests,"[10] the BPCIA prescribes that an aBLA "may not be submitted" until four years after the reference product was first licensed *and*

that a biosimilar-product license "may not be made effective" until 12 years after the reference product was first licensed.[11] In addition, the aBLA applicant must provide the RPS at least 180 days' notice before commercially marketing its "licensed" product.[12]

First Dance[13]

The tempo of the patent dance moves into high gear when an aBLA is submitted to the FDA.[14] Within 20 days after the FDA notifies the applicant that its aBLA has been accepted for review, the applicant is to give notice to the RPS by providing the sponsor with the aBLA, as well as information describing the manufacturing process for the biosimilar.[15] Within 60 days of receiving that notice, the RPS is to provide a list of patents that could reasonably be asserted against the applicant and specify those patents that it would be prepared to license to the applicant.[16] Within 60 days after receiving the list, the applicant is to respond with a detailed statement identifying why each patent on the RPS's list is invalid, unenforceable, or not infringed, or declaring that it does not intend to commercially market the biosimilar product before a particular patent expires, and also addressing the RPS's statement of readiness to license.[17] In its response, the applicant *may* also provide its own list of patents it believes could reasonably be asserted against it.[18] Then, within 60 days of receiving the applicant's response, the RPS is to provide a detailed reply regarding those patents on its initial patent list as to which the applicant has asserted non-infringement, invalidity, or unenforceability.[19]

While the RPS may later supplement its original patent list,[20] it is the original lists by both parties that form the basis of the next steps in the process that may lead to immediate first-stage litigation. That process requires the RPS and the applicant enter into good-faith negotiations regarding which listed patents will be the subject of an immediate infringement action.[21] If the parties reach agreement, the RPS must bring an action for infringement on all such patents within 30 days,[22] and the aBLA applicant must then notify the FDA.[23]

If the parties fail to reach an agreement within 15 days of starting their negotiation, the BPCIA requires them to continue in a process that would limit the scope of potential first-stage litigation.[24] The aBLA applicant first provides the RPS with the number of patents the applicant believes should be litigated.[25] That number effectively caps how many patents each party may designate on its list of patents to be litigated, and the parties exchange their lists. If the applicant claims zero patents should be litigated, the RPS may *only list one*.[26] Within 30 days of exchanging their lists, the RPS must sue for infringement on precisely those patents that appear on the combined lists,[27] and the applicant must notify the FDA.[28] Notably, the litigation is limited to *a single patent* if the applicant lists no patents, no matter how many patents the RPS designated in its original list of patents that would be infringed by the proposed biosimilar product.[29]

Given the ambitious scheduling deadlines and the time commonly taken for FDA review, any first-stage infringement litigation would likely be initiated before the FDA licenses the aBLA applicant's biosimilar product. The first-stage litigation also allows the applicant to exclude potentially meritorious patents from that litigation. To overcome these obstacles, the BPCIA patent dance provides for a second stage of patent litigation.

"Last Dance"[30]

As noted, the aBLA applicant must provide the RPS a 180-day notice before commercially marketing its 'licensed' product.[31] As the BPCIA contemplates, after receiving the notice—but before the applicant's commercial marketing begins—the RPS may seek a preliminary injunction in a second stage of patent litigation based on any patent that appeared in *any* of the original lists exchanged by the parties (either by way of initial agreement or by way of the "narrowing process"), minus those patents that were already the subject of a first-stage litigation.[32] In addition, the RPS may include additional patents that were issued to or exclusively licensed by the RPS sponsor *after* it gave the applicant its original list (non-listed patents).

Additionally, if the applicant gives timely notice to the RPS by providing the sponsor with the aBLA, as well as information describing the manufacturing process upon notification by the FDA that the application has been accepted for review,[33] then neither the RPS nor the applicant may bring a declaratory judgment action based on any non-listed patent prior to the date on which the RPS receives the 180-day notice of commercial marketing.[34] The statute permits the RPS to seek declaratory relief in the event that the applicant fails to comply with certain provisions of the "patent dance."[35]

Participating in the patent dance under the BPCIA involves more moves than the tango, salsa and bachata combined. No wonder there has been some hesitancy to hit the dance floor. There are, however, some early court decisions that have clarified the "riddle wrapped in a mystery inside an enigma" of the patent dance.

