No. __-____

IN THE
Supreme Court of the United States

APOTEX INC. AND APOTEX CORP.,
Petitioners,

v.

AMGEN INC. AND AMGEN MANUFACTURING LIMITED,
Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR A WRIT OF CERTIORARI

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QUESTIONS PRESENTED

Congress enacted the Biologics Price Competition and Innovation Act ("BPCIA") to create an expedited pathway for the approval of more affordable, life-saving "biosimilar" drugs, which are an important, but very expensive, new class of medical products. The BPCIA seeks to balance the interests of innovation and cost competition for these multi-billion dollar products by creating a framework for efficiently resolving patent disputes between a maker of a biologic drug product (referred to in the statute as a "reference product sponsor") and a would-be competitor who seeks permission to market a "biosimilar" drug product, including in the provision concerning "notice of commercial marketing," 42 U.S.C. § 262(*l*)(8)(A).

The Court of Appeals for the Federal Circuit, however, upended Congress's careful balance when it held that (1) all biosimilar applicants are required to provide a "notice of commercial marketing," even when doing so cannot advance the resolution of patent disputes, and (2) no biosimilar applicant may provide such notice before receiving a Food and Drug Administration ("FDA") license for its biosimilar product. Those holdings improperly extend by 180 days the 12-year exclusivity period Congress granted to reference product sponsors. *See* 42 U.S.C. § 262(*l*)(8)(A).

The questions presented are:

1. Whether the Federal Circuit erred in holding that biosimilar applicants that make all disclosures necessary under the BPCIA for the resolution of patent disputes (*viz.* 42 U.S.C. § 262(*l*)(2)(A)) must also provide the reference

product sponsor with a notice of commercial marketing under 42 U.S.C. § 262(*l*)(8)(A).

2. Whether the Federal Circuit improperly extended the statutory 12-year exclusivity period to 12½ years by holding that a biosimilar applicant cannot give effective notice of commercial marketing under 42 U.S.C. § 262(*l*)(8)(A) for its biosimilar product until it receives an FDA license and therefore may not commercially market its biosimilar product for 180 days after receiving its license.

CORPORATE DISCLOSURE STATEMENT

Pursuant to Rule 29.6 of the Rules of this Court, petitioners Apotex Inc. and Apotex Corp. state the following:

Apotex Inc. is an Ontario corporation and is wholly owned by Apotex Pharmaceuticals Holdings Inc. ("APHI"), which itself is wholly owned by Apotex Holdings, Inc. ("AHI"). Both APHI and AHI are Ontario corporations. Apotex Corp. is a Delaware corporation and is ultimately wholly owned by AHI. Neither Apotex Inc., Apotex Corp., APHI, nor AHI is a publicly traded company.

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Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, §§ 7001-7003, 124 Stat. 119, 804-21 ..... *passim*

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Safe and Affordable Biotech Drugs: The Need for a Generic Pathway: Hearing Before the H. Comm. on Oversight and Gov't Reform, 110th Cong. (2007) 17

Senate Comm. on Health, Education, Labor & Pensions, Press Release, *Lawmakers Praise Committee Passage of Biologics Legislation* (June 27, 2007), *available at* http://www.help.senate.gov/ranking/newsroom/press/lawmakers-praise-committee-passage-of-biologics-legislation 16

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Comment of the Staff of the Federal Trade Comm'n to Food & Drug Admin. (Oct. 27, 2015), *available at* https://www.ftc.gov/system/files/documents/advocacy_documents/ftc-staff-comment-submitted-food-drug-administration-response-fdas-request-comments-its-guidance/151028fdabiosimilar.pdf 4, 24, 25

Ctrs. for Medicare & Medicaid Servs.:

National Health Expenditures 2014 Highlights (Dec. 2015), *available at* https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/PieChartSourcesExpenditures2014.pdf 23

The Nation's Health Dollar ($3.0 Trillion), Calendar Year 2014, Where It Went (Dec. 2015), *available at* https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/highlights.pdf 23-24

Food and Drug Admin., *Memorandum re: Exclusivity Expiry for Neupogen (filgrastim) BLA 103353* (June 26, 2014), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/125553Orig1s000AdminCorres.pdf 14

Letter from John E. Dicken, Health Care Dir., GAO, to Hon. Orrin G. Hatch, Ranking Member, S. Comm. on Fin. (Jan. 31, 2012) 25

Office of Mgmt. & Budget, Exec. Office of President, *Fiscal Year 2014: Budget of the U.S. Government* (Apr. 2013), 2013), *available at* http://www.whitehouse.gov/sites/default/files/omb/budget/fy2014/assets/budget.pdf 26-27

OTHER MATERIALS

Amgen Inc., Annual Report (Form 10-K), *available at* https://www.sec.gov/Archives/edgar/data/318154/000031815416000031/amgn-12312015x10k.htm 24-25

Erwin A. Blackstone & Joseph P. Fuhr, Jr., *The Economics of Biosimilars*, 6 Am. Health & Drug Benefits 469 (Sept./Oct. 2013), *available at* http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4031732/pdf/ahdb-06-469.pdf 26

Krista H. Carver, *et al.*, *An Unofficial Legislative History of the Biologics Price Competition and Innovation Act of 2009*, 65 Food & Drug L.J. 671 (2010), *available at* https://www.cov.com/-/media/files/corporate/publications/2010/01/an-unofficial-legislative-history-of-the-biologics-price-competition-and-innovation-act-of-2009.pdf 15, 16, 19, 22

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Steve Miller, Senior V.P. & Chief Med. Officer, Express Scripts, Presentation at FTC Biosimilars Workshop: *Customer Perspective on Biosimilars* (Feb. 4, 2014), *available at* https://www.ftc.gov/system/files/documents/public_events/Follow-On%20Biologics%20Workshop%3A%20Impact%20of%20Recent%20Legislative%20and%20Regulatory%20Naming%20Proposals%20on%20Cometition/miller.pdf 3, 4, 24

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Apotex Inc. and Apotex Corp. (collectively, "Apotex") respectfully petition for a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit in this case.

INTRODUCTION

This case presents fundamental questions affecting the cost and availability of biologic "miracle medicines" to the public. The Biologics Price Competition and Innovation Act ("BPCIA") – part of the Patient Protection and Affordable Care Act of 2010 – was intended to strike a balance between encouraging price competition within this important and rapidly growing category of expensive specialty pharmaceuticals and incentivizing the development of new drugs. To do so, the BPCIA regulates two types of biologics: branded reference products and generic biosimilars. To save lives – and billions of dollars in public and private funds – the BPCIA helps to speed biosimilar medicines to market, and it facilitates the resolution of patent disputes between biosimilar applicants and reference product sponsors.

In the decision below, the Federal Circuit extended by 180 days the amount of time a biosimilar applicant must wait before marketing its product – even when the brand-name producer has all of the information it needs from the biosimilar applicant to determine whether to challenge the applicant's product. The court ruled that no biosimilar applicant may provide such notice before receiving a Food and Drug Administration ("FDA") license for its biosimilar product, even as the court recognized that the FDA has never approved a biosimilar applicant prior to the expiration of the 12-year period of exclusivity enjoyed by the branded reference. That extension confers a half-year market exclusivity period to the

brand-name producer that can be worth billions of dollars in biologics' sales.

In this case and the pending case, *Sandoz Inc. v. Amgen Inc.*, No. 15-1039 (filed Feb. 16, 2016), in which this Court has called for the views of the Solicitor General, this Court has a unique opportunity to review the errors of the Federal Circuit's statutory construction in the two distinctive factual scenarios contemplated by the BPCIA: one is this case, in which petitioner Apotex provided all the information needed for Amgen to make a determination as to whether to challenge Apotex's product on patent infringement grounds; and the other is *Sandoz*, in which the biosimilar applicant decided *not* to provide that information to the brand-name manufacturer. Erring in both cases, the Federal Circuit has contorted the patent resolution procedures established by the BPCIA.

In so doing, the Federal Circuit has upset the careful balance between biologic price competition and innovation negotiated by Congress. The Circuit-manufactured 180-day extension of the period of exclusivity conferred by Congress to brand-name manufacturers has anticompetitive effects, prolongs the collection of monopoly rents, and bolsters already-troublesome barriers to entry for biosimilars. The Federal Circuit's judicially-crafted alteration to the BPCIA, therefore, presents an issue of national importance.

Because the Federal Circuit has now decided the crucial statutory construction issues, this Court will not have another opportunity to correct that court's error in the context of multi-billion dollar biologics markets. That fact confirms the urgency of this Court granting certiorari now.

OPINIONS BELOW

The opinion of the court of appeals (App. 1a-27a) is reported at --- F.3d ---, 2016 WL 3606770. The order of the district court (App. 28a-37a) is not reported.

JURISDICTION

The court of appeals entered its judgment on July 5, 2016. The jurisdiction of this Court is invoked under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

Relevant provisions of the Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, 124 Stat. 119, are set forth at App. 76a-109a.

STATEMENT OF THE CASE

A. Statutory Background

1. Biologics are large-molecule drugs that are produced in living organisms. Some biologics are "miracle medicines" with the capacity to help patients suffering from serious diseases in ways that traditional medicines now available cannot. *Examining Food and Drug Administration Follow-On Biologics: Hearing Before the Sen. Comm. on Health, Education, Labor, and Pensions*, 110th Cong. 1 (2007) (hereinafter "*Examining Food and Drug Administration Follow-On Biologics*") (opening statement of Sen. Kennedy). Consequently, a tremendous market has developed for biologics. In 2010, four of the ten top-selling branded drugs worldwide were biologics. *See* Steve Miller, Senior V.P. & Chief Med. Officer, Express Scripts, Presentation at FTC Biosimilars Workshop: *Customer Perspective on Biosimilars* 3 (Feb. 4, 2014) (hereinafter "Miller, *Customer*

Perspective on Biosimilars").[1] Industry experts estimate that seven of the ten top-selling branded drugs this year are likely to be biologics. *Id.*

Yet biologics are also tremendously expensive. The cost of a biologic drug is on average 22 times higher than the cost of a traditional chemical or small-molecule medication. *See* Comment of the Staff of the Federal Trade Comm'n to Food & Drug Admin. 3 (Oct. 27, 2015) (hereinafter "FTC Comment").[2] And the cost keeps rising – increasing on average 10-15% each year. *See id.* In fact, the average price of biologics doubled from 2006 to 2012. *See id.*

In 2010, Congress acted to accelerate the availability of cheaper, generic versions of these expensive, branded medicines. Toward that end, Congress guaranteed the branded companies a 12-year period of exclusivity, before which the FDA cannot grant a biosimilar drug an effective license via the pathway set forth in the BPCIA. *See* 42 U.S.C. § 262(k)(7)(A). But to promote competition and prevent the high cost of biologics from further increasing the costs of health care, Congress in the BPCIA also established an abbreviated pathway for the regulatory approval of biologics that are "highly similar" to a branded reference product. *Id.* § 262(i)(2).

2. Section (k) of the BPCIA provides that, to obtain approval via the abbreviated pathway, a biosimilar applicant must submit to the FDA an abbreviated

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[1] *Available at* https://www.ftc.gov/system/files/documents/public_events/Follow-On%20Biologics%20Workshop%3A%20Impact%20of%20Recent%20Legislative%20and%20Regulatory%20Naming%20Proposals%20on%20Competition/miller.pdf.

[2] *Available at* https://www.ftc.gov/system/files/documents/advocacy_documents/ftc-staff-comment-submitted-food-drug-adminabiosimilar.pdf.

Biologics License Application ("aBLA"). *See id.* § 262(k). An aBLA relies, in part, on the branded drug company's FDA-approved license of the reference product. *See id.* The branded drug company is therefore known as the "reference product sponsor" or, simply, the "sponsor." *See id.* § 262(*l*)(1)(A).[3]

Section (*l*) of the BPCIA establishes a framework for the efficient resolution of patent disputes between the reference product sponsor and the biosimilar applicant. Twice, the statute offers the applicant the opportunity to streamline patent disputes by sharing critical information with the sponsor. And in each case, the statute offers the sponsor recourse in the event the applicant chooses not to do so.

First, under paragraphs (*l*)(2)-(*l*)(5) of the BPCIA, the parties may exchange information concerning the aBLA and those patents the sponsor reasonably believes may be infringed, thereby ultimately arriving at a list of patents subject to an immediate action for infringement per the terms of paragraph (*l*)(6). The exchange is to begin "not later than 20 days after the Secretary notifies the . . . applicant that the application has been accepted for review," by which time an applicant who elects to engage in the information exchange must "provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k), and such other information that describes the process or processes used to manufacture the biological product that is the subject of such application." 42 U.S.C. § 262(*l*)(2)(A). In the event the applicant does not provide the sponsor with that information,

[3] The various provisions of 42 U.S.C. § 262(*l*) that are the subject of this brief may be referred to as "paragraph (*l*)__" throughout.

paragraph (*l*)(9)(C) provides the sponsor with a remedy: "If a subsection (k) applicant fails to provide the application and information required under paragraph (2)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28 for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product."

Second, under paragraph (*l*)(8)(A), the applicant may "provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k)." If the applicant gives notice, then the sponsor may seek an injunction under paragraph (*l*)(8)(B): "After receiving the notice under subparagraph (A) and before such date of the first commercial marketing of such biological product, the reference product sponsor may seek a preliminary injunction prohibiting the subsection (k) applicant from engaging in the commercial manufacture or sale of such biological product until the court decides the issue of patent validity, enforcement, and infringement with respect to any patent" that was described as relevant during the information exchange outlined in paragraph (*l*)(3) and that is not already the subject of litigation. In the event the applicant does not give notice, paragraph (*l*)(9)(B) provides a remedy: "If a subsection (k) applicant fails to complete an action required of the . . . applicant under . . . paragraph (8)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28, for a declaration of infringement, validity, or enforceability of any patent" submitted to be relevant during the

information exchange described in paragraphs (*l*)(2)-(*l*)(5), including any newly issued patent deemed relevant.

3. The Federal Circuit first had occasion to interpret the BPCIA in *Amgen, Inc. v. Sandoz, Inc.*, 794 F.3d 1347 (Fed. Cir. 2015), *petition for cert. filed*, No. 15-1039 (U.S. Feb. 16, 2016). There, the biosimilar applicant Sandoz elected not to provide the information specified in paragraph (*l*)(2)(A).

The Federal Circuit held that Sandoz was not required to do so, confirming that the information exchange described in paragraphs (*l*)(2)-(*l*)(5) is optional and that paragraph (*l*)(9)(C) provides an appropriate remedy to the reference product sponsor in the event that a biosimilar applicant elects not to engage in the information exchange. *See id.* at 1357. The Federal Circuit also held that an applicant that chooses not to engage in the information exchange must provide to the sponsor the notice of commercial marketing described in paragraph (*l*)(8)(A). *See id.* at 1360. And it held that such an applicant could provide that notice of commercial marketing only after the issuance of the FDA license for its biosimilar product. *See id.* at 1358.

B. Procedural Background

1. In 2002, Amgen received a license for a brand-name biologic with the active ingredient pegfilgrastim, which provides health benefits to patients undergoing chemotherapy. App. 3a. Amgen's 12-year BPCIA-guaranteed exclusivity period for its brand-name biologic has thus expired. *Id.*

In October 2014, Apotex applied for an FDA license to market a biosimilar pegfilgrastim product in accordance with the BPCIA. App. 3a, 11a. On December 15, 2014, the FDA accepted Apotex's application

for review. App. 11a. Within 20 days, Apotex provided Amgen with a copy of its application and the other information specified in paragraph (*l*)(2)(A). Thereafter, Apotex and Amgen engaged in the exchange of patent information contemplated by paragraphs (*l*)(3)-(*l*)(5). During that exchange, Amgen stated that it held three relevant patents. App. 11a-12a. Apotex initially responded that it would commercially market its biosimilar product only after two of those three patents expired, and that the third patent, which expires in 2031, was invalid and would not in any case be infringed by the marketing of Apotex's biosimilar product. App. 11a. In addition, Apotex attempted to provide Amgen with the notice of commercial marketing described in paragraph (*l*)(8)(A) by sending Amgen a letter containing the notice. App. 11a-12a. Ultimately, the parties agreed to litigate all unexpired patents, of which there is currently only one remaining. *Id.*

2. On August 2, 2015, Amgen filed its complaint in the United States District Court for the Southern District of Florida. Amgen sought a declaration that Apotex violated paragraph (*l*)(8)(A) of the BPCIA "by not providing Amgen with an effective notice of commercial marketing after the Apotex Pegfilgrastim Product is licensed by FDA and at least 180 days before Apotex begins commercial marketing of the Apotex Pegfilgrasim Product." CAFC J.A. 56.

Amgen then sought, and the district court granted, a preliminary injunction prohibiting Apotex from commercially marketing its biosimilar product until 180 days after first receiving its FDA license and then providing a new notice of commercial marketing. App. 13a-14a. Apotex appealed the district court's grant of a preliminary injunction. App. 15a.

3. On appeal, the Federal Circuit discounted the significant factual distinctions between this case and *Sandoz* – namely, that Apotex faithfully engaged in the information exchange precipitated by the paragraph (*l*)(2)(A) disclosures and that all relevant patents had thereby already become the subject of litigation in an efficient manner. The Federal Circuit decreed, *first*, that applicants are required to provide a notice of commercial marketing "whether or not a (2)(A) notice was given" and, *second*, that "[t]he (8)(A) requirement of 180 days' post-licensure notice . . . [is] enforceable by injunction." App. 15a.

Regarding the former holding, the Federal Circuit reasoned that "[t]he language of (8)(A) is categorical" because "[i]t contains no words that make the applicability of its notice rule turn on whether the applicant took the earlier step of giving the (2)(A) notice that begins the § 262(*l*) information-exchange process" and because "[t]here . . . is no other statutory language that effectively compels a treatment of (8)(A) as non-mandatory." App. 16a. The court of appeals also rejected the argument "that paragraph (9) of § 262(*l*) makes a declaratory-judgment action, discussed in (9)(B), the exclusive remedy for violations of (8)(A)." App. 21a.

Regarding the timing of the notice of commercial marketing and the injunctive relief granted to Amgen, the Federal Circuit reasoned that the BPCIA "establishes the 12-year date only as an earliest date, not a latest date on which a biosimilar license can take effect" and that, in any case, "any . . . delay beyond 12 years should occur less and less as time goes by" because "as time passes, more and more of the reference products will be newer, and a biosimilar-product applicant, entitled to file an application a

mere four years after licensure of the reference product . . . can seek approval long before the 12-year exclusivity period is up." App. 17a.

REASONS FOR GRANTING THE PETITION

The Federal Circuit's decision misreads the BPCIA's text and upsets Congress's careful balance between cost-saving competition and life-saving innovation. Congress sought to promote the former through the creation of an abbreviated pathway for the approval of biosimilar products and the latter by preserving a 12-year exclusivity period for brand-name reference product sponsors. The Federal Circuit threw up a roadblock in the abbreviated pathway by mandating that biosimilars provide a notice of commercial marketing even when doing so cannot advance the orderly resolution of patent disputes, and – adding insult to injury – it functionally extended the 12-year exclusivity period by an extra six months. Together, those errors put a thumb on the scale in favor of reference product sponsors. If not corrected, they will substantially increase Americans' health care costs and needlessly delay access to life-saving biosimilar medications. Because no other appellate court will interpret the BPCIA, this Court's review is necessary to correct the Federal Circuit's erroneous reading of the statute on a question that affects multi-billion dollar markets for a range of life-saving drugs.

I. THE FEDERAL CIRCUIT MISREAD THE BPCIA

A. The Federal Circuit's Decision Cannot Be Reconciled With The BPCIA's Text And Structure

The BPCIA does not require a biosimilar applicant to give a notice of commercial marketing if it made the disclosures set forth in paragraph (*l*)(2)(A) and fully engaged in the subsequent patent resolution framework. Under such circumstances, a notice of commercial marketing serves no purpose.

Paragraph (*l*)(8)(A) provides that a "subsection (k) applicant shall provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k)." Although the use of the word "shall" in isolation implies a mandatory obligation, the text of the statute as a whole indicates that is not the case.

The Federal Circuit recognized as much in *Sandoz*. There, the court held that, although the BPCIA repeatedly directs that an applicant "shall" take certain actions, it is not always the case that they "must" do so. 794 F.3d at 1355. The Federal Circuit explained that "'shall' in paragraph (*l*)(2)(A) does not mean 'must'" because, among other provisions, paragraph (*l*)(9)(C) "explicitly contemplates that a subsection (k) applicant might fail to disclose the required information by the statutory deadline" and provides a consequence for the applicant's failure to do so. *Id.* at 1355-56.

That same logic applies with full force in the present case. Paragraph (*l*)(9)(B) provides a remedy to sponsors in the event that an applicant elects not to provide the notice of commercial marketing described

in paragraph (*l*)(8)(A): "*If a subsection (k) applicant fails to complete an action required of the subsection (k) applicant under . . . paragraph (8)(A)*, the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28, for a declaration of infringement, validity, or enforceability" of those patents raised during the earlier information exchange between the parties.

If paragraph (*l*)(8)(A) were mandatory for applicants who complied with paragraph (*l*)(2)(A) and engaged in the information exchange described in paragraphs (*l*)(3)-(*l*)(5), then paragraph (*l*)(9)(B) would be superfluous – sponsors would have no need of the remedy specified therein. And this Court clearly has stated that "a statute ought, upon the whole, to be so construed that, if it can be prevented, no clause, sentence, or word shall be superfluous, void, or insignificant." *TRW Inc. v. Andrews*, 534 U.S. 19, 31 (2001) (internal quotation marks omitted).

Notwithstanding the paragraph (*l*)(9)(B) remedy, the Federal Circuit erroneously implied the existence of an atextual injunctive remedy extending the 12-year exclusivity period by 180 days based upon a purely theoretical concern over a "race to court" resulting in "the hurried motion practice that [paragraph (*l*)(8)(A)] is designed to replace by ensuring a defined amount of time for pre-launch litigation." App. 24a-25a. *First*, even if the paragraph (*l*)(8)(A) notice is mandatory, nothing in that paragraph requires that the notice post-date FDA licensure of the biological product, and pre-licensure notice would guarantee sponsors adequate time to consider their legal options. *Second*, as this case illustrates, a "race to court" is unlikely ever to come to pass. Here,

Apotex provided Amgen with a pre-licensure notice of commercial marketing that adequately informed Amgen of its intentions and thus enabled Amgen to take all steps necessary to vindicate its legal rights. *See supra* pp. 7-8. Even had it not done so, however, Apotex's disclosures pursuant to paragraph (*l*)(2)(A) gave Amgen all the information it needed to pursue an orderly defense of its patent rights, such that all relevant patents are already the subject of litigation. *See supra* pp. 7-8. Indeed, the BPCIA explicitly anticipates that the sponsor will be able to generate "a list of patents for which [it] believes a claim of patent infringement could reasonably be asserted" based upon the applicant's paragraph (*l*)(2)(A) disclosures, even if not all such patents are immediately litigated. 42 U.S.C. § 262(*l*)(3)(A).

Moreover, Amgen has now tried and lost its patent case. The district court concluded that Apotex's manufacturing process does not infringe Amgen's patent. App. 59a-67a. Thus, Amgen has exhausted its patent rights and the 180-day injunction imposed by the Federal Circuit serves no logical purpose. In this instance, the Circuit's bar will operate only to keep a non-infringing, cost-saving FDA-approved biosimilar product out of the hands of consumers for an additional six months.

The Federal Circuit's assertion that the 180-day extension of the statutory exclusivity period occasioned by its holding in this case "should occur less and less as time goes by" is also inaccurate. App. 17a. The Federal Circuit supposes that, as applicants begin to model their biosimilar products on newer reference products, they will be able to "seek approval long before the 12-year exclusivity period is up." *Id.* The court then suggests that "the

FDA may . . . issue a license before the 11.5-year mark and deem the license to take effect on the 12-year date." *Id.* But that speculation by the Federal Circuit panel finds no basis in fact: there is currently no FDA policy for licensing applicants prior to the expiration of the exclusivity period.[4] The statutory imbalance between applicants and sponsors and between cost competition and innovation can be better and more swiftly resolved by reversing the Federal Circuit's erroneous decision.

B. The Federal Circuit's Decision Cannot Be Reconciled With The Legislative History And Policy Underlying The BPCIA

The Federal Circuit read the BPCIA as having the purpose of preserving the market share of reference product sponsors. In fact, the statute was intended to balance the interests of sponsors and applicants and, more broadly, to balance the national interests in innovation and cost competition. Requiring a notice of commercial marketing in all cases and extending the 12-year exclusivity window upends Congress's intended balance.

First, requiring a notice of commercial marketing in all cases cannot be justified by reference to Congress's intent to promote the introduction of biosimilar products, including by facilitating the resolution of patent disputes arising between sponsors and biosimilar applicants.

The Federal Circuit's decision erroneously requires *all* biosimilar applicants to wait an additional 180

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[4] *See* FDA, *Memorandum re: Exclusivity Expiry for Neupogen (filgrastim) BLA 103353* (June 26, 2014), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/125553Orig1s000AdminCorres.pdf.

days before undertaking to commercially market an aBLA product, notwithstanding their voluntary participation in the statutory information exchange and patent negotiation procedures. But where, as here, an applicant has made available to the sponsor the information outlined in paragraph (*l*)(2)(A), the sponsor has all the information needed to enforce its intellectual property rights, including "a copy of the application" and "such other information that describes the process or processes used to manufacture the biological product that is the subject of such application." As such, mandating the notice of commercial marketing will in most, if not all, cases in which an applicant has provided the paragraph (*l*)(2)(A) disclosures, convey a windfall upon sponsors without providing any countervailing public benefit. In this case, for example, not only did Apotex already provide Amgen with all the information Amgen needed to determine whether to litigate its intellectual property rights, but Amgen had in fact already undertaken to litigate all relevant patents, which Apotex's product was found not to infringe. The 180 day injunction therefore serves no purpose other than to preserve Amgen's exclusive market for an additional six months.

Second, the 12-year window was a carefully negotiated compromise – a "middle ground between innovator and generic interests." Krista H. Carver, *et al.*, *An Unofficial Legislative History of the Biologics Price Competition and Innovation Act of 2009*, 65 Food & Drug L.J. 617, 817 (2010) (hereinafter "*An Unofficial Legislative History*").[5] Defining an

[5] *Available at* https://www.cov.com/-/media/files/corporate/publications/2010/01/an-unofficial-legislative-history-of-the-biologics-price-competition-and-innovation-act-of-2009.pdf.

exclusivity period that would best promote both innovation and cost-saving generic competition was a key sticking point across years of legislative negotiations. *See id.* at 724-25 (noting that exclusivity proved early on to be a "troublesome" point of disagreement). In fact, even during final negotiations over the bill, proposals under consideration included exclusivity periods as long as 14 years and as short as five to seven. *See id.* An unnecessarily lengthy, unintended, and unwarranted extension of the exclusivity period will impede access to biosimilars and add hundreds of billions of dollars in costs to consumers, employers, and publicly funded programs like Medicare and Medicaid.

Weighing the competing interests of sponsors and applicants and of innovation and cost competition, legislators emphasized the need to strike a "balance" that would "allow generic companies to do what they do best – bring low-cost versions to the market." Senate Comm. on Health, Education, Labor & Pensions, Press Release, *Lawmakers Praise Committee Passage of Biologics Legislation* (June 27, 2007),[6] (statement of Sen. Hatch). Why? Quite simply, "to lower prices and extend the availability of . . . treatments to more who need them." *Id.* (statement of Sen. Clinton). The congressional record is full of testimony from lawmakers of both parties and from others who repeatedly emphasized the importance of achieving cost savings to improve patient access.

For example, in a hearing before a Subcommittee of the House Committee on Energy and Commerce, Rep. Frank Pallone, Jr. called on Congress to

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[6] *Available at* http://www.help.senate.gov/ranking/newsroom/press/lawmakers-praise-committee-passage-of-biologics-legislation.

"produce measurable savings." *Assessing the Impact of a Safe and Equitable Biosimilar Policy in the United States: Hearing Before the H. Subcomm. on Health of the Comm. on Energy and Commerce*, 110th Cong. 2 (2007) (hereinafter "*Assessing the Impact*"). Representative Nathan Deal concurred, offering that Congress had before it "an opportunity to provide patients access to a lower cost alternative for their needed medications." *Id.* at 5. Likewise, the Vice President of Human Services at Caterpillar, a United States manufacturer, told the Senate Committee on Health, Education, Labor, and Pensions that biologic drugs accounted for an outsized and increasingly unaffordable slice of the company's health care expenses, describing the rising costs as "simply not sustainable." *Examining Food and Drug Administration Follow-On Biologics* at 11. In the same hearing, Sen. Charles Schumer acknowledged the national scope of the problem and put the potential for cost savings in perspective: "Treating a patient with a biologic drug can cost $100,000 a year, total cost to the nation, $32 billion. If introducing competition in this market lowers the price of biologics even by 10 to 25 percent, the savings are astronomical."[7] *Id.* at 6.

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[7] *See also Safe and Affordable Biotech Drugs: The Need for a Generic Pathway: Hearing Before the H. Comm. on Oversight and Gov't Reform*, 110th Cong. 2-3 (2007) (statement of Rep. Waxman) ("A new path for FDA to approve generic biologicals will save patients billions in the future and will improve access to treatments and cures. . . . For the sake of patients, their families, public and private health insurance, and taxpayers, we must find a way to introduce competition to this market. When a patent expires, we owe it to consumers to find a way through competition to lower prices and still deliver a safe and effective product."); *Assessing the Impact* at 7 (statement of Rep. Ferguson) (noting importance of both patient safety and cost savings and, in particular, pointing to expectation that

Ultimately, Congress provided for a 12-year exclusivity period that was intended to be commensurate in duration and scope to the patent protection typically afforded to innovative drugs.[8] And like patent

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"follow-on biologics will save about $3.6 billion over 10 years"); *id.* at 9 (statement of Rep. Blackburn) ("When the healthcare costs are skyrocketing, and we hear this every time we come in for a committee hearing, we know that people are looking for new options for lowering drug costs."); *id.* at 10 (statement of Rep. Capps) ("Quite frankly, with no competition on the markets, biologics remain out of economic reach for most of the people who need them. I hope to hear today from witnesses on how we can balance innovation with patients' needs for cheaper, more accessible drugs."); *id.* at 11 (statement of Rep. Solis) ("The manufacture of biologic medicines has the potential to save millions of lives, and biologics account for approximately $30 billion in sales. However, the cost of developing and manufacturing these biologics are extremely high; and the average cost of a 1-day supply of biologic medicines is $45. As a result, the cost for patients, insurers, private companies, and Government payers are quickly growing. And I am very concerned about the high cost of these medicines, especially the cost of those treatments for many who lack healthcare insurance or who are underinsured."); *id.* at 12 (statement of Rep. Wilson) ("I commend the chairman and members of his committee for their determination to tackle this issue to see whether there is something we can do so that we create a pathway for generics that might be at less cost for a new class and a new kind of therapy in the area of medicine.").

[8] *See Biologics and Biosimilars: Balancing Incentives for Innovation: Hearing Before the H. Comm. on the Judiciary*, 111th Cong. 8 (2009) (hereinafter "*Biologics and Biosimilars*") (statement of Rep. Eshoo) ("[T]o preserve the existing incentives for investment and innovation the Pathway for Biosimilars Act provides a data exclusivity period equivalent to patent protections for small molecules. The Congressional Budget Office has determined that 11.5 years is the average length of time that drugs are marketed under patent. In other words, innovative drugs and biologics typically stay on the market for about 12 years before facing competition. My legislation maintains this level of protection for biologics.").

protections, the 12-year exclusivity period is not open-ended. Indeed, the congressional sponsor of key patent resolution provisions underscored the point: "In order to protect the rights of all parties and ensure that all patent disputes involving a biosimilar are resolved *before, and I emphasi[ze] the word before*, the expiration of the data-exclusivity period, H.R. 1548 also establishes a simple, streamlined patent resolution process."[9] *Biologics and Biosimilars* at 9 (statement of Rep. Eshoo) (emphasis added); *see also Assessing the Impact* at 116 (statement of Bruce Downey, Chairman of the Board, Generic Pharmaceutical Association) ("[T]here needs to be a mechanism that allows [patent] issues to be decided before there is a launch of the product that allows both innovator and generic companies to manage the risks that they confront and . . . *also allows for the earliest lawful entry of the product and doesn't allow the litigation post-exclusivity period, post-patent to delay the launch of a product*.") (emphasis added). The Federal Circuit's assertion to the contrary undermines Congress's explicit effort to make cost-saving biosimilars available at the earliest possible date consistent with continuing innovation. *See* App. 16a-17a.

II. THIS COURT SHOULD ACT NOW TO CORRECT THE FEDERAL CIRCUIT'S MISREADING OF THE BPCIA

The BPCIA is a new law, and the Federal Circuit's decisions in *Sandoz* and in this case are the first to

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[9] The patent resolution provisions of H.R. 1548, 111th Cong. (2009), were substantially incorporated into the BPCIA's final text. *See An Unofficial Legislative History* at 802-06 (describing how patent provisions of H.R. 1548 were incorporated into final legislation).

interpret it. But the novelty of the important questions raised in this petition ought not cause this Court to defer its review of them.[10]

There will never be a circuit split concerning the meaning of the BPCIA. The Federal Circuit "has exclusive jurisdiction over appeals from all United States District Courts in patent litigation." *Cardinal Chem. Co. v. Morton Int'l, Inc.*, 508 U.S. 83, 89 (1993). Nor can this Court expect that the notice issue will further percolate in the Federal Circuit, which has now definitively indicated that *all* applicants will be required to provide a post-approval notice and to delay the commercial introduction of their biosimilar product by 180 days. Indeed, the Federal Circuit repeatedly has declined to revisit its holding that the paragraph (*l*)(8)(A) notice of commercial marketing is mandatory. *First*, the court declined to review its holding in *Sandoz* en banc. *See* Order, *Sandoz*, No. 15-1499 (Fed. Cir. Oct. 16, 2015) (per curiam). Then, in this case, the Federal Circuit declined the opportunity to distinguish its holding in *Sandoz*. It did so notwithstanding that Apotex complied with the information exchange and patent negotiation provisions of the law, and that all relevant patents identified in that process had already become the subject of litigation. If neither one of those circumstances induced the Federal Circuit to distinguish its decision in *Sandoz*, there is

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[10] In addition to this case and *Sandoz*, several other suits have already been filed under the BPCIA. *See Janssen Biotech, Inc. v. Celltrion Healthcare Co.*, No. 1:15-cv-10698 (D. Mass. filed Mar. 6, 2015); *Amgen Inc. v. Hospira, Inc.*, No. 1:15-cv-839 (D. Del. filed Sept. 18, 2015); *Immunex Corp. v. Sandoz Inc.*, No. 2:16-cv-1118 (D.N.J. filed Feb. 26, 2016); *Amgen Inc. v. Sandoz Inc.*, No. 2:16-cv-1276 (D.N.J. filed Mar. 4, 2016).

simply no set of circumstances in which it can be expected to do so.

This Court routinely has granted certiorari petitions in similar cases of national importance coming from the Federal Circuit. For example, this Court has taken cases construing the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, known more commonly as the Hatch-Waxman Act. *See*, *e.g.*, *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 132 S. Ct. 1670, 1675 (2012) (whether counterclaim provision under 21 U.S.C. § 355(j)(5)(C)(ii)(I) authorized challenge to accuracy of use code); *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 665 (1990) (whether exemption from infringement under 35 U.S.C. § 271(e)(1) applied to medical devices). Allowing the Federal Circuit's decision to stand would introduce new areas of significant uncertainty into the law. For example, if the "commercial marketing" of a biosimilar product is enjoined until 180 days after the FDA licenses that product, as the Federal Circuit has ruled, then courts can expect significant litigation regarding the scope of that injunction as pharmaceutical companies attempt to negotiate the real-world consequences of delayed launch.

III. THE COURT SHOULD GRANT THIS CASE AND THE *SANDOZ* PETITION CURRENTLY PENDING BEFORE THIS COURT BECAUSE BOTH CASES PRESENT DISTINCTIVE AND RECURRING FACT PATTERNS UNDER THE BPCIA

The Federal Circuit's decisions in *Sandoz* and in this case should be considered together. To take the full measure of the BPCIA, the Court should consider the Federal Circuit's imposition of the paragraph

(*l*)(8)(A) notice requirement and 180 day injunction in two distinctive contexts addressed in the statute: when the applicant fully engages in the information exchange precipitated by paragraph (*l*)(2)(A) (as in this case) and when the applicant does not (as in *Sandoz*). The Court has called for the views of the Solicitor General in the *Sandoz* case, and should consider this petition in conjunction with that one.

Even if the Court declines to grant the petition for certiorari in *Sandoz*, however, it should grant the petition in this case. Congress plainly expected that applicants and sponsors would engage in the information exchange and patent negotiations described in paragraphs (*l*)(2)-(*l*)(5) and (*l*)(7).[11] The Court

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[11] *See Biologics and Biosimilars* at 9 (statement of Rep. Eshoo) ("H.R. 1548 also establishes a simple, streamlined patent resolution process. This process would take place within a short window of time, roughly 6 to 8 months after the biosimilar application has been filed with the FDA. It will help ensure that litigation surrounding relevant patents will be resolved expeditiously and prior to the launch of the biosimilar product, providing certainty to the applicant, the reference product manufacturer, and the public at large. . . . Once a biosimilar application is accepted by the FDA, the agency will publish a notice identifying the reference product and a designated agent for the biosimilar applicant. After an exchange of information to identify the relevant patents at issue, the applicant can decide to challenge any patents' validity or applicability."); *id.* at 197 (statement of Teresa S. Rea, President, American Intellectual Property Law Association) ("[H.R. 1548] addresses the need for an exchange of information concerning the follow-on product to allow a preliminary infringement analysis. The notice and certification provisions in H.R. 1548 would limit the patents that may be challenged to those which the patent holder believes are infringed by the follow-on product."); *see also An Unofficial Legislative History* at 802-06 (describing how the patent provisions of H.R. 1548 were incorporated into the final legislation); *Assessing the Impact* at 116 (statement of Bruce Downey) ("I think we need to have a provision that would

should therefore evaluate the meaning of the paragraph (*l*)(8)(A) notice provision against the background actions Congress intended. That is the case here, where Apotex conscientiously engaged in the statutory information exchange, from which Amgen received all the information required to enable it to litigate its relevant patents.

IV. THIS CASE PRESENTS QUESTIONS OF SIGNIFICANT NATIONAL IMPORTANCE

The Federal Circuit's erroneous decision will substantially increase the total health care costs of the United States government and the American people, and it will delay patient access to more affordable biosimilar medicines.

Health care spending accounts for a huge part of the American economy – at least 17.5% of America's Gross Domestic Product, according to the Centers for Medicare and Medicaid Services ("CMS"). *See* CMS, *National Health Expenditures 2014 Highlights* 1, 2 (Dec. 2015).[12] And prescription drug costs in turn account for a large portion of health care spending – approximately $300 billion of $3 trillion, or 10%, again according to CMS. *See* CMS, *The Nation's*

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permit resolution of intellectual property disputes in advance of launching the product. . . . Many of these products do not have one or two patents, but 30, 40 patents and there are disagreements about whether we infringe or if they are valid, and there needs to be a mechanism that allows those issues to be decided before there is a launch of the product that allows both innovator and generic companies to manage the risks that they confront.").

[12] *Available at* https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/highlights.pdf.

Health Dollar ($3.0 Trillion), Calendar Year 2014, Where It Went (Dec. 2015).[13]

New competition between branded reference products and biosimilars can help ameliorate those rising healthcare costs: the FTC estimates that biosimilars will cost up to 30% less than brand biologic drugs. *See* FTC Comment at 5. That discount is expected to translate into major savings for consumers, including public-sector health plans and the federal government. For example, the Ohio Public Employees Retirement System anticipates that the introduction of new biosimilars will save its health plan $129 million over 10 years. *See* Joyce Frieden, *Biosimilars Hold Promise, Questions*, MedPage Today (June 21, 2016).[14] And industry estimates suggest that competition between brand biologic products and biosimilars could save Americans overall, including the federal government, as much as $250 billion by 2024. *See* Miller, *Customer Perspective on Biosimilars* at 7. Lower prices also mean better consumer access to "the most promising medicines for the treatment of a variety of medical conditions for which patients have no other alternative." FTC Comment at 2-3. In contrast, delaying the entry of a biosimilar pegfilgrastim product by six months would cost the government and health payers up to about $600 million in lost savings and impair consumer access. *See* Amgen

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[13] *Available at* https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/PieChartSourcesExpenditures2014.pdf.

[14] *Available at* http://www.medpagetoday.com/publichealthpolicy/healthpolicy/58691.

Inc., Annual Report 42 (Form 10-K) (Feb. 16, 2016);[15] FTC Comment at 5.