"I Can't Dance"[36]

In *Sandoz Inc. v. Amgen Inc. et al.*,[37] recently decided by the U.S. Supreme Court, applicant Sandoz notified RPS Amgen that the FDA had accepted for review Sandoz's aBLA application, and that it would commence commercial marketing of the biosimilar product immediately upon FDA approval—whenever that may be.[38] Sandoz refused

to provide Amgen with its aBLA or other relevant information, and its notice of commercial marketing was only a general notice—not specific to a date and not directed to a biosimilar product that had received actual licensure from the FDA.

The two issues before the Court in *Sandoz* were: 1) whether §262(l)(2)(A)'s requirement that an applicant provide the RPS with its aBLA and manufacturing information is enforceable by an injunction under either federal or state law, and 2) whether an applicant must provide notice *after* the FDA licenses its biosimilar, or if it may also provide effective notice *before* licensure.[39]

The Court held that an injunction under federal law is not available to enforce the disclosure requirements under the BPCIA.[40] After engaging in a comprehensive analysis of the interplay between the patent dance of the BPCIA and the amendments to the patent statute to implement that statutory regime, the Court concluded that when an applicant fails to comply with the disclosure requirements, the BPCIA authorizes the RPS[41] to bring an immediate declaratory judgment action for artificial infringement as defined in the patent statute.[42] In such event, the BPCIA, therefore, vests in the RPS the control that the applicant would otherwise have exercised over the scope and timing of the patent litigation.[43] It also deprives the applicant of the certainty that it could have obtained by bringing a declaratory judgment action prior to marketing its product. The BPCIA, therefore, provides a specific remedy to RPS, of which injunctive relief is excluded.[44]

While the Court in *Sandoz* concluded that the BPCIA does not permit injunctive relief against an applicant for failing to provide the required disclosures, the Court left open the door regarding whether state law may permit that equitable remedy. The Court remanded the matter to the Federal Circuit for a determination of whether California state law would allow injunctive relief.[45]

As to the second issue, the Court held that the applicant may provide notice either before or after receiving FDA approval.[46] The BPCIA requires that the applicant give notice at least 180 days before the date of first commercial marketing of a licensed biological product.[47] Because the term "licensed" modifies the phrase "commercial marketing" rather than "notice," "commercial marketing" is the point in time by which the biosimilar must be "licensed." As such, the statute's use of the word "licensed" merely reflects the fact that, on the "date of the first commercial marketing," the product must be "licensed."[48] Under this interpretation, the applicant may provide notice either

before or after receiving FDA approval.

"Dancing Machine"[49]

In *Amgen Inc. v. Apotex Inc.*,[50] the CAFC revisited the issue of whether an aBLA applicant could avoid the 180-day commercial marketing notice requirement. In this case, however, applicant Apotex did provide the RPS with its aBLA and the additional required information, and the parties engaged in a first-stage dance, resulting in an infringement action filed by Amgen. Yet, as in the prior matter before the CAFC, Apotex merely provided Amgen with a "general notice" of its intended commercial marketing activities without specifying a date or a licensed product. In the infringement litigation, Amgen sought and obtained a preliminary injunction against Apotex, compelling it to provide a (8)(A) notice if and when it receives a license from the FDA, and to delay any commercial marketing for 180 days from that notice. The court granted the injunction, and Apotex appealed.

The CAFC affirmed.[51] First noting that the appeal does not involve the merits of the infringement allegations, the court emphasized that RPS's motion for a preliminary injunction concerned what will happen *if and when* the FDA licenses Apotex's proposed biosimilar product. The court rejected Apotex's distinction, holding that the "commercial-marketing provision is mandatory and enforceable by injunction even for an applicant [that has otherwise properly performed the dance]."[52]

In *AbbVie Inc. v. Amgen Inc.*,[53] RPS AbbVie filed an infringement action against aBLA applicant Amgen regarding AbbVie's reference product Humira® (adalimumab). According to the complaint, the underlying technology of Humira® involves more than 100 issued U.S. patents, 61 of which AbbVie identified in its initial list.[54] Unable to agree on the patents to be litigated, the parties proceeded to the 'scope narrowing' phase of the dance and ultimately agreed upon 10 patents to litigate, all of which were the subject of the filed complaint.