The Federal Circuit's decision will delay Americans' realization of those economic and medical benefits – thwarting Congress's years-long effort to close the biologics loophole in the Hatch-Waxman Act. *See FTC v. Actavis, Inc.*, 133 S. Ct. 2223, 2234 (2013).

That Act sought to ensure Americans would receive the economic and medical benefits of generic drugs by facilitating their entrance into the markets for traditional small-molecule chemical medicines. *See Caraco Pharm.*, 132 S. Ct. at 1676; *Eli Lilly & Co.*, 496 U.S. at 676. And it was successful. Following the law's enactment, a surge of cheaper generic products produced significant savings for consumers. According to the Government Accountability Office ("GAO"), the United States health care system saved more than $1 trillion from 1999 to 2010 by substituting small-molecule generic chemical drugs for their brand-name counterparts. *See* Letter from John E. Dicken, Health Care Dir., GAO, to Hon. Orrin G. Hatch, Ranking Member, S. Comm. on Fin. 4, 10 (Jan. 31, 2012).

But, "[w]hen the Hatch-Waxman law was enacted, Congress did not include biologics because at the time, such drugs were not providing the major innovations and advances . . . the biological sciences have brought over the past 20 years." *Examining Food and Drug Administration Follow-On Biologics* at 2 (statement of Sen. Kennedy). As a result, biologics remained stubbornly resistant to the cost

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[15] *Available at* https://www.sec.gov/Archives/edgar/data/318154/000031815416000031/amgn-12312015x10k.htm. Amgen's domestic sales of its pegfilgrastim product were approximately $4 billion in 2015.

competition making traditional drugs more affordable. *See* Joanna M. Shepherd, *Biologic Drugs, Biosimilars, and Barriers to Entry*, 25 Health Matrix 139, 144-46 (2015).[16]

The BPCIA thus completed a project three decades in the making: to balance cost competition and innovation for all types of pharmaceuticals. And its framework for the abbreviated approval of biosimilars is arguably even more essential to healthcare today than when the Hatch-Waxman Act was enacted in 1984. Biosimilars face significant barriers to market entry that are higher than those typically confronting small-molecule generic chemical drugs, including difficulties associated with manufacturing, marketing, storage, distribution, delivery devices, immunogenicity (*i.e.*, adverse reactions in a patient due to live organisms), and special requirements for pharmacovigilance (*i.e.*, post-sale monitoring). *See* Erwin A. Blackstone & Joseph P. Fuhr, Jr., *The Economics of Biosimilars*, 6 Am. Health & Drug Benefits 469, 471 (Sept./Oct. 2013).[17]

To ensure that Americans are able to realize the benefits of biosimilars and of continued brand-name biologic innovation, Congress specifically prescribed a 12-year period of exclusivity for brand-name reference products.[18] By extending that exclusivity

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[16] *Available at* http://scholarlycommons.law.case.edu/cgi/viewcontent.cgi?article=1021&context=healthmatrix.

[17] *Available at* http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4031732/pdf/ahdb-06-469.pdf.

[18] In fact, the President's Office of Management and Budget ("OMB") recently proposed reducing the market exclusivity period afforded to reference product sponsors from 12 years to 7 years in order to achieve $3 billion in savings over 10 years to Federal health programs including Medicare and Medicaid. *See* OMB, Exec. Office of President, *Fiscal Year 2014: Budget of*

period, the Federal Circuit's decision impedes Americans' access to life-saving biosimilar drugs and could add billions of dollars to household and government health care costs.

CONCLUSION

The petition for a writ of certiorari should be granted.

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the U.S. Government 40 (Apr. 2013), *available at* http://www.whitehouse.gov/sites/default/files/omb/budget/fy2014/assets/budget.pdf.

Respectfully submitted,

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September 9, 2016

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UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

No. 2016-1308

AMGEN INC., AMGEN MANUFACTURING LIMITED,
Plaintiffs-Appellees,
v.

APOTEX INC., APOTEX CORP.,
Defendants-Appellants.

Appeal from the United States District Court
for the Southern District of Florida
No. 0:15-cv-61631-JIC, Judge James I. Cohn.

[Decided: July 5, 2016]

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* * *

Before WALLACH, BRYSON, AND TARANTO, *Circuit Judges*.

TARANTO, *Circuit Judge*.

This appeal involves an action brought by Amgen Inc. and Amgen Manufacturing Limited (collectively Amgen) against Apotex Inc. and Apotex Corp. (collectively Apotex) under the Biologics Price Competition and Innovation Act of 2009 (Biologics Act or BPCIA). Apotex has an application pending with the Food and Drug Administration, filed under the Biologics Act, that seeks permission to begin marketing a product allegedly "biosimilar" to Amgen's FDA-approved Neulasta®. For such an applicant, the Biologics Act

lays out a step-by-step process for exchanging information and channeling litigation about patents relevant to the application. Apotex and Amgen proceeded several steps into that process, leading to the present suit in which Amgen alleges that Apotex's proposed marketing would infringe an Amgen patent.

This appeal, however, does not involve the merits of the infringement allegations. Rather, it involves Amgen's motion for a preliminary injunction concerning what will happen if and when the FDA licenses Apotex's proposed biosimilar product. Amgen sought a preliminary injunction to enforce a provision of the Biologics Act that requires a biosimilar-product applicant to give notice 180 days before commercially marketing its FDA-licensed product, 42 U.S.C. § 262(*l*)(8)(A). We held in *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347, 1357-58 (Fed. Cir. 2015), among other things, that the 180-day period runs from *post*-licensure notice. Here, the district court, agreeing with Amgen, preliminarily enjoined Apotex from entering the market unless it has given Amgen notice after receiving the requested FDA license and then waited 180 days.

We affirm. In *Amgen v. Sandoz*, we held that the commercial-marketing provision is mandatory, with the 180-day period beginning only upon post-licensure notice, and that an injunction was proper to enforce the provision against Sandoz, a biosimilar-product applicant that had entirely skipped the statutory process of information exchange and patent-litigation channeling. Apotex argues that a different result is required here—that the commercial-marketing provision is not mandatory and may not be enforced by an injunction—because it, unlike Sandoz, did launch the statutory process for

exchanging patent information and channeling patent litigation. We reject the asserted distinction. We hold that the commercial-marketing provision is mandatory and enforceable by injunction even for an applicant in Apotex's position.

BACKGROUND

Amgen markets FDA-approved Neulasta®, whose active ingredient is pegfilgrastim, a human-engineered protein that, in patients undergoing chemotherapy, can stimulate the production of neutrophils (a type of white blood cell) and thereby decrease the incidence of infection. Amgen received a biologics license from the FDA for Neulasta® in 2002 pursuant to 42 U.S.C. § 262(a). In 2014, Apotex filed an application for an FDA license to market a biosimilar version of Neulasta®, invoking the "abbreviated pathway for regulatory approval of follow-on biological products that are 'highly similar' to a previously approved product ('reference product')," as described in *Amgen v. Sandoz*, 794 F.3d at 1351. Congress created that route to FDA licensure in the Biologics Act in 2010. 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*. Apotex's application is pending.

A

When Amgen obtained its license, it had to show that its biological product, Neulasta®, was "safe, pure, and potent." 42 U.S.C. § 262(a)(2)(C)(i)(I). The Biologics Act authorizes enterprises like Apotex to gain approval, after a time, for a product sufficiently similar to the "reference product," without repeating all of the work of the pioneer, the "reference product sponsor" (defined at *id.* § 262(*l*)(1)(A)).

Under § 262(k), an applicant may obtain a license by demonstrating, among other things, that its product is "biosimilar" to a reference product. In so doing, it may use publicly available information about the reference product's safety, purity, and potency to support its application. *Id.* § 262(k)(2)(A)(i), (iii). For the purpose of "balancing innovation and consumer interests," Pub. L. No. 111-148, § 7001(b), 124 Stat. at 804, Congress prescribed that a biosimilar-product application under § 262(k) "may not be submitted" until four years after the reference product was first licensed under § 262(a) and that a biosimilar-product license "may not be made effective" until twelve years after the reference product was first licensed. 42 U.S.C. § 262(k)(7)(A), (B).

1

Of particular relevance here, the Biologics Act contains a detailed, multi-part subsection, § 262(*l*), that is focused in various ways on potential patent disputes between the reference product sponsor and biosimilar-product applicant. That subsection by its terms provides for two stages of litigation—one under paragraph (6), the other under paragraph (8). In this opinion, we will often refer to paragraphs and subparagraphs within that subsection without repeating the "§ 262(*l*)"; unless otherwise made clear, any such shorthand references are to that subsection. We also will usually call the § 262(k) applicant simply the "applicant."

The § 262(*l*) provisions of principal present significance are as follows. Under (2)(A), within 20 days after the FDA notifies the applicant that its application has been accepted for review, the applicant is to give notice to the reference product sponsor by providing the application as well as information

describing the manufacturing process. § 262(*l*)(2)(A). Under (3)(A), within 60 days of receiving that notice, the reference product sponsor is to provide a list of patents that could reasonably be asserted against the applicant and specify which it would be prepared to license to the applicant. § 262(*l*)(3)(A). Under (3)(B), within 60 days after receiving that list, the applicant is to respond with a detailed statement identifying why each patent on the reference product sponsor'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 reference product sponsor's statement of readiness to license. § 262(*l*)(3)(B)(ii), (iii). The applicant, in its response, *may* also provide its own list of patents that it believes could reasonably be asserted against it. § 262(*l*)(3)(B)(i). Under (3)(C), then, within 60 days of receiving the applicant's (3)(B) response, the reference product sponsor is to provide a detailed reply regarding those patents on its (3)(A) list as to which the applicant has asserted non-infringement, invalidity, or unenforceability. § 262(*l*)(3)(C).

While the reference product sponsor may later supplement its (3)(A) list under paragraph (7), it is the original lists under (3) that form the basis of the next steps in the process leading to immediate litigation under paragraph (6). Those steps begin with paragraph (4), which requires that the reference product sponsor and the applicant enter into good-faith negotiations over which of the patents listed under (3) will be the subject of an immediate patent-infringement action. § 262(*l*)(4)(A). If the parties reach agreement, (6)(A) provides that the reference product sponsor must bring an action for

infringement on all such patents within 30 days. § 262(*l*)(6)(A); *see* 35 U.S.C. § 271(e)(2)(C)(i). The applicant must then notify the FDA. § 262(*l*)(6)(C).

If the parties do not reach agreement within 15 days of starting their negotiation, (4)(B) directs the parties to paragraph (5) for the process that determines the scope of immediate litigation. § 262(*l*)(4)(B). That process gives the applicant a scope-limiting ability, based on an exchange of lists of patents to be litigated. The applicant tells the reference product sponsor how many patents will be on the applicant's list; that number caps how many patents the reference product sponsor may list, except that if the applicant lists none, the reference product sponsor may list one; and the two sides exchange lists. § 262(*l*)(5). Within 30 days, under (6)(B), the reference product sponsor must sue for infringement on precisely those patents that appear on the combined lists. § 262(*l*)(6)(B). And the applicant must notify the FDA. § 262(*l*)(6)(C). Notably, the immediate litigation is limited to a single patent if the applicant lists no patents, no matter how many patents the reference product sponsor designated in (3)(A) as reasonably assertable against the making, selling, etc., of the proposed biosimilar product. § 262(*l*)(5)(B)(ii)(II).

Given the deadlines set in § 262(*l*), and the time commonly taken for FDA review, we may assume that the early litigation under paragraph (6) will be initiated before the FDA licenses the applicant's biosimilar product. But the Biologics Act—having provided for a narrowing of the scope of the paragraph (6) litigation, including by allowing the applicant to exclude potentially meritorious patents

from that litigation—provides, in paragraph (8), for a second stage of patent litigation.

Paragraph (8) does so by first requiring, in (8)(A), that the applicant give the reference product sponsor notice at least 180 days before commercially marketing its "licensed" product. § 262(*l*)(8)(A). We held in *Amgen v. Sandoz* that the notice starting the 180-day clock must follow, not precede, the licensure. 794 F.3d at 1357-58. (8)(B) then declares that, after receiving the (8)(A) post-licensure notice but before the applicant's commercial marketing begins, the reference product sponsor may seek a preliminary injunction based on any patent within either of two classes. The first class, expressly described in (8)(B), consists of the patents that appeared on any of the original paragraph (3) lists, minus patents that were the subject of paragraph (6) litigation (by agreement under (4) or by the narrowing process under (5)). § 262(*l*)(8)(B). The second class consists of certain patents that were issued to or exclusively licensed by the reference product sponsor after it gave the applicant its (3)(A) list. As to those patents, paragraph (7) prescribes an information exchange and states that they "shall be subject to paragraph (8)," § 262(*l*)(7)—which evidently means that patents within (7) are to be treated as falling under (8)(B). For this second-stage litigation, (8)(C) requires that the parties reasonably cooperate to expedite new discovery needed in connection with the preliminary-injunction motion. § 262(*l*)(8)(C).

Paragraph (9) of § 262(*l*) reinforces the just-described channeling of litigation and provides incentives for the applicant to proceed in those channels. It does so by addressing when declaratory-judgment actions are or are not available in certain

circumstances—in (9)(C), as to applicants that simply bypass the process of information exchange that begins with (2)(A); and in (9)(A) and (B), as to applicants that begin but do not complete the process.

(9)(C) addresses an applicant that does not even provide the first-step notice under (2)(A). For such an applicant, the reference product sponsor, but not the applicant, may bring an action under 28 U.S.C. § 2201 for a declaratory judgment of "infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product." § 262(*l*)(9)(C). The subject of such action is not limited by reference to any patent lists.

(9)(A) and (B) together address an applicant that does provide the (2)(A) notice. (9)(A) protects the two-stage litigation scheme under paragraphs (6) and (8): it declares that neither side may bring a declaratory-judgment action relating to any patent described in (8)(B) for the second-stage litigation until after the (post-licensure) 180-day notice of commercial marketing under (8)(A) is received. § 262(*l*)(9)(A).[1] Then, (9)(B) reinforces the applicant's incentives to complete the orderly process: it specifies that the (9)(A) bar on declaratory-judgment actions is lifted for the reference product sponsor, but not for the applicant, if an applicant that has given the (2)(A) notice "fails to complete an action required" of the applicant at specified steps past the (2)(A) step. The specified applicant duties are those prescribed by paragraph (3)(B)(ii) (responding to the reference product

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[1] The Declaratory Judgment Act, 28 U.S.C. § 2201(b), states: "For limitations on actions brought with respect to drug patents see" 21 U.S.C. §§ 355, 360b and 42 U.S.C. § 262. The Biologics Act added the § 262 reference. *See* Pub. L. No. 111-148, § 7002(c)(2), 124 Stat. at 816.

sponsor's (3)(A) list); by paragraph (5) (furnishing lists defining the first-stage litigation in the absence of agreement); by paragraph (6)(C)(i) (notifying the FDA of the first-stage litigation); by paragraph (7) (responding to the reference product sponsor's update of its (3)(A) list); and by paragraph (8)(A) (providing a 180-day notice before commercial marketing of the licensed product). A failure of the applicant at any of those stages lifts the (9)(A) bar on the reference product sponsor, allowing it to bring a declaratory-judgment action on any patent on its (3)(A) list as supplemented under (7). § 262(*l*)(9)(B).

2

Besides setting out the foregoing regime, the Biologics Act amended the infringement provision of the Patent Act, 35 U.S.C. § 271, in a way that is tied to that regime. *See* Pub. L. No. 111-148, § 7002(c)(1), 124 Stat. at 815-16. As amended, 35 U.S.C. § 271(e)(2) provides that, in two circumstances, it is "an act of infringement" for a person "to submit" "an application seeking approval of a biological product" if the purpose is to obtain approval "to engage in the commercial manufacture, use, or sale of a . . . biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent." 35 U.S.C. § 271(e)(2)(C)(i), (ii). The two circumstances involve, respectively, an applicant that has launched the Biologics Act information-exchange process we have described and an applicant that has not.

Specifically, one circumstance is when the patent "is identified in the list of patents described in" paragraph (3), "including as provided under" paragraph (7), of the Biologics Act's patent provisions described above. 35 U.S.C. § 271(e)(2)(C)(i). Filing the

biosimilar application is an act of infringement of patents that the reference product sponsor has listed through the Biologics Act's prescribed processes, which occurs only when the applicant has provided the (2)(A) notice. The other circumstance involves an applicant that "fails to provide the application and information required" under (2)(A). In that case, filing the biosimilar application is an act of infringement as to a patent that "could be identified pursuant to" (3)(A), *i.e.*, a patent that the reference product sponsor could identify as one it believes "could reasonably be asserted" with respect to the biosimilar product at issue. 35 U.S.C. § 271(e)(2)(C)(ii).

35 U.S.C. § 271(e)(4) addresses remedies for such infringements. Subparagraphs (B) and (C) authorize injunctions and damages, and subparagraph (D) states that "the court shall order a permanent injunction" against infringement of a patent in certain cases decided in the Biologics Act's first-stage (paragraph (6)) litigation. 35 U.S.C. § 271(e)(4)(D). Section 271(e)(4) adds that those remedies "are the only remedies which may be granted by a court for an act of infringement described in paragraph (2)," except for attorney's fees. 35 U.S.C. § 271(e)(4).

35 U.S.C. § 271(e)(6), however, then limits the just-described remedies in two ways evidently designed to reinforce the reference product sponsor's incentives to follow the distinctive Biologics Act's patent process where the applicant has launched that process. *First*: If the reference product sponsor is late in bringing the first-stage infringement action under § 262(*l*)'s paragraph (6), *i.e.*, does so more than 30 days after the scope of that litigation has been determined under (4) or (5), the only remedy the reference product sponsor can get in that action is a reasonable royalty.

35 U.S.C. § 271(e)(6)(A), (B).[2] *Second*: If a patent that the reference product sponsor should have included on its (3)(A) list or its (7) supplement "was not timely included," then the owner of that patent may not sue for infringement under 35 U.S.C. § 271 with respect to the biological product at issue. 35 U.S.C. § 271(e)(6)(C).

B

In October 2014, Apotex filed a biologics license application with the FDA under 42 U.S.C. § 262(k), listing Amgen's Neulasta® as the reference product, and the FDA accepted Apotex's application for review on December 15, 2014. On December 31, 2014, Apotex provided Amgen a copy of the application and information detailing Apotex's pegfilgrastim manufacturing process, complying with § 262(*l*)'s paragraph (2)(A). Amgen provided Apotex its (3)(A) list on February 27, 2015, identifying three patents, and Apotex provided its (3)(B) patent-specific response on April 17, 2015. In that response, Apotex certified that it did not intend to begin commercial marketing before two of the patents had expired and, as to the remaining patent, described bases for asserting non-infringement and invalidity. The same day, Apotex sent a letter to Amgen stating that it was thereby providing notice of future commercial marketing pursuant to (8)(A), though Apotex lacked (as it still lacks) an FDA license. On June 16, 2015, Amgen furnished Apotex its (3)(C) reply regarding validity and infringement. The parties then negotiated under (4) and agreed to an immediate action under (6)(A)

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[2] The same restriction applies if the reference product sponsor timely brought a paragraph (6) action that "was dismissed without prejudice or was not prosecuted to judgment in good faith." 35 U.S.C. § 271(e)(6)(A)(ii)(II).

for infringement of the two then-extant patents; Amgen filed that action on August 6, 2015; and when one of the patents expired in October 2015, that action became about only one patent, U.S. Patent No. 8,952,138.

C

Just before that action was filed, this court decided *Amgen v. Sandoz*. The court held first that a biosimilar-product applicant cannot be compelled to provide notice of FDA review under (2)(A) and that an infringement suit under 35 U.S.C. § 271(e)(2) is the reference product sponsor's remedy if the applicant does not provide such notice. The court stressed that 35 U.S.C. § 271(e)(2)(c)(ii) declares precisely that conduct—filing an application and failing to give the (2)(A) notice—to constitute an infringement (of a patent that could have been listed under (3)(A)) and that § 271(e)(4) declares the monetary and injunctive remedies in a suit for that infringement to be the exclusive remedies for that conduct. 794 F.3d at 1354-57.

The court next addressed the (8)(A) requirement of a 180-day notice of commercial marketing. The court held that the (8)(A) notice must be a notice given after FDA licensure of the biosimilar product, not before, and that pre-licensure notices are of no legal effect for purposes of (8)(A). *Id.* at 1358. It explained that the statutory 180-day period runs from licensure, "at which time the product, its therapeutic uses, and its manufacturing processes are fixed" by licensure. *Id.* The purpose, the court explained, is to "provide[] a defined statutory window during which the court and the parties can fairly assess the parties' rights prior to the launch of the biosimilar product," the alternative being a rush in

decision-making about requesting or issuing a preliminary injunction. *Id.*; *see id.* at 1360 ("The purpose of [(8)(A)] is clear: requiring notice of commercial marketing be given to allow the [reference product sponsor] a period of time to assess and act upon its patent rights.").

The court then concluded that (8)(A) is "mandatory": "A question exists . . . concerning whether the 'shall' provision in [(8)(A)] is mandatory. We conclude that it is." *Id.* at 1359. The court added that (8)(A) is "a standalone notice provision," not dependent on the earlier information-exchange provisions. *Id.* at 1359-60. And for the case before it, involving an applicant (Sandoz) that did not provide notice of FDA review under (2)(A), and hence did not come under (9)(B), there could be no basis for finding the declaratory-judgment action referred to in (9)(B) to be the exclusive remedy for an (8)(A) violation. *Id.* On that basis, the court held it appropriate to enjoin commercial marketing until 180 days after the post-licensure notice. *Id.* at 1362.

D

In the present case, Amgen filed a motion in October 2015 asking the district court to issue a preliminary injunction that would require Apotex to provide an (8)(A) notice if and when it receives a license and to delay any commercial marketing for 180 days from that notice. The parties stipulated that Amgen will be irreparably harmed if Apotex enters the market without giving the requested 180 days' notice, the balance of the hardships favors Amgen, and the public interest favors the issuance of an injunction. The decision whether to grant the preliminary-injunction motion, therefore, turned on Amgen's likelihood of success on the legal question

presented: whether the (8)(A) notice requirement is a mandatory one enforceable by injunction as to an applicant (such as Apotex) that, unlike Sandoz in *Amgen v. Sandoz*, gave the (2)(A) notice to launch the information-exchange process leading to the paragraph (6) infringement suit. Notably, there is no dispute that Apotex's pre-licensure April 2015 notice is of no effect under (8)(A) as construed in *Amgen v. Sandoz*.

The district court agreed with Amgen and granted a preliminary injunction. The court noted that "[t]he [BPCIA] is intended to provide an orderly process for evaluating patent claims in the context of biosimilar products." J.A. 6. In particular, the (8)(A) notice-of-commercial-marketing requirement "'provides a defined statutory window during which the court and the parties can fairly assess the parties' rights prior to the launch of the biosimilar product.'" *Id.* (quoting *Amgen v. Sandoz*, 794 F.3d at 1358). The court concluded: "That defined statutory window exists for all biosimilar products that obtain FDA licenses, regardless of whether the subsection (k) applicant complies with § 262(*l*)(2)." *Id.* The court disagreed with Apotex's contention that this conclusion should be rejected in order to avoid adding 180 days to § 262(k)(7)'s 12-year exclusivity period for reference product sponsors. J.A. 7. The court also disagreed with Apotex's contention that paragraph (9) establishes that the exclusive remedy for failure to provide the (8)(A) notice of commercial marketing is a declaratory judgment on the patent-law merits of the patents at issue, no matter how rushed the litigation of those issues might be without the 180 days' notice. *Id.*

Apotex appeals the district court's grant of a preliminary injunction. We have jurisdiction under 28 U.S.C. § 1292(a)(1) and (c)(1).

DISCUSSION

We review a district court's grant of a preliminary injunction for abuse of discretion, which may be established when a district court's decision is based on an error of law. *Endo Pharm. Inc. v. Actavis, Inc.*, 746 F.3d 1371, 1373-74 (Fed. Cir. 2014); *U.S. Commodity Futures Trading Comm'n v. Hunter Wise Commodities, LLC*, 749 F.3d 967, 973 (11th Cir. 2014). Here, the district court's grant of an injunction rested on its interpretation of a statute, a question of law we review de novo. *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1374 (Fed. Cir. 2006). We agree with the district court: that Apotex gave a (2)(A) notice provides only a factual distinction, not a legally material distinction, between its situation and that of Sandoz in *Amgen v. Sandoz*. The (8)(A) requirement of 180 days' post-licensure notice before commercial marketing, we conclude, is a mandatory one enforceable by injunction whether or not a (2)(A) notice was given.

Paragraph (8)(A) provides that "[t]he subsection (k) applicant *shall* provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k)." § 262(*l*)(8)(A) (emphasis added). The word "shall" generally indicates that the directive is mandatory. *See Nat'l Ass'n of Home Builders v. Defs. of Wildlife*, 551 U.S. 644, 661-62 (2007); *Lopez v. Davis*, 531 U.S. 230, 241 (2001); *Lexecon Inc. v. Milberg Weiss Bershad Hynes & Lerach*, 523 U.S. 26, 35 (1998). We ruled in *Amgen v. Sandoz* that this language is,

indeed, "mandatory," and we did not say that it was mandatory only in no-(2)(A)-notice circumstances. 794 F.3d at 1359.

The language of (8)(A) is categorical in the sense relevant here. It contains no words that make the applicability of its notice rule turn on whether the applicant took the earlier step of giving the (2)(A) notice that begins the § 262(*l*) information-exchange process. And in *Amgen v. Sandoz* we stated that (8)(A) was "a standalone notice provision" not dependent on the information-exchange processes that begin with (2)(A). *Id.* at 1359-60.

There also is no other statutory language that effectively compels a treatment of (8)(A) as non-mandatory, contrary to the usual meaning of its "shall" terms. In this respect, (8)(A) differs materially from (2)(A). For (2)(A), as this court explained in *Amgen v. Sandoz*, the language of 35 U.S.C. § 271(e)(2) & (4) forces (2)(A)'s "shall" not to be a term of enforceable compulsory obligation. Section 271(e)(2)(C)(ii) declares to be an act of infringement the filing of a biosimilar-product application coupled to a failure to give the (2)(A) notice, and § 271(e)(4) declares that the patent-merits infringement suit, with specified damages and injunctive relief, is the exclusive remedy for that combination. Compelling the applicant to provide the (2)(A) notice would go beyond that remedy, thus contradicting the congressional command that the infringement remedies of § 271(e)(4) are "'the *only* remedies which may be granted by a court for an act of infringement described in [§ 271(e)(2)].'" *Amgen v. Sandoz*, 794 F.3d at 1356 (quoting § 271(e)(4); emphasis added by *Amgen v. Sandoz*). For (8)(A), in contrast, as *Amgen v. Sandoz* necessarily recognized

in finding it "mandatory," there is no comparable textual source of a contradiction that would be created by following the usual mandatory-character interpretation.

Amgen v. Sandoz likewise disposes of Apotex's argument that giving (8)(A) its plain meaning would effectively extend, by six months, the 12-year exclusivity period given to a reference product sponsor by § 262(k)(7). *See* 794 F.3d at 1358. Notably, § 262(k)(7) by its terms establishes the 12-year date only as an earliest date, not a latest date, on which a biosimilar license can take effect. Even when entry is delayed under (8)(A) to what amounts to 12 years plus 180 days after the reference product sponsor's licensure, the result is consistent with § 262(k)(7).

Moreover, it is implicit in the Biologics Act that any such delay beyond 12 years should occur less and less as time goes by. Doubtless, there will be some exclusivity periods beyond 12 years in the early years of the Biologics Act, as biosimilars are introduced for reference products licensed well before the Act was adopted in 2010. But as time passes, more and more of the reference products will be newer, and a biosimilar-product applicant, entitled to file an application a mere four years after licensure of the reference product, § 262(k)(7)(B), can seek approval long before the 12-year exclusivity period is up. *See Amgen v. Sandoz*, 794 F.3d at 1358 (the "extra 180 days will not likely be the usual case, as [biosimilar-product applications] will often be filed during the 12-year exclusivity period"). In such circumstances, we have been pointed to no reason that the FDA may not issue a license before the 11.5-year mark and deem the license to take effect on the 12-year date—a possibility suggested by § 262(k)(7)(A)'s

language about when the FDA approval may "be made effective." And we read (8)(A) as allowing the 180-day notice of commercial marketing to be sent as soon as the license issues, even if it is not yet effective, because it is at the time of the license that "the product, its therapeutic uses, and its manufacturing processes are fixed." *Id.* at 1358.

In any event, the established and evident purpose of (8)(A) covers applicants that file (2)(A) notices as well as those that do not. As this court explained in *Amgen v. Sandoz*, the purpose is to ensure that, starting from when the applicant's product, uses, and processes are fixed by the license, the necessary decision-making regarding further patent litigation is not conducted under time pressure that will impair its fairness and accuracy. *Id.* at 1358, 1360. At the least, the reference product sponsor needs time to make a decision about seeking relief based on yet-to-be litigated patents, and a district court needs time for litigants to prepare their cases, in a complicated area, to provide a reliable basis for judgment. While that may not be true in every single case, Congress clearly made a categorical fixed-period judgment in (8)(A)—as it did elsewhere in the Biologics Act—and we have explained that the "statute must be interpreted as it is enacted, not especially in light of particular, untypical facts of a given case." *Id.* at 1358.

That litigation-focused purpose extends to applicants that launch and pursue the information-exchange process of § 262(*l*). For those applicants as for others, the final biosimilar product cannot be known with certainty until the FDA license issues. Moreover, as we have described, § 262(*l*) affirmatively contemplates two stages of litigation

(under paragraphs (6) and (8)), and it contemplates that the first stage of litigation may omit patents the reference product sponsor has good grounds to assert, whether patents already in the hands of the reference product sponsor or patents newly in its hands under paragraph (7). It gives the applicant substantial authority to force such a limitation on the scope of the first-stage litigation.[3] And it provides for the reference product sponsor to "seek a preliminary injunction" after the licensure and (8)(A) notice. *See* § 262(*l*)(8)(B). The 180-day period gives the

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[3] Such applicant control is part of the design. *See Assessing the Impact of a Safe and Equitable Biosimilar Policy in the United States: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Commerce*, 110th Cong. 119 (2007) (statement of Bruce Downey, chairman of the Generic Pharmaceutical Ass'n and CEO of Barr Pharmaceuticals, Inc.) ("a biological patent system should provide a mechanism for litigating only those patent disputes that the generic company believes would delay its launch"); *Biologics and Biosimilars: Balancing Incentives for Innovation: Hearing Before the Subcomm. on Courts & Competition Policy of the H. Comm. on the Judiciary*, 111th Cong. 209-10 (2009) (statement of Teresa Stanek Rea, President of the American Intellectual Property Law Ass'n) ("Under H.R. 1427, pre-launch litigation of any patent is entirely within the control of the follow-on applicant . . . ."); Michael P. Dougherty, *The New Follow-on-Biologics Law: A Section by Section Analysis of the Patent Litigation Provisions in the Biologics Price Competition and Innovation Act of 2009*, 65 Food & Drug L.J. 231, 238 (2010) ("a significant feature of the Biologics Act" is that "it allows the applicant to limit litigation at this early stage of the application process to one patent"); Krista Hessler Carver, Jeffrey Elikan, & Erica Lietzan, *An Unofficial Legislative History of the Biologics Price Competition and Innovation Act of 2009*, 65 Food & Drug L.J. 671, 816 (2010) ("the BPCIA may operate to prevent patentees from asserting the relevant patents during the initial phase of litigation because the biosimilar applicant dictates how many patents can be asserted in the first instance").

reference product sponsor time to assess its infringement position for the final FDA-approved product as to yet-to-be-litigated patents. And if there is such litigation, it gives the parties and the district court the time for adjudicating such matters without the reliability-reducing rush that would attend requests for relief against immediate market entry that could cause irreparable injury.

This is evident on the face of § 262(*l*). And the Biologics Act's legislative history confirms the aim to avoid the uncertainties and deficiencies associated with a process in which requests for temporary restraining orders and preliminary injunctions are presented and adjudicated on short notice. *See*, *e.g.*, *Biologics and Biosimilars: Balancing Incentives for Innovation: Hearing Before the Subcomm. on Courts & Competition Policy of the H. Comm. on the Judiciary*, 111th Cong. 201-02 (2009) (statement of Teresa Stanek Rea, President of the American Intellectual Property Law Ass'n) (without a pre-launch patent-dispute mechanism, "patent disputes in this area would strain the federal judiciary by requiring—in preliminary injunction proceedings—resolution of the complex legal and scientific questions involved with each biosimilar product launch . . . in a pressurized context and without the benefit of a complete evidentiary record"); *id.* at 80 (statement of Jeffrey Kushan, on behalf of the Biotechnology Industry Organization) ("forcing patent disputes to commence only after a biosimilar has been placed on the market . . . will raise the prospect that a court will not enforce the exclusive rights of the patent by issuing an injunction preventing the continued marketing of the biosimilar"); *id.* at 9 (statement of Rep. Anna Eshoo) ("[A] simple,

streamlined patent resolution process . . . will help ensure that litigation surrounding relevant patents will be resolved expeditiously and prior to the launch of the biosimilar product, providing certainty to the applicant, the reference product manufacturer, and the public at large."); *Emerging Health Care Issues: Follow-On Biologic Drug Competition: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Commerce*, 111th Cong. 17-18 (2009) (statement of Rep. Marsha Blackburn); *Assessing the Impact of a Safe and Equitable Biosimilar Policy in the United States: Hearing Before the Subcomm. on Health of the H. Comm. on Energy & Commerce*, 110th Cong. 85 (2007) (statement of Dr. David Schenkein, Vice President, Clinical Hematology/Oncology, Genentech, Inc.); *see also An Unofficial Legislative History of the Biologics Price Competition and Innovation Act of 2009*, 65 Food & Drug L.J. at 798-800.

Apotex's final argument is that paragraph (9) of § 262(*l*) makes a declaratory-judgment action, discussed in (9)(B), the exclusive remedy for violations of (8)(A). We reject that contention.

Apotex has not asserted that (8)(A) creates no privately enforceable right, even when asserted as part of an infringement action concerning patent rights whose fair and unhurried adjudication (8)(A) is designed to protect. Nor has it identified any statutory commitment to a government agency of responsibility or authority to enforce or to seek to enforce the (8)(A) command. Instead, Apotex suggests that the only remedy for an applicant's unilateral denial to the reference product sponsor of the 180-day period for post-licensure litigation decision-making is a declaratory-judgment action on a patent—which

(9)(B) permits if the applicant "fails to complete" any one of several steps, including the giving of the (8)(A) notice. § 262(*l*)(9)(B).

We cannot infer such an exclusive-remedy conclusion from paragraph (9). The Supreme Court long ago ruled that the federal courts' "equitable jurisdiction is not to be denied or limited in the absence of a clear and valid legislative command," whether "in so many words, or by a necessary and inescapable inference." *Porter v. Warner Holding Co.*, 328 U.S. 395, 398 (1946); *see Mitchell v. Robert DeMario Jewelry, Inc.*, 361 U.S. 288, 291 (1960); *United States v. Oakland Cannabis Buyers' Coop.*, 532 U.S. 483, 496 (2001). Under that standard, or indeed under a straightforward understanding of paragraph (9) as it relates to (8)(A), we do not find that paragraph (9) establishes that a declaratory-judgment action is the sole remedy for violating (8)(A).

Apotex cannot point to any text providing for exclusivity. Nothing in paragraph (9) declares the exclusivity of the declaratory-judgment actions to which it refers—either in (9)(B) as it applies to an (8)(A) violation or more generally. (9)(A) bars certain declaratory-judgment actions, and (9)(B) & (C) state only that, in certain circumstances, the reference product sponsor "may bring" such an action. § 262(*l*)(9)(B), (C). There is no language that excludes other remedies for the conduct described.

Apotex's argument is therefore for an implied exclusivity of declaratory-judgment remedies. But it is clear that there is no such exclusivity implied by paragraph (9) generally. Most notably, when (9)(C) says that a declaratory-judgment action may be brought under 28 U.S.C. § 2201 if an applicant does not give the (2)(A) notice, *see* § 262(*l*)(9)(C), it plainly

does not imply exclusivity of that remedy: as *Amgen v. Sandoz* confirms, (9)(C) does not exclude the monetary and injunctive infringement remedies expressly authorized by 35 U.S.C. § 271(e)(4) for what is, after all, an infringement under § 271(e)(2). *See Amgen v. Sandoz*, 794 F.3d at 1357 ("when a subsection (k) applicant fails the disclosure requirement, 42 U.S.C. § 262(*l*)(9)(C) *and* 35 U.S.C. § 271(e) expressly provide the only remed*ies*") (emphases added); *id.* at 1359 (same). Nor has Apotex shown that (9)(B), when it applies, implicitly negates 35 U.S.C. § 271(e)(4)'s provision of damages and injunctive remedies (if otherwise appropriate and not curtailed by 35 U.S.C. § 271(e)(6)) for an application that is deemed by 35 U.S.C. § 271(e)(2)(C)(i) to be an infringement of a patent on a list under § 262(*l*)(3) (necessarily after a (2)(A) notice).[4] Against this generally *non*-exclusive character of the paragraph (9) declaratory-judgment remedy, it would be surprising to infer exclusivity of that remedy specifically for an (8)(A) violation.

This court did not declare otherwise when it said in *Amgen v. Sandoz* "that paragraph (*l*)(9)(B) specifies the consequence for a subsequent failure to comply with paragraph (*l*)(8)(A) after the applicant has complied with paragraph (*l*)(2)(A)." 794 F.3d at 1359. We read that statement to mean only that, when

[4] We need not explore how the timing of actions for such Title 35 remedies is affected by § 262(*l*). We make the narrower point that (9)(B) does not make declaratory judgments exclusive and thereby wipe out the remedies expressly provided for in 35 U.S.C. § 271(e)(4). We need not say to what extent, if at all, a similar point applies to remedies provided for in, *e.g.*, 35 U.S.C. §§ 283, 284 for activities, such as actual or imminent market entry, that might be infringements under portions of 35 U.S.C. § 271 other than subsection (e)(2).

there is noncompliance with (8)(A), the consequence *for the (9)(A) bar on declaratory judgments* is specified by (9)(B). That understanding reflects the express, limited language of (9)(B) and its evident connection to (9)(A). The court in *Amgen v. Sandoz* thus did not establish that the full remedial consequence of (8)(A) noncompliance is a declaratory-judgment action on the merits of the patents.

Such an exclusivity conclusion regarding (8)(A) would, in fact, make little sense. In the ordinary case, a declaratory-judgment action would not actually enforce the categorical "standalone," "mandatory" (8)(A) notice right, which would not be the subject of a declaratory-judgment patent-merits action. 794 F.3d at 1359-60. A declaratory-judgment action on the patent merits in the ordinary case would not serve (8)(A)'s essential purpose or, therefore, be a meaningful remedy *for the (8)(A) violation*.

In particular, relegating a reference product sponsor to a patent-merits declaratory-judgment action would introduce the very problem of rushed decision-making as to the patent merits that it is (8)(A)'s purpose to avoid. Noncompliance with (8)(A) means either entering the market without giving a post-licensure notice or giving a notice but then jumping the gun and entering the market before 180 days have passed. In either event, a reference product sponsor is likely not to know that the applicant will fail to provide the actual 180-day commercial-marketing notice required by (8)(A) until the applicant begins commercial marketing or, at least, declares that it may begin such marketing at any moment. The reference product sponsor will have to race to court for immediate relief to avoid irreparable harm from market entry, and the parties and the

court, in dealing with a request for a temporary restraining order or a preliminary injunction, will engage in precisely the hurried motion practice that (8)(A) is designed to replace by ensuring a defined amount of time for pre-launch litigation. (9)(B) as a "remedy" is so gross a mismatch for the (8)(A) right that it cannot fairly be treated, in the absence of any statutory language so stating, as the exclusive remedy for (8)(A)'s violation.

The mention of (8)(A) in (9)(B) seems to play a limited role in the provision, whose primary purpose is to provide an incentive for an applicant to fulfill its obligations along § 262(*l*)'s litigation-channeling path once it starts on the path by giving a (2)(A) notice. (9)(A) bars specified declaratory-judgment actions until the (8)(A) notice is received, and without a further direction from Congress, that bar would by its terms last precisely until the (8)(A) notice is received. But Congress did go further in (9)(B), by identifying several earlier points in time at which the (9)(A) bar is lifted, for the reference product sponsor, if the applicant "fails to complete" any of the specified actions the applicant is obliged to take in the process designed to lead up to and end with the (8)(A) notice. With respect to the other actions listed in (9)(B)—namely, those required by (3)(B)(ii), (5), (6)(C)(i), and (7)—the bar is lifted earlier than otherwise would be implicit in (9)(A). With respect to a failure to complete an action required by (8)(A), it appears that (9)(B) also goes beyond what is implicit in (9)(A) by authorizing a declaratory judgment as to an applicant that sends an (8)(A) notice (which upon receipt brings the (9)(A) bar to an end by (9)(A)'s terms) but then enters the market before 180 days have passed—which may be a "fail[ure] to complete" an

action required by (8)(A). But even if (9)(B) does not have that application, it would still make sense for (8)(A) to be included in the (9)(B) list solely for completeness, to bring the chronological list of (9)(A)-bar-lifting actions to its end point. It is hardly an unfamiliar role for a statutory provision to make explicit what otherwise would be implicit; such a provision is not superfluous. *See*, *e.g.*, *Ali v. Fed. Bureau of Prisons*, 552 U.S. 214, 226 (2008); *Fort Stewart Sch. v. Fed. Labor Relations Auth.*, 495 U.S. 641, 646 (1990).