In the complaint, AbbVie further alleged that Amgen failed to confirm that it intended to comply with the 180-day notice requirement of commercial marketing, and asserted a claim seeking to compel Amgen to comply and to enjoin Amgen from launching its product until 180 days after Amgen provided the appropriate notice under (8)(A). In its responsive pleading to the complaint, Amgen asserted that it intended to fully comply with its obligations under BPCIA concerning the 180-day notice as interpreted by the CAFC in *Amgen v. Sandoz* and *Amgen v. Apotex*. Amgen's biosimilar product (adalimumab) has since been approved. A 20-day bench trial is scheduled for Nov. 4, 2019.

The statutory requirement that the aBLA applicant provide a 180-day notice of commercial marketing of a licensed biosimilar to the RPS surfaced again in the matter of *Amgen Inc., et al v. Hospira, Inc.*[55] In *Hospira*, RPS Amgen, maker of the reference product Epogen® (epoetin alfa), filed an infringement action against aBLA applicant Hospira. Hospira provided a purported notice of commercial marketing, which Amgen alleged was legally defective under the BPCIA. In the first count of its infringement complaint, Amgen sought a declaratory judgment that Hospira's refusal to provide proper notice of commercial marketing violates the BPCIA. Before answering the complaint, Hospira filed a motion to dismiss the declaratory judgment claim, arguing that the BPCIA does not provide a private cause of action regarding the notice requirement.

The district court denied Hospira's motion, finding that the rationale of *Apotex, supra*, applied with equal force to the declaratory judgment claim asserted by Amgen.[56] Placing substance over form, the court noted that seeking a declaratory judgment on the issue is tantamount to seeking a preliminary injunction, stating "Plaintiffs explicitly request 'a declaration of its rights under the statute and injunctive relief requiring [Defendant] to provide [Plaintiffs] with legally effective notice of commercial marketing…'Absent the availability of declaratory relief, Plaintiffs would simply seek an injunction."[57]

In *Immunex Corp., et al v. Sandoz Inc., et al*,[58] there was a dance, but not as the BPCIA instructs. In *Immunex*, a matter venued in the District of New Jersey, the aBLA application was filed for a biosimilar to Immunex's[59] Enbrel® (etanercept) product. On or about 20 days after the FDA accepted the aBLA for review, Sandoz provided RPS Immunex with remote access to a Sandoz-hosted database of thousands of TIFF images purporting to comprise the aBLA and additional required information. Immunex claimed the material failed to fully comply with the BPCIA requirements but, nevertheless, provided Sandoz with a list of patents for which a claim of infringement could be reasonably asserted based on the aBLA's etanercept product. Sandoz responded by "stating that it no longer wished to follow the strictures of the BPCIA," and insisted Immunex file an action for patent infringement within 30 days. Sandoz also provided Immunex with additional information relating to the manufacturing process of its biosimilar product.[60]

In light of the circumstances, Immunex filed an immediate first-stage infringement action, asserting five patents. Sandoz has agreed not to commercially launch its product, although the date has not been made publically available. A bench trial is scheduled before Judge Claire C. Cecchi, D.J., for April 17, 2018.

"Dancing in the Dark"[61]

In yet another matter involving Amgen and Sandoz, *Sandoz Inc. v. Amgen Inc.*,[62] Sandoz filed an action against

Amgen and Hoffman-LaRoche seeking a declaratory judgment that their two patents are invalid and unenforceable, and will not be infringed if Sandoz uses, offers to sell or sells, or imports a drug product that is biosimilar to Amgen's Enbrel® (etanercept) product. At the time it filed suit, however, Sandoz had not (and had not at the time the CAFC issued its opinion) filed its aBLA for its contemplated product with the FDA, and had only just begun certain testing required for the filing. Having no reason to delve into the "riddle wrapped in a mystery inside an enigma" of the BPCIA, the CAFC affirmed the dismissal of the matter by the district court on the basis that Sandoz did not allege an injury of sufficient immediacy and reality to create subject matter jurisdiction.[63]

"Dancing with Myself"[64]

By the year 2020, biologics are estimated to account for nearly 25 percent of the world's pharmaceutical sales.[65] Currently, biologics account for eight out of the world's top 10 best-selling drugs.[66] Yet, the exponential complexity of large molecule biologic pharmaceuticals—and their research, development and commercialization—as compared to small molecule chemical drugs, necessarily translates into more complex patents and resolution of patent infringement claims related to such biotechnology.