Apotex would infer an outsize consequence from the mere modesty of the role played by (9)(B)'s mention of (8)(A). Apotex's proposed inference from (9)(B) would implicitly make (8)(A) neither mandatory nor standalone, despite (8)(A)'s language, and would reintroduce the very problems of rushed litigation—over patents the applicant is empowered to prevent being litigated earlier—that (8)(A) was enacted to avoid. The inference that Congress rendered unavailable direct injunctive enforcement of (8)(A)'s plain terms is unwarranted.

We conclude that an applicant must provide a reference product sponsor with 180 days' post-licensure notice before commercial marketing begins, regardless of whether the applicant provided the (2)(A) notice of FDA review. Because the parties here stipulated to the remaining preliminary-injunction factors, *see eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388, 394 (2006), we affirm the district court's grant of a preliminary injunction without addressing those factors.

CONCLUSION

For the foregoing reasons, we affirm the district court's grant of a preliminary injunction.

AFFIRMED

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

Case No. 15-61631-CIV-COHN/SELTZER

AMGEN, INC. AND
AMGEN MANUFACTURING LIMITED,
Plaintiffs,

v.

APOTEX INC. AND APOTEX CORP.,
Defendants.

[Filed Dec. 9, 2015]

ORDER ON MOTION FOR PRELIMINARY INJUNCTION

THIS CAUSE has come before the Court upon the Motion of Plaintiffs Amgen Inc. and Amgen Manufacturing Limited (collectively "Amgen") for a Preliminary Injunction DE [42]. Amgen seeks a preliminary injunction enjoining the Defendants, Apotex Inc. and Apotex Corp. (collectively "Apotex") from marketing its pegfilgrastim product until 180 days after it notifies Amgen of approval by the Federal Drug Administration ("FDA"). Amgen's Motion for Preliminary Injunction is based upon the Biologics Price Competition and Innovation Act of 2009 ("BCPIA"), 42 U.S.C.A. § 262 *et seq.*, in particular § 262(*l*)(8)(A).

For purposes of this motion, the parties have stipulated that three of the four elements needed for the issuance of a preliminary injunction are met: Apotex does not contest the elements of irreparable harm, balance of hardships or the public interest being

served by an injunction. *See Bryan v. Hall Chem. Co.*, 993 F.2d 831, 835 (11th Cir. 1993) (discussing the showing needed for issuance of a preliminary injunction). The parties have presented evidence and argument on the final element: the likelihood of Amgen's success on the merits, and the Court heard oral argument on December 3, 2015. The only issue before the Court is whether the BCPIA requires a company such as Apotex to give a company such as Amgen 180 days notice of its intent to market a licensed biosimilar product (as Amgen claims) or whether (as Apotex argues) the BCPIA merely makes the 180 days notice provision optional at the discretion of the applicant.

The BCPIA is a complex statute that attempts to establish "an abbreviated pathway for regulatory approval of follow-on biological products that are 'highly similar' to a previously approved product ('reference product')." *Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347, 1351 (Fed. Cir. 2015). Typically, the maker of a biological product must obtain licensing from the Food and Drug Administration ("FDA") through the submission of clinical data that prove the safety and efficacy of its product. *Id.* In an attempt to "balance innovation and price competition," the BCPIA allows the filing of abbreviated applications ("aBLA" or "subsection (k) application") for approval of biological products that are "biosimilar" or "interchangeable" with a previously approved reference product. *Id.* This process allows a biosimilar or interchangeable product to be approved using publicly available clinical data that was produced and obtained by the sponsor of the reference product ("reference product sponsor" or "RPS"). 42 U.S.C. § 262(k)(2)-(5). The innovator RPS

is protected through a statutory 12-year period of exclusivity and the right to file "infringement suits based on a biosimilar application prior to FDA approval and prior to marketing of the biological product." *Sandoz*, 795 F.3d at 1352.

As part of this abbreviated process, a subsection (k) applicant submits an aBLA to the FDA, and then provides the RPS with a copy of the aBLA and information about the product's manufacturing. 42 U.S.C. § 262(*l*)(2). The parties then exchange lists of patents they believe may be impinged by the biosimilar product and the RPS has 30 days within which to file a patent infringement action on the listed patents. *Id.* § 262(*l*)(6). If and when the biosimilar product is approved by the FDA for sale and use, § 262(*l*)(8) provides that the biosimilar applicant "shall" provide the RPS with 180 days notice of approval before marketing the biosimilar product for sale and use in the United States. *Id.* § 262(*l*)(8). This 180-day period "allows the RPS a period of time to seek a preliminary injunction based on patents that the parties initially identified during information exchange but were not selected for the immediate infringement action, as well as any newly listed or licensed patents (collectively, 'non-listed patents'), *id.* § 262(*l*)(7)-(8)." *Sandoz*, 794 F.3d at 1352. If the biosimilar applicant fails to comply with certain provisions of subsection (*l*), including § 262(*l*)(8), the RPS (but not the applicant) may seek declaratory relief. 42 U.S.C. § 262(*l*)(9)(B) and (C).

Amgen is an RPS that developed, manufactures and markets a biologic therapy known as Neulasta, which is approved by the FDA for use in treating certain cancer patients receiving chemotherapy. Apotex submitted an aBLA to the FDA, seeking approval of

a biosimilar version of Neulasta. Apotex complied with the BCPIA and disclosed its aBLA and information about its manufacturing process to Amgen, pursuant to § 262(*l*)(2). Based upon the list of patents compiled by the parties, Amgen filed this action to enforce two of its patents. Apotex has informed Amgen that it will not notify Amgen when and if it obtains FDA approval for its biosimilar product and it will not provide the 180 days commercial marketing notice as required in § 262(*l*)(8). Amgen requests injunctive relief in the form of an order requiring Apotex to provide Amgen with notice of FDA approval of Apotex's pegfilgrastim product and to refrain from marketing its licensed product for at least 180 days from the date of such notice.

As previously stated, the issue is whether the commercial marketing notice and 180 day period in § 262(*l*)(8) is mandatory. Paragraph 262(*l*)(8) provides that "[t]he subsection (k) applicant *shall* provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product *licensed* under subsection (k)." 42 U.S.C. § 262(*l*)(8)(A) (emphases added). "The word 'shall' is ordinarily the language of command." *In re Tennyson*, 611 F.3d 873, 877 (11th Cir. 2010), *quoting Alabama v. Bozeman*, 533 U.S. 146, 153, 121 S.Ct. 2079, 2085, 150 L.Ed.2d 188 (2001) (quotation omitted). However, in the realm of statutory construction, "shall" may sometimes mean "may." "Use of the word 'shall' generally indicates a mandatory intent unless a convincing argument to the contrary is made." *Sierra Club v. Train*, 557 F.2d 485, 489 (5th Cir. 1977). And that is where the parties lead us: Amgen argues that "shall" means shall

in all cases, while Apotex argues that "shall" means shall only in some cases.

The Federal Circuit addressed the meaning of "shall" as used in§ 262(*l*)(8)(A) in the *Sandoz* case, 794 F.3d 1347, but left some ambiguity which this Court must now address. In *Sandoz*, the subsection (k) applicant submitted the abbreviated application allowed by the BCPIA, but did not provide the RPS with its aBLA or manufacturing process as contemplated by § 262(*l*)(2). Even though § 262(*l*)(2) contained the word "shall," the Federal Circuit, in a two-person majority, ruled that "shall" in the context of § 262(*l*)(2) is not mandatory. *Sandoz*, 794 F.3d at 1355-57. The court then stated that the word "shall" in the context of § 262(*l*)(8)(A) *does* mean "mandatory." 794 F.3d at 1359. "Paragraph (*l*)(8)(A) is a standalone notice provision in subsection (*l*), and Sandoz concedes as much. . . . . The purpose of paragraph (*l*)(8)(A) is clear: requiring notice of commercial marketing be given to allow the RPS a period of time to assess and act upon its patent rights." *Id.* at 1359-60. However, the *Sandoz* decision was limited to situations where the subsection (k) applicant "completely fails to provide its aBLA and the required manufacturing information to the RPS by the statutory deadline . . . ." *Id.* at 1360. Because the situation was not before it, the court did not address whether the notice provision of § 262(*l*)(8)(A) applies where the applicant, like Apotex, *did* share the information required by § 262(*l*)(2).

Apotex would have this Court limit the *Sandoz* decision, and the mandatory nature of § 262(*l*)(8)(A), to instances where the applicant did not comply with § 262(*l*)(2) and make the notice provision of § 262(*l*)(8)(A) optional in instances where the

applicant did comply with § 262(*l*)(2). This scenario was addressed by Judge Chen in his dissent to the *Sandoz* decision: "While the result in the latter scenario comes from the plain language of the statute, not so with the former. Nothing in the statute supports this peculiar outcome." *Sandoz*, 794 F.3d at 1371 (Chen, J., dissenting). This Court agrees. The scenario proposed by Apotex would result in confusion and uncertainty, as well as inconsistent results, depending on which route a subsection (k) applicant chooses to travel. Nothing in the statute or the *Sandoz* decision leads to or supports such a result; neither the statute nor the *Sandoz* decision condition the 180 day notice provision of § 262(*l*)(8)(A) upon a subsection (k) applicant's compliance with § 262(*l*)(2).

The BCPIA is intended to provide an orderly process for evaluating patent claims in the context of biosimilar products. Indeed the *Sandoz* court (in the unanimous portion of the decision) recognized that "[g]iving notice after FDA licensure, once the scope of the approved license is known and the marketing of the proposed biosimilar product is imminent, allows the RPS to effectively determine whether, and on which patents, to seek a preliminary injunction from the court. Requiring that a product be licensed before notice of commercial marketing ensures the existence of a fully crystallized controversy regarding the need for injunctive relief. It provides a defined statutory window during which the court and the parties can fairly assess the parties' rights prior to the launch of the biosimilar product." *Id.* at 1358. That defined statutory window exists for all biosimilar products that obtain FDA licenses,

regardless of whether the subsection (k) applicant complies with § 262(*l*)(2).

The *Sandoz* court also discounted Apotex's argument that the notice provision of § 262(*l*)(8)(A) unfairly gives the RPS an additional 180 days of exclusivity. Noting that Sandoz filed its aBLA 23 years after the RPS's product was initially approved, the *Sandoz* court agreed that the RPS received an "extra" 180 days, but stated "that is apparently the way the law, business, and the science evolved. That extra 180 days will not likely be the usual case, as aBLAs will often be filed during the 12-year exclusivity period for other products. A statute must be interpreted as it is enacted, not especially in light of particular, untypical facts of a given case." *Id.*

Indeed, the "extra" 180 days afforded to Amgen by the injunction it seeks will likely result in a more crystallized patent litigation before this Court. As Amgen concedes, depending on when the FDA grants Apotex's product a license, one of the patents Amgen has filed suit on in this Court may well expire before the 180 day period ends; under Apotex's construction of § 262(*l*)(8)(A), the Court would be forced to rule on the validity of that patent now, even though that patent claim may be moot by the end of the 180 day period. This fact helps illustrate the value and the purpose of applying the 180 day notice provision to all biosimilar applicants.

Finally, the Court disagrees with Apotex's argument that making § 262(*l*)(8)(A) mandatory for all subsection (k) applicants would render the penalty provisions of § 262(*l*)(9) superfluous. Subsection § 262(*l*)(9) gives the RPS the option to file a declaratory judgment action if the subsection (k) applicant fails to comply with § 262(*l*)(8)(A) , but it is not an

exclusive remedy. As the *Sandoz* court ruled, an injunction to compel compliance with the 180-day notice provision of § 262(*l*)(8)(A) is another remedy. The BCPIA simply does not give the subsection (k) applicant the power to nullify the RPS' statutory right to 180 days notice of approval prior to marketing based on whether or not the subsection (k) applicant complies with § 262(*l*)(2). As Judge Newman stated in her dissent in *Sandoz*, "[s]ubsection 262(*l*)(9) provides jurisdiction in the district court when a subsection (k) applicant fails to comply with subsection (*l*), but it does not ratify non-compliance; While 'a party may waive any provision, either of a contract or of a statute, intended for his benefit' . . . . the party cannot waive or disregard a provision that benefits those in an adverse position." *Sandoz*, 794 F.3d at 1366 (Newman, J., dissenting), quoting *United States v. Mezzanatto*, 513 U.S. 196, 201 (1995).

On the record before the Court, Amgen has established (1) that Apotex does not intend to comply with § 262(*l*)(8)(A) of the BCPIA; (2) that it would suffer irreparable harm if Apotex were to commence marketing its product without complying with § 262(*l*)(8)(A); (3) that the balance of hardships weighs in favor of Amgen; (4) that the public interest will be served by an injunction; and (5) that Amgen has a substantial likelihood of prevailing on the merits. The Court finds that the requested injunctive relief is appropriate. *See*, *Sandoz*, 794 F.3d at 1360 (enjoining Sandoz from marketing its biosimilar product before 180 days from the date it gave notice of FDA approval).

Rule 65(e), Federal Rules of Civil Procedure, requires the Court to establish an amount of a bond

to secure the costs and damages the enjoined party may sustain if the injunction is wrongfully issued. Nevertheless, "it is well-established that 'the amount of security required by the rule is a matter within the discretion of the trial court . . . [, and] the court may elect to require no security at all.'" *City of Atlanta v. Metro. Atlanta Rapid Transit Auth.*, 636 F.2d 1084, 1094 (5th Cir. Unit B 1981); *BellSouth Telecomms., Inc. v. MCImetro Access Transmission Servs.*, 425 F.3d 964, 971 (11th Cir. 2005).

The Court finds that no bond is necessary. There are no factual disputes before the Court. It is undisputed that Apotex is not currently approved by the FDA to market its biosimilar product and is not conducting such marketing. The requested preliminary injunction will require Apotex to notify Amgen when and if it receives FDA approval and will prohibit Apotex from marketing the approved product for 180 days after the notice is provided. This injunction maintains the status quo and leaves the parties in the position mandated by § 262(*l*)(8)(A). Apotex presented evidence of its projected income during the first 180 days of marketing its biosimilar product and requests a bond in that amount, but as the Court has found, Apotex is prohibited by statute from marketing its product for 180 days after it obtains FDA licensure. Apotex will lose nothing to which it is otherwise entitled by the entry of this injunction. Therefore, for the reasons discussed herein, it is hereby

ORDERED AND ADJUDGED that Amgen's Motion for Preliminary Injunction DE [42] be and the same is **GRANTED**. If the FDA approves Apotex's Biologics License Application for its pegfilgrastim product, Apotex must provide Amgen with at least

180 days notice before the date of the first commercial marketing of the biological product approved by the FDA. 42 U.S.C. § 262(*l*)(8)(A). Apotex and those acting in concert with it are enjoined from any commercial marketing of its biosimilar pegfilgrastim product, including selling that product or offering it for sale for use in the United States, until Apotex gives Amgen proper notice, at least 180 days before first commercial marketing but not before its pegfilgrastim biosimilar product is licensed by the FDA, and the 180-day notice period is exhausted. No bond is required to be posted by Amgen.

DONE AND ORDERED in Chambers, Fort Lauderdale, Florida, this 9th day of December, 2015.

/s/ JAMES I. COHN

JAMES I. COHN
UNITED STATES DISTRICT JUDGE

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

Case No. 15-61631-CIV-COHN/SELTZER

AMGEN, INC. AND
AMGEN MANUFACTURING LIMITED,
Plaintiffs,

v.

APOTEX INC. AND APOTEX CORP.,
Defendants.

[Filed Sept. 6, 2016]

FINDINGS OF FACT AND CONCLUSIONS OF LAW

THIS CAUSE came before the Court for nonjury trial on July 11, 2016 through July 18, 2016. The parties provided the Court with revised proposed findings of fact and conclusions of law on August 18, 2016 [DE 262-65]. The Court has considered all submissions and the evidence presented at trial, and is otherwise advised in the premises.

Plaintiffs Amgen Inc. and Amgen Manufacturing Limited (collectively, "Amgen") sued Defendants Apotex Inc. and Apotex Corp. (collectively, "Apotex") under the Biologics Price Competition and Innovation Act ("BPCIA") for infringement of U.S. Patent No. 8,952,138 (the "'138 Patent"). Amgen is the owner of all rights, title, and interest in the '138 Patent, which covers a process of protein refolding. Apotex filed abbreviated Biologics License Application ("aBLA") Nos. 761026 and 761027 seeking approval from the U.S. Food & Drug Administration ("FDA")

to market biosimilar versions of Amgen's Neulasta (Pegfilgrastim) and Neupogen (Filgrastim) products, respectively. Amgen alleges that aBLA Nos. 761026 and 761027 infringe the '138 Patent under 35 U.S.C. § 271(e)(2)(C)(i), and also allege that the commercial manufacture, use, sale, offer for sale, or importation of Apotex's Pegfilgrastim and Filgrastim products will infringe the asserted claims of the '138 Patent under 35 U.S.C. § 271(a) and/or (g). Apotex alleges that the process described in its aBLAs falls outside the scope of the asserted claims of the '138 Patent and seeks a declaratory judgment of non-infringement and invalidity for lack of enablement.

For the reasons set forth below, the Court finds that Amgen has not met its burden to prove that Apotex's process for refolding Filgrastim and Pegfilgrastim infringe, either literally or under the doctrine of equivalents, each limitation of the '138 Patent. Additionally, the Court finds that Apotex has established that its process, as described in aBLA Nos. 761026 and 761027, does not infringe the '138 Patent. Having found no infringement, the Court shall dismiss without prejudice Apotex's counterclaim for invalidity.[1]

Pursuant to Federal Rule of Civil Procedure 52, the Court issues the following Findings of Fact and Conclusions of Law.

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[1] Apotex also argued at trial that its Pegfilgrastim product does not infringe the '138 Patent because pegylation of Filgrastim constitutes a "material change" to the claimed process. Because the Court finds no infringement, this argument is now moot.

I. FINDINGS OF FACT

A. The '138 Patent

1. The '138 Patent is entitled "Refolding Proteins Using a Chemically Controlled Redox State." The '138 Patent issued on February 10, 2015, to inventors Joseph Edward Shultz, Roger Hart, and Ronald Nixon Keener, III, was assigned to Amgen Inc. The '138 Patent claims priority to Provisional U.S. Application No. 61/219,257, which was filed on June 22, 2009.

1. The Asserted Claims of the '138 Patent

2. Amgen asserted claims 1-3, 6-7, 13, 15-17, and 22-23 of the '138 Patent against Apotex. Claims 2-3, 6-7, 13, 15-17, and 22-23 depend from claim 1.

3. Claim 1 of the '138 Patent states:

> **1.** A method of refolding a protein expressed in a non-mammalian expression system and present in a volume at a concentration of 2.0 g/L or greater comprising:
>
> (a) contacting the protein with a refold buffer comprising a redox component comprising a final thiol-pair ratio having a range of 0.001 to 100 and a redox buffer strength of 2 mM or greater and one or more of:
>
> (i) a denaturant;
>
> (ii) an aggregation suppressor; and
>
> (iii) a protein stabilizer;
>
> to form a refold mixture;
>
> (b) incubating the refold mixture; and
>
> (c) isolating the protein from the refold mixture.

4. Claim 2 of the '138 Patent states:

> **2.** The method of claim 1, wherein the final thiol-pair ratio is selected from the group consisting of

0.05 to 50, 0.1 to 50, 0.25 to 50, 0.5 to 50, 0.75 to 40, 1.0 to 50 and 1.5 to 50, 2 to 50, 5 to 50, 10 to 50, 15 to 50, 20 to 50, 30 to 50 or 40 to 50.

5. Claim 3 of the '138 Patent states:

3. The method of claim 1, wherein the thiol-pair buffer strength is selected from the group consisting of greater than or equal to 2.25 mM, 2.5 mM, 2.75 mM, 3 mM, 5 mM, 7.5 mM, 10 mM and 15 mM.

6. Claim 6 of the '138 Patent states:

6. The method of claim 1, wherein the protein is present in the volume in a soluble form.

7. Claim 7 of the '138 Patent states:

7. The method of claim 1, wherein the protein is recombinant.

8. Claim 13 of the '138 Patent states:

13. The method of claim 1, wherein the non-mammalian expression system is one of a bacterial expression system and a yeast expression system.

9. Claim 15 of the '138 Patent states:

15. The method of claim 1, wherein the protein stabilizer is selected from the group consisting of arginine, proline, poly-ethylene glycols, non-ionic surfactants, ionic surfactants, polyhydric alcohols, glycerol, sucrose, sorbitol, glucose, Tris, sodium sulfate, potassium sulfate and osmolytes.

10. Claim 16 of the '138 Patent states:

16. The method of claim 1, wherein the aggregation suppressor is selected from the group consisting of arginine, proline, polyethylene glycols, non-ionic surfactants, ionic surfactants, polyhydric alcohols, glycerol, sucrose, sorbitol, glucose,

Tris, sodium sulfate, potassium sulfate and osmolytes.

11. Claim 17 of the '138 Patent states:

17. The method of claim 1, wherein the thiol-pairs comprise at least one component selected from the group consisting of glutathione-reduced, glutathione-oxidized, cysteine, cystine, cysteamine, cystamine and betamercaptoethanol.

12. Claim 22 of the '138 Patent states:

22. The method of claim 1, wherein the isolating comprises contacting the mixture with an ion exchange separation matrix.

13. Claim 23 of the '138 Patent states:

23. The method of claim 1, wherein the isolating further comprises a filtration step.

2. Claim Construction

14. In its Claim Construction Order and Sealed Omnibus Order, the Court construed certain terms of the '138 Patent as follows:

Claim Term	Court's Construction
"a protein . . . present in a volume at a concentration of 2.0 g/L or greater"	A protein as it existed in a volume before contacting the volume with a refold buffer. The protein concentration in the volume is 2.0 g/L or greater.

"refold mixture"	A mixture formed from contacting (1) the volume in which the concentration of protein is 2.0 g/L or greater with (2) the refold buffer. The refold mixture has a high protein concentration, where "high protein concentration" is at or above about 1 g/L protein.
"refold buffer"	A preparation that supports the renaturation of protein to a biologically active form. The refold buffer comprises (1) a redox component and (2) one or more of (i) a denaturant, (ii) an aggregation suppressor, and (iii) a protein stabilizer.
"redox component"	Any thiol-reactive chemical or combinations of such chemicals, or solution comprising such a chemical or chemicals that facilitates a reversible thiol exchange with another thiol or the cysteine residues of a protein. The redox component comprises a final thiol-pair ratio in the range of 0.001-100 and a redox buffer strength of 2 mM or greater.
"final thiol-pair ratio"	Defined by the following equation: $\frac{[reductant]^2}{[oxidant]}$ where the concentrations are the concentrations in the redox component.

"redox buffer strength"	Also called "buffer thiol strength," "thiol-pair buffer strength," or "thiol-pair strength," defined by the following equation: $2[oxidant] + [reductant]$ where the concentrations are the concentrations in the redox component.
"2 mM or greater"	2 mM or greater, wherein the redox buffer strength is effectively bounded at a maximum of 100 mM.
"protein"	Any chain of at least five naturally or non-naturally occurring amino acids linked by peptide bonds including but not limited to the protein of interest.

B. Apotex's Manufacturing Process

15. Apotex's refolding process for its Pegfilgrastim and Filgrastim products is described in detail in aBLA Nos. 761026 and 761027, respectively (hereinafter "Apotex's aBLAs"). Apotex's aBLAs seek FDA licensure to market biosimilar versions of Amgen's Neulasta (Pegfilgrastim) and Neupogen (Filgrastim) products, respectively.

16. Apotex's refolding process includes an "upstream" process and a "downstream" process. The end product of Apotex's upstream process is inclusion bodies. During the upstream process, Apotex performs multiple washes of the inclusion bodies with a buffer and water. Following each of these washes, the inclusion bodies are centrifuged to separate a wet "pellet" of inclusion bodies from the supernatant (liquid). The wet inclusion bodies are weighed at the conclusion of the upstream process and then frozen.

The inclusion bodies remain frozen in storage until they are used in Apotex's downstream process.

17. Apotex's aBLAs specify that between 144 grams (hereinafter "grams" or "g") and 216 grams of inclusion bodies are used to begin Apotex's downstream process. In addition to specifying the wet weight of inclusion bodies carried from the upstream process into Apotex's downstream process, Apotex's aBLAs specify the amount of inclusion bodies as a concentration, as shown in the table below, which is equivalent to 0.9 to 1.4 grams per Liter (hereinafter "Liter" or "L") of Apotex's Refolding Buffer.

Table S.2.2-26: Inclusion Bodies Solubilization Operating Parameters

Operating Parameter	Operating Range	Set Point
IB amount per L of Refolding Buffer (160 L)	0.9 - 1.4 g/L	1.1 g/L
IB Solubilization Buffer volume	5.4 - 5.6 L	5.5 L
Amount of DTT added to solubilized IBs	4.44 - 5.55 g	5.00 g
Mixing time for reduction of solubilized IBs	20 - 40 min	30 min

DTT = dithiothreitol; IB = Inclusion Body

This concentration is determined by dividing the lowest and highest amounts of inclusion bodies—144 g and 216 g, respectively—by the nominal volume of the refold buffer tank, which is 160 L.

18. The first step in Apotex's downstream process is solubilization of the inclusion bodies. After the inclusion bodies are thawed in a small amount of water, they are dissolved in Apotex's solubilization

buffer, resulting in a solution having a volume of 7.2 L. The solubilized inclusion bodies are then reacted with dithiothreitol ("DTT") to reduce the proteins into their primary, unfolded structure.

19. According to Apotex's aBLAs specifications, and shown in the table below, the concentration of Filgrastim in the solubilization buffer is 4.24 to 11.80 milligrams (hereinafter "milligrams" or "mg") per milliliter (hereinafter "milliliter" or "mL"), which is the same as 4.24 to 11.80 g/L.

Table S.2.2-27: Inclusion Bodies Solubilization Performance Parameters

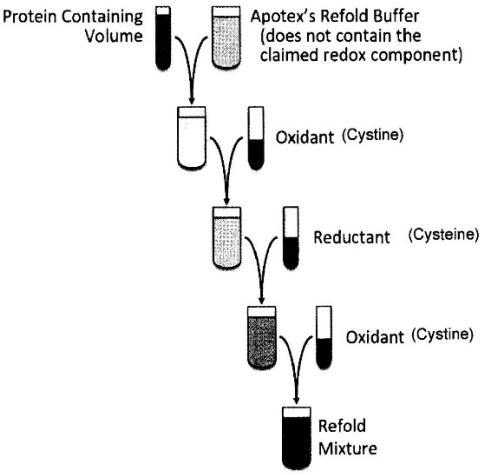
Performance Parameter	Categorization	Acceptance Criterion	Expected Range
Solubilized IB purity by UPLC M1	CPP	≥ 75%	—
Solubilized IB rHu-met-GCSF Concentration by UPLC M1	KPP	—	4.24 - 11.80 mg/mL*
Solubilized IB Endotoxin (Post-filtration)	CPP	NMT 500 EU/mg	—
Solubilized IB Bioburden (Post-filtration)	CPP	NMT 1 CFU/10 mL	—
*Based on the ranging studies that were carried out using a Design of Experiments (DoE) approach, the qualified upper limit for the concentration of protein entering the refolding unit operation is 11.8 mg/mL.			

20. Apotex's specification for the concentration of Filgrastim in the solubilization buffer limits the

concentration of Filgrastim that is present in subsequent manufacturing processes. For example, the upper limit of the Filgrastim concentration in Apotex's refold mixture is 0.531 g/L. This upper limit is determined by taking the highest possible concentration of Filgrastim in the solubilization buffer—11.80 mg/mL (or 11.80 g/L)—and multiplying by the volume of the solubilization buffer, which is 7.2 L, and then dividing by the volume of the refold mixture, which is 160 L.

21. As further shown in Table S.2.2-27: Inclusion Bodies Solubilization Performance Parameters, *supra,* Apotex's aBLAs specify that in the solubilization buffer at least 75 percent of the total protein present must be Filgrastim. This specification for the Filgrastim purity limits the amount of total protein in Apotex's refold mixture to a maximum of 0.708 g/L. This total protein amount is calculated by dividing the maximum Filgrastim concentration by 0.75 (or dividing by 75 percent).

22. Turning to Apotex's refolding process, the following schematic is illustrative:



23. The composition and quantity of ingredients in Apotex's Refolding Buffer, Cystine Solution, and Cysteine Solution are shown below in Table S.2.2-33.

Table S.2.2-33:
Refolding – Solution Composition

Solution	Component	Quantity
Refolding Buffer, pH 9.0 ± 0.2, Conductivity 17.5 ± 1.5 mS/cm	Arginine base	16.8 ± 0.02 kg
	Tris base	1940.00 ± 0.02 g
	Sorbitol	8.0 ± 0.8 kg
	EDTA disodium dehydrate	118.80 ± 0.02 g
	WFI Ph. Eur., IP, USP	q.s. to 168.0 kg
Cystine Solution	Cystine	13.2 ± 3.6 g
	0.2 N Hydrochloric Acid	440 ± 4 mL
Cysteine Solution	Cysteine	2.500 ± 0.25 g
	WFI Ph. Eur., IP, USP	32.00 ± 0.32 mL
Tris = Tris (hydroxymethy) aminomethane; WFI = Water for Injection; USP = United States Pharmacopoeia		

24. The first step in Apotex's refolding process is to create Apotex's Refolding Buffer (the orange container in the schematic) and to add it to the refolding vessel. Solubilized and reduced inclusion bodies (royal blue) are then slowly added to Apotex's Refolding Buffer over 90 minutes.

25. After the solubilized and reduced inclusion bodies are added to Apotex's Refolding Buffer, the Cystine Solution (purple) and Cysteine Solution (pink) are added in a stepwise manner. According to the

aBLAs, first 360 mL of the Cystine Solution (purple) is added to Apotex's Refolding Buffer to "neutralize DTT." Next, 32 mL of the Cysteine Solution (pink) is added to Apotex's Refolding Buffer to "break S-H (thiosulfide) bonds." Finally, 80 mL of Cystine Solution is added to "reduce the free S moieties so they were not available to form intramolecular disulfide bonds after refolding."

26. After the stepwise addition of the Cystine and Cysteine Solutions, Apotex incubates the refold mixture for at least 18 hours. Then, Apotex isolates the Filgrastim protein using a series of isolation steps.

27. The protein that results from Apotex's manufacturing process is Filgrastim Critical Intermediate ("Filgrastim CI"), which is both the starting material for Apotex's Filgrastim product and the critical intermediary for its Pegfilgrastim product.

C. Apotex Does Not Infringe the Asserted Claims of the '138 Patent.

28. As discussed in detail below, Amgen has not met its burden to show that Apotex's refolding process, as defined by Apotex's aBLAs, infringes the asserted claims of the '138 Patent, either literally or under the doctrine of equivalents. Specifically, Amgen has not established by a preponderance of the evidence that Apotex's process has: (1) a "high protein concentration" at or above about 1 g/L; and (2) a redox component having a redox buffer strength of 2 to 100 mM.

29. Moreover, Apotex has shown that its manufacturing process, both as defined in its aBLAs and in practice, does not infringe the '138 Patent.

1. Apotex's Refolding Process Does Not Include a Refold Mixture Having a Protein Concentration At or Above about 1 g/L.

30. Each asserted claim of the '138 Patent requires a "refold mixture" having "a high protein concentration, where 'high protein concentration' is at or above about 1 g/L protein." Amgen asserts that Apotex's refolding process literally meets this claim element, and did not allege infringement of this element under the doctrine of equivalents.

31. As discussed in detail below, Amgen did not meet its burden to show by a preponderance of the evidence that Apotex's refolding process literally uses a protein concentration in Apotex's refold mixture that is "at or above about 1 g/L." To the contrary, the Court finds that Apotex's aBLAs require a total protein concentration in Apotex's refold mixture that is well below "at or above about 1 g/L." Therefore, the Court finds that Apotex's aBLAs do not define an infringing process.

32. The Court finds that Amgen's failure to prove that Apotex's refolding process literally infringes the asserted claims of the '138 Patent is established by: (i) the testimony of Amgen's expert Dr. Richard C. Willson, III and Apotex's experts Dr. Jason Dowd and Dr. Anne S. Robinson that Apotex's inclusion bodies are not wholly protein; (ii) Dr. Dowd's and Dr. Robinson's testimony that Apotex's aBLAs specifications for the amount of inclusion bodies of 0.9 to 1.4 g/L is not reliable for determining protein concentration in the refold mixture because the inclusion bodies are wet at the time of weighing and are mostly water; (iii) the fact that Dr. Willson's opinion that the washed inclusion bodies are almost entirely pure protein did not account for the water present in those

inclusion bodies; and (iv) Amgen's lack of evidence that the actual protein concentration in Apotex's refold mixture is "at or above about 1 g/L."

33. Further, the Court finds that Apotex's non-infringement is established by: (i) Apotex's aBLAs that require a specific protein concentration range in the refold mixture that is outside the range of "at or above about 1 g/L"; and (ii) Apotex's batch records, which show that the protein concentration in the refold mixture of actual manufactured batches is outside the range of "at or above about 1 g/L."

a. Amgen did not prove that Apotex's specification for inclusion bodies defines the protein concentration in the refold mixture.

34. Amgen's theory of infringement of the protein concentration limitation requires a finding that the inclusion bodies in Apotex's downstream process are primarily pure protein. Specifically, Amgen maintains that the 0.9 to 1.4 g/L inclusion body concentration specification in Apotex's aBLAs is roughly equivalent to the total protein concentration.

35. The Court does not find that Apotex's inclusion bodies are substantially pure protein. In reaching this conclusion, the Court credits the testimony of Apotex's experts, Dr. Dowd and Dr. Robinson, that Apotex's inclusion bodies are composed of approximately two-thirds water at the time of weighing.

36. Amgen's theory that Apotex's inclusion body specification defines the protein concentration, as explained by Dr. Willson, does not sufficiently account for the water weight present in the inclusion bodies at the time of weighing.

37. Additionally, no evidence affirmatively shows that Apotex's centrifugation process removes water

from Apotex's inclusion bodies. Dr. Willson's testimony that Apotex "pours off the liquid containing the stuff that got washed off" during centrifugation speaks to the amount of liquid on the outside of the inclusion bodies, but it does not establish how much liquid remains in them.

38. In light of Dr. Robinson's deposition testimony describing the inclusion bodies after centrifugation and at the time of weighing as a "wet pellet" and the specifications in Apotex's batch records (described in the following section), Amgen knew or should have known that the inclusion bodies contained water.

39. Apotex's pre-litigation letters to Amgen, which incorrectly equate the inclusion body concentration with protein concentration, are not probative on the issue of protein concentration. Statements in the pre-litigation letters are not binding on Apotex, and the Court credits Dr. Dowd's testimony that the statements at issue in these letters are factually incorrect.

40. Based on the above, the Court finds that Apotex's aBLAs specifications of 0.9 to 1.4 g/L merely require an amount of inclusion bodies to be used as an input in Apotex's refolding process, but do not specify the amount of protein present in those inclusion bodies. Thus, the Court finds that Amgen has failed to meet its burden to show by a preponderance of the evidence that Apotex's refolding process literally infringes the protein concentration claim limitation.

b. Apotex's aBLAs specify a protein concentration separate from an inclusion body concentration.

41. The maximum concentration of total protein in Apotex's refold mixture process is limited by Apotex's aBLAs specifications to 0.708 g/L. The Court credits

the opinions and calculations of Dr. Dowd and Dr. Robinson in reaching this conclusion.

42. Apotex's aBLAs specify the concentration of Filgrastim in Apotex's solubilization buffer, and this specification limits the concentration of Filgrastim that is present in subsequent manufacturing steps.

43. As shown in Table S.2.2-27: Inclusion Bodies Solubilization Performance Parameters, *supra*, Apotex's aBLAs restrict Apotex's process from exceeding 11.80 g/L of Filgrastim in 7.2 L of solubilization buffer.

44. The upper limit of the Filgrastim concentration in Apotex's refold mixture is 0.531 g/L. This is determined by taking the highest possible concentration of Filgrastim in the solubilization buffer—11.80 g/L—and multiplying by the volume of the solubilization buffer, which is 7.2 L, and then dividing by the volume of the refold mixture, which is 160 L.

45. As further shown in Table S.2.2-27: Inclusion Bodies Solubilization Performance Parameters, *supra,* Apotex's aBLAs also specify that in the solubilization buffer at least 75 percent of the total protein present must be Filgrastim. This specification for the Filgrastim purity effectively limits the amount of total protein in Apotex's refold mixture to a maximum of 0.708 g/L. This is calculated by dividing the maximum Filgrastim concentration in the refold mixture—0.531 g/L—by 0.75 (or dividing by 75 percent).

46. If Apotex's manufacturing process was to deviate from the amount and quantity of Filgrastim specified in the Apotex aBLAs submitted to the FDA, Apotex would be required to discard that batch. The Court credits the testimony of Dr. Dowd in reaching this conclusion.

47. Amgen cited no evidence to contradict that Apotex's aBLAs specifications limit the maximum protein concentration in Apotex's refold mixture to 0.708 g/L. Evidence that Apotex advertised that it uses a bioreactor capable of utilizing a higher protein concentration is irrelevant to the infringement inquiry because this bioreactor is used for protein synthesis and is not involved in any way in Apotex's refolding process for Filgrastim.

48. Because Apotex's aBLAs limit the amount of total protein in Apotex's refold mixture to a maximum of 0.708 g/L, the Court finds that Apotex's aBLAs specifications directly address the infringement inquiry and define a protein refolding process having a total protein concentration less than "at or above about 1 g/L protein." For these reasons, the Court finds that Apotex's refolding process does not infringe the asserted claims.

c. Batch records show that the products that Apotex will likely market are manufactured by a *non-infringing process.*

49. Apotex's batch records, which were submitted to the FDA with Apotex's aBLAs, show that Apotex's protein refolding process, in practice, has not and will not use a protein concentration in Apotex's refold mixture that is within the scope of "at or above about 1 g/L protein," as required by claim 1 of the '138 Patent.

50. Apotex's batch records document the way in which Apotex has made its Filgrastim and Pegfilgrastim products. Apotex's batch records report both the amount of wet inclusion bodies that are used to begin Apotex's refolding process, as well as the total amount of protein present in those inclusion bodies. Apotex's batch records also confirm that the total wet

weight of the inclusion bodies are used to calculate the 0.9 to 1.4 g/L inclusion body concentration in the refold mixture.

51. Apotex's batch records reflect that inclusion bodies from Apotex's upstream process are weighed wet prior to being placed into cold storage for up to 90 days. That Apotex's inclusion bodies are frozen suggests that water is present with the inclusion bodies.

52. After the inclusion bodies have been solubilized, Apotex measures the total protein concentration using an optical density measurement at 280 nanometers, also referred to as "OD280." Apotex uses the OD280 measurement in the solubilization buffer to calculate the total amount of protein that was present in Apotex's inclusion bodies and records this amount in its batch records.

53. The batch records show that, in the 91 times that Apotex has run its manufacturing process, the average protein content in Apotex's inclusion bodies has been 36 percent, with the balance of Apotex's inclusion bodies—on average, 64 percent by weight—being water. Further, in the 91 times that Apotex has run its manufacturing process, the highest protein concentration in the refold mixture has been 0.56 g/L, which is well below the claimed "at or above 1 g/L." The Court credits Dr. Dowd's testimony in reaching these findings.

54. In addition to measuring the protein concentration in the solubilization buffer, Apotex measures the protein concentration in its refold mixture using the OD280 measurement. However, this second measurement of protein concentration (taken in the refold mixture) reports an artificially higher amount of protein because cysteine and cystine are present

at high concentrations, and both absorb light at 280 nanometers. Although the measurement of protein concentration in the refold mixture is not a reliable indicator of protein concentration, a clear explanation exists for the difference between the OD280 measurements from the solubilization buffer and the refold mixture. Thus, the higher OD280 measurement of protein concentration in the refold mixture does not render unreliable the OD280 measurement in the solubilization buffer.

55. For these reasons, the Court finds that Apotex's batch records provide an accurate record of Apotex's manufacturing process, which does not literally infringe any of the asserted claims of the '138 Patent.

2. Apotex's Refolding Process Does Not Include a Redox Component Having a Redox Buffer Strength of 2 to 100 mM or Its Equivalent.

56. Each of the asserted claims of the '138 Patent requires a "redox component comprising . . . a redox buffer strength of 2 mM or greater," wherein the redox buffer strength is effectively bounded at a maximum of 100 mM.