The common idiomatic expression "it takes two to tango"[67]—in which more than one person or other entity is paired in an inextricably related and active manner—exemplifies the BPCIA patent dance. While the BPCIA provides a complex, mechanical approach to resolving patent disputes involving biologics, the few litigation matters arising under the statute have shown a modicum of flexibility regarding the nature of the dance. Applicants are afforded the lead in first-stage litigation, but should they refuse to fully participate, the sponsor's rights are fully protected for potential second-stage litigation. In addition, a sponsor must be provided at least 180 days' notice by the applicant before commercial marketing of a licensed biosimilar, so the reference product sponsor may initiate second-stage infringement litigation regarding any and all claims it wishes to pursue that have not yet been determined, and seek the necessary injunctive relief.

Whether the BPCIA and its patent resolution process will accomplish the legislation's objective of providing a "biosimilar pathway balancing innovation and consumer interests" for biologics as successfully as the Hatch-Waxman Act did for small-molecule chemical pharmaceuticals has yet to be determined. Indeed, it may take a decade of regulatory action and infringement litigation to draw any reasoned conclusion. Until then, reference product sponsors and biosimilar applicants have a sophisticated dance—"a riddle wrapped in a mystery inside an enigma"—to follow, with the courts providing necessary guidance to the best of their ability. ⚖

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ENDNOTES

1. Title of the hit song by the Ramones from their 1977 album *Rocket to Russia*. Originally titled "Do You Want to Dance," the song was written and recorded in 1958 by American R&B singer Bobby Freeman. The song was subsequently recorded by a number of artists, including the Beach Boys, who released it as a single on Feb. 15, 1965. It peaked at number 12 on the *Billboard* Hot 100 and was the highest-charting Beach Boys song to feature Dennis Wilson on lead vocals. The arrangement used by the Ramones borrowed heavily from the Beach Boys, albeit with a hard-driving punk delivery punctuated by the distinctive lead vocals of Joey Ramone (Jeffrey Ross Hyman).
2. Pub. L. No. 111-148, §§7001–7003, 124 Stat. 119, 804–21 (2010).
3. *Amgen Inc. et al. v Sandoz Inc.*, 794 F.3d 1347, 1351(Fed. Cir. 2015), note 1.
4. 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*.).
5. BPCIA, Pub. L. No. 111-148, §7001(b), 124 Stat. at 804.
6. Pub. L. No. 98-417, 98 Stat. 1585 (1984).
7. "The Dance" was written and composed by Tony Arata and recorded by Garth Brooks as the 10th and final track from his 1990 self-titled debut album, *Garth Brooks*. The song was also released as the album's fourth and final single in April 1990. It is considered by many to be Brooks' signature song. In a 2015 interview with Patrick Kielty of BBC Radio 2, Brooks credits the back-to-back success of both "The Dance" and its follow up "Friends in Low Places" for his success.
8. 42 U.S.C. §262(a)(2)(C)(i)(I) (hereinafter, all citations to 42 U.S.C. §262 omit "42 U.S.C.").
9. §262(l)(1)(A).
10. Pub. L. No. 111-148, §7001(b), 124 Stat. at 804.
11. §262(k)(7)(A), (B).
12. §262(l)(8)(A).
13. The "first dance" is an element in a number of traditions, being an opening of a certain dance function, *e.g.*, ball, prom, wedding, etc.
14. *See, generally*, §262(l).
15. §262(l)(2)(A).
16. §262(l)(3)(A).
17. §262(l)(3)(B)(ii), (iii).
18. §262(l)(3)(B)(i).
19. §262(l)(3)(C).
20. §262(l)(7).
21. §262(l)(4)(A).
22. §262(l)(6)(A); *see also* 35 U.S.C. §271(e)(2)(C)(i).
23. §262(l)(6)(C).
24. §262(l)(4)(B).
25. §262(l)(5)(A).

26. §262(l)(5).

27. §262(l)(6)(B).

28. §262(l)(6)(C).

29. §262(l)(5)(B)(ii)(II).

30. "Last Dance" is a song by Donna Summer from the soundtrack album to the 1978 film *Thank God It's Friday*. "Last Dance" became a critical and commercial success, winning the Academy and Golden Globe Award for Best Original Song, the Grammy Award for Best Female R&B Vocal Performance, and peaking at number three on the *Billboard* Hot 100 chart, all in 1978.