57. The claim specifies a minimum redox buffer strength because, as the Patent states, "[a]t lower redox buffer strengths, the overall system becomes much more difficult to control." The imposition of an effective maximum redox buffer strength is to address solubility limitations.

58. Apotex's process does not literally include the claimed redox component that has an oxidant (cystine) and a reductant (cysteine) combined together outside of the refold mixture. Nor does Apotex's process literally include the claimed redox buffer strength. These conclusions are not in dispute.

59. Instead, Amgen argues that Apotex's process has (1) an equivalent redox component (2) that equivalently satisfies the buffer strength limitation.

60. The Court will assume, without deciding, that the Cysteine and Cystine Solutions added in a stepwise manner in Apotex's refolding process is the equivalent of the claimed redox component.

61. The Court does find, however, that Amgen has failed to meet its burden to prove that the hypothetical redox component in Apotex's process—the combination of Apotex's Cysteine and Cystine Solutions in a hypothetical volume—satisfies the redox buffer strength claim limitation under the doctrine of equivalents.

62. Specifically, Amgen has not proven by a preponderance of the evidence that the redox buffer strength of Apotex's hypothetical redox component is insubstantially different from the claimed redox buffer strength of 2 to 100 mM.

63. The maximum possible combined volume of Apotex's Cystine and Cysteine Solutions is 476.32 mL (444 mL of Cystine Solution plus 32.32 mL of Cysteine Solution). Thus, the maximum possible volume of Apotex's hypothetical redox component is 476.32 mL.

64. The redox buffer strength of Apotex's hypothetical redox component ranges from 214 to 340 mM.

65. Thus, Apotex's process uses a smaller volume of more concentrated redox component than is claimed in the '138 Patent to achieve its desired redox conditions.

66. According to Dr. Willson, when using a redox component with a redox buffer strength of 100 mM (within the limitation of the claim), one would need

to practice the claimed method with a total volume of 1.0 L to 1.6 L of such a redox component to deliver the same number of molecules of cystine and cysteine to the refold mixture as in Apotex's process.

67. A volume of 1 to 1.6 L is two to three times greater than the volume of the hypothetical redox component.

68. The difference between a redox component in a 476.32 mL volume and a 1 to 1.6 L volume, particularly when its components are added in a stepwise manner, is substantial. The Court credits Dr. Robinson's opinion in reaching this conclusion.

69. Amgen's evidence is insufficient that simply increasing the redox component volume will serve substantially the same function in substantially the same way to achieve substantially the same result as practicing a volume with the claimed redox component strength. Dr. Willson did not specify what liquid would be used to increase the volume of the hypothetical redox component in Apotex's process to achieve the desired redox buffer strength. Dr. Willson also acknowledged that he did not know where equivalence would be lost by increasing the volume of the redox component volume. Additionally, Dr. Willson did not perform any experiments or present any evidence that increasing the volume of the redox component would result in an insubstantial difference.

70. Additionally, Apotex's aBLAs specify the volume of each Cystine and Cysteine Solution allowed in its manufacturing process. A batch utilizing combined redox chemical solutions with a volume of 1 to 1.6 L is not possible under Apotex's aBLAs. Apotex's process does not, and cannot, meet the claim

requirement of a redox buffer strength effectively bounded at a maximum of 100 mM.

II. CONCLUSIONS OF LAW

Amgen has not met its burden to prove that Apotex's process for manufacturing its Filgrastim and Pegfilgrastim products meets each and every claim limitation of the '138 Patent. Specifically, Amgen has not proven by a preponderance of the evidence that Apotex's process literally meets the protein concentration claim limitation or equivalently meets the redox buffer strength claim limitation. Thus, no finding of infringement is warranted. Apotex, however, is entitled to a judgment of non-infringement because it has proven that its manufacturing process does not satisfy at least one of the Patent's claim limitations.

"Patent infringement, whether literal or by equivalence, is an issue of fact, which the patentee must prove by a preponderance of the evidence." *Siemens Med. Sols. USA, Inc. v. Saint-Gobain Ceramics & Plastics, Inc.*, 637 F.3d 1269, 1279 (Fed. Cir. 2011). Determining infringement requires a two-step analysis: (1) the patent claims must be construed to ascertain their scope and meaning; and (2) the claims, as properly construed, must be compared to the accused method or product. *SmithKline Diagnostics, Inc. v. Helena Labs. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988). The Court previously construed the asserted claims, leaving the issue of infringement for trial.

To prove infringement, the patentee must show that an accused method meets each and every limitation of a claim, either literally or under the doctrine of equivalents. *Deering Precision Instruments, L.L.C. v. Vector Distrib. Sys., Inc.*, 347 F.3d 1314, 1324 (Fed. Cir. 2003). "To show literal infringement of a patent,

a patentee must supply sufficient evidence to prove that the accused product or process meets every element or limitation of a claim." *Rohm & Haas Co. v. Brotech Corp.*, 127 F.3d 1089, 1092 (Fed. Cir. 1997) (citing *Lemelson v. United States*, 752 F.2d 1538, 1551 (Fed. Cir. 1985)). Under the doctrine of equivalents, a "process that does not literally infringe upon the express terms of a patent claim may nonetheless be found to infringe if there is 'equivalence' between the elements of the accused . . . process and the claimed elements of the patented invention." *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21 (1997) (citation omitted). Because Amgen has conceded that Apotex's process does not literally satisfy some limitations of claim 1 of the '138 Patent, Amgen proceeds on a theory of infringement by equivalence.

A dependent claim "incorporate[s] by reference all the limitations of the claim to which it refers." 35 U.S.C. § 112. If an independent claim is not infringed, then each corresponding dependent claim cannot be infringed. *See Wahpeton Canvas Co., Inc. v. Frontier, Inc.*, 870 F.2d 1546, 1553 (Fed. Cir. 1989) ("It is axiomatic that dependent claims cannot be found infringed unless the claims from which they depend have been found to have been infringed . . . .").

A. Amgen Has Not Met Its Burden to Prove Literal Infringement of the Protein Concentration Claim Limitation.

Amgen did not meet its burden to show by a preponderance of the evidence that Apotex's refolding process literally uses a protein concentration in Apotex's refold mixture that is "at or above 1 g/L." Nor did Amgen proffer evidence or assert that Apotex's

refolding process meets this limitation under the doctrine of equivalents.

Under the BPCIA, the "submission" of an aBLA to the FDA, which seeks approval to commercially market a biosimilar biologic product, is an act of infringement of the patents identified by the parties during the BPCIA information exchange process. 35 U.S.C. § 271(e)(2)(C)(i); *Amgen Inc. v. Apotex Inc.*, 2016 WL 3606770, at *4. Similar to the Hatch-Waxman Act (which is analogous to the BPCIA in some respects, *see Amgen Inc. v. Sandoz Inc.*, 794 F.3d 1347, 1351 (Fed. Cir. 2015)), the ultimate infringement question, however, is determined by traditional patent law principles. *See Sunovion Pharmaceuticals, Inc. v. Teva Pharmaceuticals USA, Inc.*, 731 F.3d 1271, 1278 (Fed. Cir. 2013). If the process that an aBLA applicant is asking the FDA to approve falls within the scope of an asserted patent claim, a judgment of infringement must necessarily ensue. *Id.*

To determine infringement, a court compares the patent claim to the aBLAs specification, which is "what [the applicant] has asked the FDA to approve as a regulatory matter." *Id.*; *see also Abbott Labs. v. TorPham, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002) ("Because drug manufacturers are bound by strict statutory provisions to sell only those products that comport with the ANDA's description of the drug, an ANDA specification defining a proposed generic drug in a manner that directly addresses the issue of infringement will control the infringement inquiry."). If the aBLA applicant has asked the FDA to approve a process within the scope of the claim, it is an infringement as a matter of law. *See Sunovion*, 731 F.3d at 1280. Manufacturing guidelines, batch

records, product samples, and certifications pledging not to infringe cannot be used to overcome that infringement. *See id.* at 1278-80. This other evidence is considered only if the aBLA is "silent" with respect to the claim limitations of the patents-in-suit. *See Meds. Co. v. Mylan Inc.*, 72 F. Supp. 3d 837, 887 (N.D. Ill. 2014) (citing *Ferring B.V. v. Watson Labs., Inc.-Fla.*, 764 F.3d 1382, 1387 (Fed. Cir. 2014)). It is the burden of the patentee to prove by a preponderance of the evidence that the alleged infringer will likely market an infringing product, and that burden is never shifted to the alleged infringer. *See Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1568-70 (Fed. Cir. 1997).

Here, Amgen asserts that Apotex's aBLAs speak directly to the issue of infringement because Apotex's aBLAs contain process specifications for inclusion bodies. However, Amgen has not established that Apotex's specification for inclusion bodies defines a protein concentration in the refold mixture. Instead, the Court finds extensive evidence that Apotex's inclusion bodies are wet at the time they are weighed and are on average about two-thirds water. Further, whether Apotex refers to the inclusion bodies as a "pellet" or a "paste," does not change the fact that water constitutes the majority of Apotex's inclusion bodies at the time of weighing. Nor is this finding changed because Apotex's pre-litigation letters under 42 U.S.C. § 262(*l*)(3)(8) incorrectly referred to the inclusion body concentration as the protein concentration. These letters were not part of Apotex's aBLAs, were never filed with the FDA, do not impact the process and product approved by the FDA, and are not controlling. *See Takeda Chem. Indus., Ltd. v. Mylan Labs., Inc.*, 549 F.3d 1381, 1390-91 (Fed. Cir.

2008) ("It is clear from the district court's opinion that it . . . [did not] limit the filers to the theories raised in their certification letters.").

Apotex, however, did prove that its aBLAs specify a protein concentration separate from an inclusion body concentration. Based on the highest allowable Filgrastim concentration required by Apotex's aBLAs, the maximum total protein concentration allowable in Apotex's refold mixture is restricted at 0.708 g/L. Therefore, Apotex's aBLAs specifications directly show that the total protein concentration in Apotex's refold mixture is outside the "at or above about 1 g/L protein" range required by the Court's construction of the claim element "refold mixture." Amgen cited no relevant evidence contradicting that Apotex's aBLAs specifications effectively limit the maximum protein concentration in Apotex's refold mixture to 0.708 g/L. As a result, the Court finds that Apotex's aBLAs specifications directly address the infringement inquiry and define a protein refolding process having a total protein concentration less than "at or above about 1 g/L protein." *See Sunovion*, 731 F.3d at 1279-80 (citing *Bayer*, 212 F.3d at 1250) ("In *Bayer*, we upheld a summary judgment of no literal infringement because the generic manufacturer's ANDA specification itself required that the proposed product have a specific surface area outside of the range claimed by the innovator's asserted patent."). For at least these reasons, the Court finds that Apotex's refolding process does not infringe the asserted claims.

Furthermore, even if Apotex's aBLAs had been silent on the issue of protein concentration, Apotex's batch records show that the drug products it intends to market are manufactured by a non-infringing

process. In the 91 times that Apotex has run its manufacturing process, the highest protein concentration in the refold mixture has been 0.56 g/L, which is well below the claimed "at or above about 1 g/L" limitation. Apotex submitted its batch records, which include an outline for each step in the manufacturing process with operating parameters, to the FDA along with the aBLAs, and there is no evidence that the FDA has questioned the accuracy of Apotex's measurements. Thus, Apotex's batch records support a finding that judgment of non-infringement is proper because Apotex's refolding process for the drugs it intends to market does not infringe any asserted claim of the '138 Patent under 35 U.S.C. § 271(e)(2). *See Glaxo*, 110 F.3d at 1568-70.

B. Amgen Has Not Met Its Burden to Prove Equivalent Infringement of the Redox Buffer Strength Claim Limitation.

Amgen has not proven that Apotex's protein refolding process infringes the redox buffer strength claim limitation of the '138 Patent under the doctrine of equivalents. A patent is infringed under the doctrine of equivalents if the difference(s) between a claim limitation and the corresponding element in the accused process is "insubstantial" ("insubstantial differences" test). *See Warner-Jenkinson*, 520 U.S. at 39-40 (1997). Alternatively, an element in the accused process is equivalent to a claim limitation only if it performs substantially the same function, in substantially the same way, to yield substantially the same result ("function-way-result" test). *See id.* at 38-40 (citing *Union Paper-Bag Mach. Co. v. Murphy*, 97 U.S. 120, 125 (1877)). Which test to apply depends on the facts of the case, because "[d]ifferent linguistic frameworks may be more suitable to

different cases, depending on their particular facts." *Warner-Jenkinson*, 520 U.S. at 40.

"What constitutes equivalency must be determined against the context of the patent, the prior art, and the particular circumstances of the case." *Graver Tank & Mfg. Co. v. Linde Air Products Co.*, 339 U.S. 605, 609 (1950). The doctrine of equivalents "must be applied to individual elements of the claim, not to the invention as a whole." *Warner-Jenkinson*, 520 U.S. at 29. The patentee must demonstrate that a claim element is found equivalently in the accused product or process by a preponderance of the evidence. *Id.*, 520 U.S. at 37. The equivalence must have been known at the time of the alleged infringement to a person having ordinary skill in the art. *Graver Tank*, 339 U.S. at 609.

In addition to Amgen's failure to prove that Apotex's protein refolding process literally satisfies the protein concentration limitation, Amgen has not established that Apotex's process equivalently satisfies the limitation of a "redox buffer strength of 2mM or greater." Assuming without deciding that Apotex's hypothetical redox component is equivalent to the claimed redox component, the redox buffer strength of this hypothetical redox component would be 214 to 340 mM. This value is more than two to three times greater than the maximum redox buffer strength of 100 mM permitted under the Court's claim construction. Amgen has established neither that this is an insubstantial difference nor that a redox buffer strength of 214 to 340 mM performs substantially the same function, in substantially the same way, to yield substantially the same result as the claimed redox buffer strength in the redox component.

The relevant inquiry is whether a redox component with a redox buffer strength of 214 to 340 mM is insubstantially different from a redox component with a redox buffer strength of 100 mM. To demonstrate equivalence, Dr. Willson adjusted the volume of the hypothetical redox component from approximately 472 mL to 1.0 to 1.6 L, adding an unspecified liquid, in an effort to make the redox buffer strength of Apotex's hypothetical redox component meet the redox buffer strength claim limitation. In other words, Amgen attempts to show equivalence by significantly altering Apotex's process. This cannot be done. Apotex is bound by the specifications in its aBLAs and cannot, in practice, increase the volume of its redox component to a volume of 1.0 to 1.6 L without facing serious legal penalties. Moreover, adjusting the volume of the hypothetical redox component to reach a desired redox buffer strength that is not actually utilized in Apotex's process renders meaningless the maximum limit of 100 mM because one could simply adjust the volume of any redox component with a redox component greater than 100 mM to make it fall within the claimed limitation. *See Warner-Jenkinson*, 520 U.S. at 29 ("It is important to ensure that the application of the doctrine [of equivalents], even as to an individual element, is not allowed such broad play as to effectively eliminate that element in its entirety.").

For all of the reasons above, judgment of no infringement under the doctrine of equivalents is appropriate because Amgen has failed to prove by a preponderance of the evidence that a redox buffer strength 214 to 340 mM in the redox component is insubstantially different from the claimed redox buffer strength. Because the process defined in

Apotex's aBLAs does not infringe claim 1, dependent claims 2, 3, 6, 7, 13, 15, 16, 17, 22, and 23 that depend from claim 1 similarly are not infringed. *See Teledyne McCormick Selph*, 558 F.2d at 1004.

C. Apotex's Invalidity Counterclaim Shall Be Dismissed.

Having found that the manufacturing process defined in Apotex's aBLAs does not infringe the '138 Patent, the Court declines to render an opinion as to whether the '138 Patent is invalid for lack of enablement. The Federal Circuit has indicated that "a district court can dismiss an invalidity counterclaim when it finds noninfringement or dismisses an infringement claim with prejudice." *AstraZeneca LP v. Breath Ltd.*, 542 F. App'x 971, 981 (Fed. Cir. 2013), as amended on reh'g in part (Dec. 12, 2013) (citing *Liquid Dynamics Corp. v. Vaughan Co., Inc.*, 355 F.3d 1361, 1371 (Fed. Cir. 2004) ("A district court judge faced with an invalidity counterclaim challenging a patent that it concludes was not infringed may either hear the claim or dismiss it without prejudice, subject to review only for abuse of discretion."); *Nystrom v. TREX Co., Inc.*, 339 F.3d 1347, 1351 & n.* (Fed. Cir. 2003) ("[T]he district court could have dismissed the counterclaim without prejudice (either with or without a finding that the counterclaim was moot) following the grant of summary judgment of non-infringement."); *Phonometrics, Inc. v. N. Telecom Inc.*, 133 F.3d 1459, 1468 (Fed. Cir. 1998) ("We have previously held that a district court has discretion to dismiss a counterclaim alleging that a patent is invalid as moot where it finds no infringement.")). "Where . . . non-infringement is clear and invalidity is not plainly evident, it is appropriate to treat only the infringement issue." *Leesona Corp. v. United*

States, 530 F.2d 896, 906 n.9 (Ct. Cl. 1976) (citation omitted). Even after the invalidity counterclaim has been tried, the district court may dismiss the invalidity counterclaim without prejudice where "the non-infringement judgment firmly and clearly resolves the case, and [the defendant] has not shown how a judgment of invalidity would provide any additional benefit." *AstraZeneca LP*, 542 F. App'x at 981-82.

Here, a judgment of Apotex's non-infringement firmly and clearly resolves this case. Apotex has not shown how a finding of invalidity of the '138 Patent would provide any additional benefit beyond a judgment of non-infringement. Moreover, unlike Apotex's non-infringement, the issue of invalidity is not plainly evident to the Court based on the evidence presented at trial. Accordingly, the Court defers judgment on the issue of invalidity of the '138 Patent and will dismiss the invalidity counterclaim without prejudice.

D. This Is Not an Unusual Case Warranting an Attorneys' Fee Award.

Under 35 U.S.C. § 271(e)(4), a court may award reasonable attorneys' fees under 35 U.S.C. § 285 to the prevailing party in exceptional cases. An exceptional case is "simply one that stands out from others with respect to the substantive strength of a party's litigating position (considering both the governing law and the facts of the case) or the unreasonable manner in which the case was litigated." *Octane Fitness, LLC v. ICON Health & Fitness, Inc.*, 134 S. Ct. 1749, 1756 (2014); *see also ILOR, LLC v. Google, Inc.*, 631 F.3d 1372, 1380 (Fed. Cir. 2011) (reversing district court finding that case was exceptional where neither plain language of claim, specification, nor prosecution history showed that patentee's claim

construction "was so unreasonable that no reasonable litigant could believe it would succeed"). Attorneys' fees are limited to exceptional cases "in order to avoid penalizing a party for merely defending or prosecuting a lawsuit, and are awarded to avoid a gross injustice." *Revlon, Inc. v. Carson Prod. Co.*, 803 F.2d 676, 679 (Fed. Cir. 1986) (internal citations and quotations omitted).

Determining whether a case is "exceptional" is a case-by-case exercise that should consider the totality of the circumstances. *Id.* "The determination whether a case is 'exceptional' is indisputably committed to the discretion of the district court." *Lumen View Tech. LLC v. Findthebest.com, Inc.*, 811 F.3d 479, 482 (Fed. Cir. 2016) (citing *Highmark Inc. v. Allcare Health Mgmt. Sys., Inc.*, 134 S. Ct. 1744, 1749 (2014)).

The Court does not find this case "exceptional." Amgen's actions in asserting its patent rights were reasonable. The Court has no reason to doubt that Amgen brought this case upon a good faith belief that Apotex's process practices each claim of the '138 Patent. The substantive strength of Amgen's litigating position certainly was not so weak that no reasonable litigant would think its claims could succeed. To the contrary, Amgen advanced a cogent argument for a finding of infringement, and it should not be penalized simply because the Court found Apotex's evidence and arguments more convincing. Furthermore, Amgen litigated this case in a reasonable and professional manner. No manifest injustice will result if attorneys' fees are not awarded.

III. CONCLUSION

For the foregoing reasons, it is **ORDERED AND ADJUDGED** that a separate Final Judgment will be

entered in favor of Defendants Apotex Inc. and Apotex Corp. and against Plaintiffs Amgen Inc. and Amgen Manufacturing Limited on the issue of infringement consistent with the Findings of Fact and Conclusions of Law herein.

DONE AND ORDERED in Chambers at Fort Lauderdale, Broward County, Florida, this 6th day of September, 2016.