31. §262(l)(8)(A).

32. § 262(l)(8)(B).

33. §262(l)(2)(A).

34. §262(l)(9)(A).

35. §262(l)(9)(B)–(C).

36. "I Can't Dance" is the fourth track from the 1992 Genesis album *We Can't Dance* and was the second single from the album. The song peaked at number seven on both the U.S. *Billboard* Hot 100 and the UK Singles Chart, and received a Grammy Award nomination for Best Pop Performance by a Duo or Group with Vocals in 1993.

37. *Sandoz Inc. v Amgen Inc., et al.*, Slip Opinion, Nos. 15–1039 and 15–1195, 582 U. S. ___ (2017) (decided June 12, 2017).

38. Sandoz's Zaraxio™ (filgrastim-sndz) product was the first biologic approved under the BPCIA and was approved as a biosimilar of Amgen's Neupogen® (filgrastim) product.

39. Slip opinion at 1-2.

40. Slip opinion at 12-13.

41. §262(l)(2)(A), §262(l)(9)(C).

42. 35 U.S.C. §271(e)(2)(C)(ii).

43. §262(l)(9)(C).

44. Slip opinion at 12 ("The remedy provided by §262(l)(9)(C) excludes all other federal remedies, including injunctive relief.").

45. *Id*. at 15.

46. *Id*. at 16.

47. §262(l)(8)(A).

48. *See* §262(a)(1)(A).

49. "Dancing Machine" was recorded by The Jackson 5, and released as a single in 1974. "Dancing Machine" hit No. 1 in *Cash Box* and reached No. 2 on the *Billboard* Hot 100. In addition, the song hit No. 1 on the R&B charts and *Billboard* ranked it as the No. 5 song for 1974. "Dancing Machine" brought The Jackson 5 their second Grammy Award nomination in 1975 for Best R&B Performance by a Duo or Group with Vocals, losing to Rufus and Chaka Khan's "Tell Me Something Good."

50. *Amgen Inc., et al v. Apotex Inc., et al*, No. 2016-1308, CAFC (Slip Opinion dated July 5, 2016).

51. *Id.* at 3, 25.

52. *Id.* at 4.

53. *AbbVie Inc., et al v. Amgen Inc., et al*, No. 1:16-666 (D. Del.).

54. AbbVie provided Amgen with a nearly 1,500-page statement claiming that Amgen's biosimilar product would infringe more than 1,100 claims of 60 AbbVie patents. Complaint, ¶42.

55. *Amgen Inc., et al v. Hospira, Inc.*, No. 15-839 (D. Del.) (Slip Opinion dated Aug. 5, 2016).

56. *Id.* at 6.

57. *Id.* (citations omitted).

58. *Immunex Corp., et al v. Sandoz Inc., et al*, No. 2:16-1118 (D.N.J.).

59. While Immunex Corporation was acquired by Amgen Inc. in 2002, it is the first named plaintiff in this litigation. The other named plaintiffs are Amgen Manufacturing, Limited and Hoffmann-LaRoche Inc.

60. *Immunex Corp., et al v. Sandoz Inc., et al, supra*, Complaint, ¶61 (Feb. 26, 2016).

61. "Dancing in the Dark" was written and performed by Bruce Springsteen on his iconic 1984 album *Born in the U.S.A.* The song spent four weeks at number two on the *Billboard* Hot 100 and sold over one million singles in the U.S. alone. As the first single released from the album, "Dancing in the Dark" became his biggest hit. *Born in the U.S.A.* is Springsteen's best-selling album.

62. *Sandoz Inc. v. Amgen Inc., et. al*, No. 2014-1693(CAFC) (Slip Opinion dated Dec. 5, 2014).

63. *Id.* at 2.

64. "Dancing with Myself" was written by singer Billy Idol and bassist Tony James, and first recorded by their band Generation X in 1979. The song failed to achieve success. In late 1981 Idol, now a solo artist, remixed and re-released "Dancing with Myself" as a single in the U.S., incorporating a milder sound and more danceable beat. The release became his first hit in America and propelled him into a 1980's pop icon.

65. *Wall Street Journal*, China Emerges as Powerhouse for Biotech Drugs, April 10, 2017.

66. *Id. citing* Frost & Sullivan.

67. The tango is a dance that requires two partners moving in relation to each other, sometimes in tandem, sometimes in opposition.