/s/ JAMES I. COHN

JAMES I. COHN
UNITED STATES DISTRICT JUDGE

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF FLORIDA

Case No. 15-61631-CIV-COHN/SELTZER

AMGEN, INC. AND
AMGEN MANUFACTURING LIMITED,
Plaintiffs,

v.

APOTEX INC. AND APOTEX CORP.,
Defendants.

[Filed Sept. 6, 2016]

FINAL JUDGMENT

THIS CAUSE came before the Court in a nonjury trial on July 11, 2016 through July 18, 2016, after which the Court found that Defendants Apotex Inc. and Apotex Corp. (collectively, "Apotex") have not infringed claims 1-3, 6, 7, 13, 15-17, and 22-23 (the "Asserted Claims") of U.S. Patent No. 8,952,138 ("the '138 Patent") held by Plaintiffs Amgen Inc. and Amgen Manufacturing Limited (collectively, "Amgen"). The Court entered separately its Findings of Fact and Conclusions of Law [DE 267]. Pursuant to Federal Rule of Civil Procedure 58, it is hereby

ORDERED AND ADJUDGED as follows:

1. Judgment is entered in favor of Apotex and against Amgen on:

a. Amgen's claims of infringement under 35 U.S.C. § 271(e)(2)(C)(i): Amgen's First Count in each of Amgen's Complaints in this consolidated action [DE 1 in Case No. 15-62081; DE 1 in Case No. 15-61631];

b. Amgen's claims seeking declaratory judgments of infringement under 35 U.S.C. § 271(g): Amgen's Second Count of Amgen's Filgrastim Complaint [DE 1 in Case No. 15-62081] and Amgen's Third Count of Amgen's Pegfilgrastim Complaint [DE 1 in Case No. 15-61631]; and

c. Apotex's counterclaims regarding non-infringement of the '138 Patent: First Counterclaim (Declaratory Judgment of Non-Infringement of the '138 Patent) in each of Apotex's Answers, Affirmative Defenses, and Counterclaims in this consolidated action [DE 47 (incorporating DE 35) in Case No. 15-61631; DE 64 in Case No. 15-61631].

2. Judgment is entered in favor of Amgen and against Apotex on the following issues based on the Court's previous decision on December 9, 2015 [DE 71], the relevant part of which was affirmed by the United States Court of Appeals for the Federal Circuit on July 5, 2016 [DE 259]:

a. Amgen's claims for Declaratory Judgment that Apotex's Notice of Commercial Marketing Violates 42 U.S.C. § 262(*l*)(8)(A): Amgen's Fourth Count in each of Amgen's Complaints in this consolidated action [DE 1 in Case No.15-62081; DE 1 in Case No. 15-61631];

b. Apotex's counterclaims for Declaratory Judgment that Subsection (k) Applicants Who Have Complied with 42 U.S.C. § 262(*l*)(2)(A) May Elect Not to Provide Notice of Commercial Marketing to the Reference Product Sponsor, Subject to the Consequences Set Forth in 42 U.S.C. § 262(*l*)(9)(B): Apotex's Fifth Counterclaim in Apotex's Pegfilgrastim Counterclaims [DE 47 (incorporating DE 35) in Case No. 15-61631] and

Apotex's second Seventh Counterclaim in Apotex's Filgrastim Counterclaims [DE 64 in Case No. 15-61631]; and

c. Apotex's counterclaims for Declaratory Judgment of No Injunctive Relief Under BPCIA: Apotex's Sixth Counterclaim in Apotex's Pegfilgrastim Counterclaims [DE 47 (incorporating DE 35) in Case No. 15-61631] and Apotex's Eighth Counterclaim in Apotex's Filgrastim Counterclaims [DE 64 in Case No. 15-61631].

3. In addition, consistent with the Court's grant of a preliminary injunction in favor of Amgen on December 9, 2015 [DE 71], affirmed by the United States Court of Appeals for the Federal Circuit on July 5, 2016 [DE 259], permanent injunctive relief is appropriate. If the FDA approves Apotex's aBLA for its Pegfilgrastim Product, Apotex must provide Amgen with at least 180 days' notice before the date of the first commercial marketing of the biological product approved by the FDA. 42 U.S.C. § 262(*l*)(8)(A). Apotex and those acting in concert with it are enjoined from any commercial marketing of Apotex's Pegfilgrastim Product, including selling that product or offering it for sale for use in the United States, until Apotex gives Amgen proper notice, at least 180 days before first commercial marketing but not before Apotex's Pegfilgrastim Product is licensed by the FDA, and the 180-day notice period is exhausted.

4. Likewise, if the FDA approves Apotex's aBLA for its Filgrastim Product, Apotex must provide Amgen with at least 180 days' notice before the date of the first commercial marketing of the biological product approved by the FDA. 42 U.S.C. § 262(*l*)(8)(A). Apotex and those acting in concert with it are enjoined

from any commercial marketing of Apotex's Filgrastim Product, including selling that product or offering it for sale for use in the United States, until Apotex gives Amgen proper notice, at least 180 days before first commercial marketing but not before Apotex's Filgrastim Product is licensed by the FDA, and the 180-day notice period is exhausted.

5. In addition, judgment is hereby entered in favor of Amgen and against Apotex on Apotex's counterclaim for Declaratory Judgment of Unenforceability of the '138 Patent for Patent Misuse: Apotex's Fourth Counterclaim in Apotex's Pegfilgrastim Counterclaims [DE 47 (incorporating DE 35) in Case No. 15-61631] and Apotex's Sixth Counterclaim in Apotex's Filgrastim Counterclaims [DE 64 in Case No. 15-61631]. Apotex neither provided evidence on this counterclaim at trial nor identified it as a trial issue in the parties' Joint Pretrial Stipulation [DE 217].

6. Apotex's counterclaims regarding invalidity of the '138 Patent for lack of enablement[1]—Apotex's Fifth Affirmative Defense (Invalidity) and Second Counterclaim (Declaratory Judgment on Invalidity of the '138 Patent) in each of Apotex's Answers, Affirmative Defenses, and Counterclaims in this consolidated action [DE 47 (incorporating DE 35) in Case

[1] The Court previously entered judgment in favor of Amgen and against Apotex on Apotex's Fifth Affirmative Defense and Second Counterclaim in each of Apotex's Answers, Affirmative Defenses, and Counterclaims in this consolidation action [DE 47 (incorporating DE 35) in Case No. 15-61631; DE 64 in Case No. 15-61631] solely with respect to (i) anticipation, (ii) lack of written description, (iii) indefiniteness, and (iv) obviousness. *See* DE 245.

No. 15-61631; DE 64 in Case No. 15-61631]—**are DISMISSED without prejudice.**

7. The Clerk of Court is directed to **CLOSE** these cases and **DENY as moot** any pending motions.

DONE AND ORDERED in Chambers at Fort Lauderdale, Broward County, Florida, this 6th day of September, 2016.

/s/ JAMES I. COHN

JAMES I. COHN

UNITED STATES DISTRICT JUDGE

STATUTORY PROVISIONS INVOLVED

Public Law 111-148

111th Congress

An Act

Entitled The Patient
Protection and Affordable Care Act.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

* * *

TITLE VII—IMPROVING ACCESS TO INNOVATIVE MEDICAL THERAPIES

Subtitle A—Biologics Price Competition and Innovation

SEC. 7001. SHORT TITLE.

(a) IN GENERAL.—This subtitle may be cited as the "Biologics Price Competition and Innovation Act of 2009".

(b) SENSE OF THE SENATE.—It is the sense of the Senate that a biosimilars pathway balancing innovation and consumer interests should be established.

SEC. 7002. APPROVAL PATHWAY FOR BIOSIMILAR BIOLOGICAL PRODUCTS.

(a) LICENSURE OF BIOLOGICAL PRODUCTS AS BIOSIMILAR OR INTERCHANGEABLE.—Section 351 of the Public Health Service Act (42 U.S.C. 262) is amended—

(1) in subsection (a)(1)(A), by inserting "under this subsection or subsection (k)" after "biologics license"; and

(2) by adding at the end the following:

"(k) LICENSURE OF BIOLOGICAL PRODUCTS AS BIOSIMILAR OR INTERCHANGEABLE.—

"(1) IN GENERAL.—Any person may submit an application for licensure of a biological product under this subsection.

"(2) CONTENT.—

"(A) IN GENERAL.—

"(i) REQUIRED INFORMATION.—An application submitted under this subsection shall include information demonstrating that—

"(I) the biological product is biosimilar to a reference product based upon data derived from—

"(aa) analytical studies that demonstrate that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components;

"(bb) animal studies (including the assessment of toxicity); and

"(cc) a clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are sufficient to demonstrate 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;

"(II) the biological product and reference product utilize the same mechanism or mechanisms of action for the condition or conditions of use prescribed, recommended, or suggested in the proposed labeling, but

only to the extent the mechanism or mechanisms of action are known for the reference product;

"(III) the condition or conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product have been previously approved for the reference product;

"(IV) the route of administration, the dosage form, and the strength of the biological product are the same as those of the reference product; and

"(V) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

"(ii) DETERMINATION BY SECRETARY.—The Secretary may determine, in the Secretary's discretion, that an element described in clause (i)(I) is unnecessary in an application submitted under this subsection.

"(iii) ADDITIONAL INFORMATION.—An application submitted under this subsection—

"(I) shall include publicly-available information regarding the Secretary's previous determination that the reference product is safe, pure, and potent; and

"(II) may include any additional information in support of the application, including publicly-available information with respect to the reference product or another biological product.

"(B) INTERCHANGEABILITY.—An application (or a supplement to an application) submitted under this subsection may include information demonstrating that the biological product meets the standards described in paragraph (4).

"(3) EVALUATION BY SECRETARY.—Upon review of an application (or a supplement to an application) submitted under this subsection, the Secretary shall license the biological product under this subsection if—

"(A) the Secretary determines that the information submitted in the application (or the supplement) is sufficient to show that the biological product—

"(i) is biosimilar to the reference product; or

"(ii) meets the standards described in paragraph (4), and therefore is interchangeable with the reference product; and

"(B) the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).

"(4) SAFETY STANDARDS FOR DETERMINING INTERCHANGEABILITY.—Upon review of an application submitted under this subsection or any supplement to such application, the Secretary shall determine the biological product to be interchangeable with the reference product if the Secretary determines that the information submitted in the application (or a supplement to such application) is sufficient to show that—

"(A) the biological product—

"(i) is biosimilar to the reference product; and

"(ii) can be expected to produce the same clinical result as the reference product in any given patient; and

"(B) for a biological 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 without such alternation or switch.

"(5) GENERAL RULES.—

"(A) ONE REFERENCE PRODUCT PER APPLICATION.—A biological product, in an application submitted under this subsection, may not be evaluated against more than 1 reference product.

"(B) REVIEW.—An application submitted under this subsection shall be reviewed by the division within the Food and Drug Administration that is responsible for the review and approval of the application under which the reference product is licensed.

"(C) RISK EVALUATION AND MITIGATION STRATEGIES.—The authority of the Secretary with respect to risk evaluation and mitigation strategies under the Federal Food, Drug, and Cosmetic Act shall apply to biological products licensed under this subsection in the same manner as such authority applies to biological products licensed under subsection (a).

"(6) EXCLUSIVITY FOR FIRST INTERCHANGEABLE BIOLOGICAL PRODUCT.—Upon review of an application submitted under this subsection relying on the same reference product for which a prior biological product has received a determination of

interchangeability for any condition of use, the Secretary shall not make a determination under paragraph (4) that the second or subsequent biological product is interchangeable for any condition of use until the earlier of—

"(A) 1 year after the first commercial marketing of the first interchangeable biosimilar biological product to be approved as interchangeable for that reference product;

"(B) 18 months after—

"(i) a final court decision on all patents in suit in an action instituted under subsection (*l*)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

"(ii) the dismissal with or without prejudice of an action instituted under subsection (*l*)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

"(C)(i) 42 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has been sued under subsection (*l*)(6) and such litigation is still ongoing within such 42-month period; or

"(ii) 18 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has not been sued under subsection (*l*)(6).

For purposes of this paragraph, the term 'final court decision' means a final decision of a court from which no appeal (other than a petition to the United States

Supreme Court for a writ of certiorari) has been or can be taken.

"(7) EXCLUSIVITY FOR REFERENCE PRODUCT.—

"(A) EFFECTIVE DATE OF BIOSIMILAR APPLICATION APPROVAL.—Approval of an application under this subsection may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a).

"(B) FILING PERIOD.—An application under this subsection may not be submitted to the Secretary until the date that is 4 years after the date on which the reference product was first licensed under subsection (a).

"(C) FIRST LICENSURE.—Subparagraphs (A) and (B) shall not apply to a license for or approval of—

"(i) a supplement for the biological product that is the reference product; or

"(ii) a subsequent application filed by the same sponsor or manufacturer of the biological product that is the reference product (or a licensor, predecessor in interest, or other related entity) for—

"(I) a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength; or

"(II) a modification to the structure of the biological product that does not result in a change in safety, purity, or potency.

"(8) GUIDANCE DOCUMENTS.—

"(A) IN GENERAL.—The Secretary may, after opportunity for public comment, issue guidance in accordance, except as provided in subparagraph (B)(i), with section 701(h) of the Federal Food, Drug, and Cosmetic Act with respect to the licensure of a biological product under this subsection. Any such guidance may be general or specific.

"(B) PUBLIC COMMENT.—

"(i) IN GENERAL.—The Secretary shall provide the public an opportunity to comment on any proposed guidance issued under subparagraph (A) before issuing final guidance.

"(ii) INPUT REGARDING MOST VALUABLE GUIDANCE.—The Secretary shall establish a process through which the public may provide the Secretary with input regarding priorities for issuing guidance.

"(C) NO REQUIREMENT FOR APPLICATION CONSIDERATION.—The issuance (or non-issuance) of guidance under subparagraph (A) shall not preclude the review of, or action on, an application submitted under this subsection.

"(D) REQUIREMENT FOR PRODUCT CLASS-SPECIFIC GUIDANCE.—If the Secretary issues product class-specific guidance under subparagraph (A), such guidance shall include a description of—

"(i) the criteria that the Secretary will use to determine whether a biological product is highly similar to a reference product in such product class; and

"(ii) the criteria, if available, that the Secretary will use to determine whether a biological

product meets the standards described in paragraph (4).

"(E) CERTAIN PRODUCT CLASSES.—

"(i) GUIDANCE.—The Secretary may indicate in a guidance document that the science and experience, as of the date of such guidance, with respect to a product or product class (not including any recombinant protein) does not allow approval of an application for a license as provided under this subsection for such product or product class.

"(ii) MODIFICATION OR REVERSAL.—The Secretary may issue a subsequent guidance document under subparagraph (A) to modify or reverse a guidance document under clause (i).

"(iii) NO EFFECT ON ABILITY TO DENY LICENSE.—Clause (i) shall not be construed to require the Secretary to approve a product with respect to which the Secretary has not indicated in a guidance document that the science and experience, as described in clause (i), does not allow approval of such an application.

"(*l*) PATENTS.—

"(1) CONFIDENTIAL ACCESS TO SUBSECTION (k) APPLICATION.—

"(A) APPLICATION OF PARAGRAPH.—Unless otherwise agreed to by a person that submits an application under subsection (k) (referred to in this subsection as the 'subsection (k) applicant') and the sponsor of the application for the reference product (referred to in this subsection as the 'reference product sponsor'), the provisions of this

paragraph shall apply to the exchange of information described in this subsection.

"(B) IN GENERAL.—

"(i) PROVISION OF CONFIDENTIAL INFORMATION.—When a subsection (k) applicant submits an application under subsection (k), such applicant shall provide to the persons described in clause (ii), subject to the terms of this paragraph, confidential access to the information required to be produced pursuant to paragraph (2) and any other information that the subsection (k) applicant determines, in its sole discretion, to be appropriate (referred to in this subsection as the 'confidential information').

"(ii) RECIPIENTS OF INFORMATION.—The persons described in this clause are the following:

"(I) OUTSIDE COUNSEL.—One or more attorneys designated by the reference product sponsor who are employees of an entity other than the reference product sponsor (referred to in this paragraph as the 'outside counsel'), provided that such attorneys do not engage, formally or informally, in patent prosecution relevant or related to the reference product.

"(II) IN-HOUSE COUNSEL.—One attorney that represents the reference product sponsor who is an employee of the reference product sponsor, provided that such attorney does not engage, formally or informally, in patent prosecution relevant or related to the reference product.

"(iii) PATENT OWNER ACCESS.—A representative of the owner of a patent exclusively

licensed to a reference product sponsor with respect to the reference product and who has retained a right to assert the patent or participate in litigation concerning the patent may be provided the confidential information, provided that the representative informs the reference product sponsor and the subsection (k) applicant of his or her agreement to be subject to the confidentiality provisions set forth in this paragraph, including those under clause (ii).

"(C) LIMITATION ON DISCLOSURE.—No person that receives confidential information pursuant to subparagraph (B) shall disclose any confidential information to any other person or entity, including the reference product sponsor employees, outside scientific consultants, or other outside counsel retained by the reference product sponsor, without the prior written consent of the subsection (k) applicant, which shall not be unreasonably withheld.

"(D) USE OF CONFIDENTIAL INFORMATION.—Confidential information shall be used for the sole and exclusive purpose of determining, with respect to each patent assigned to or exclusively licensed by the reference product sponsor, whether a claim of patent infringement could reasonably be asserted if the subsection (k) applicant engaged in the manufacture, use, offering for sale, sale, or importation into the United States of the biological product that is the subject of the application under subsection (k).

"(E) OWNERSHIP OF CONFIDENTIAL INFORMATION.—The confidential information disclosed under this paragraph is, and shall remain, the property of the subsection (k) applicant. By

providing the confidential information pursuant to this paragraph, the subsection (k) applicant does not provide the reference product sponsor or the outside counsel any interest in or license to use the confidential information, for purposes other than those specified in subparagraph (D).

"(F) EFFECT OF INFRINGEMENT ACTION.—In the event that the reference product sponsor files a patent infringement suit, the use of confidential information shall continue to be governed by the terms of this paragraph until such time as a court enters a protective order regarding the information. Upon entry of such order, the subsection (k) applicant may redesignate confidential information in accordance with the terms of that order. No confidential information shall be included in any publicly-available complaint or other pleading. In the event that the reference product sponsor does not file an infringement action by the date specified in paragraph (6), the reference product sponsor shall return or destroy all confidential information received under this paragraph, provided that if the reference product sponsor opts to destroy such information, it will confirm destruction in writing to the subsection (k) applicant.

"(G) RULE OF CONSTRUCTION.—Nothing in this paragraph shall be construed—

"(i) as an admission by the subsection (k) applicant regarding the validity, enforceability, or infringement of any patent; or

"(ii) as an agreement or admission by the subsection (k) applicant with respect to the competency, relevance, or materiality of any confidential information.

"(H) EFFECT OF VIOLATION.—The disclosure of any confidential information in violation of this paragraph shall be deemed to cause the subsection (k) applicant to suffer irreparable harm for which there is no adequate legal remedy and the court shall consider immediate injunctive relief to be an appropriate and necessary remedy for any violation or threatened violation of this paragraph.

"(2) SUBSECTION (k) APPLICATION INFORMATION.—Not later than 20 days after the Secretary notifies the subsection (k) applicant that the application has been accepted for review, the subsection (k) applicant—

"(A) shall provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k), and such other information that describes the process or processes used to manufacture the biological product that is the subject of such application; and

"(B) may provide to the reference product sponsor additional information requested by or on behalf of the reference product sponsor.

"(3) LIST AND DESCRIPTION OF PATENTS.—

"(A) LIST BY REFERENCE PRODUCT SPONSOR.—Not later than 60 days after the receipt of the application and information under paragraph (2), the reference product sponsor shall provide to the subsection (k) applicant—

"(i) a list of patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted by the reference product sponsor, or by a patent owner that has granted an exclusive license to

the reference product sponsor with respect to the reference product, if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application; and

"(ii) an identification of the patents on such list that the reference product sponsor would be prepared to license to the subsection (k) applicant.

"(B) LIST AND DESCRIPTION BY SUBSECTION (k) APPLICANT.—Not later than 60 days after receipt of the list under subparagraph (A), the subsection (k) applicant—

"(i) may provide to the reference product sponsor a list of patents to which the subsection (k) applicant believes a claim of patent infringement could reasonably be asserted by the reference product sponsor if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application;

"(ii) shall provide to the reference product sponsor, with respect to each patent listed by the reference product sponsor under subparagraph (A) or listed by the subsection (k) applicant under clause (i)—

"(I) a detailed statement that describes, on a claim by claim basis, the factual and legal basis of the opinion of the subsection (k) applicant that such patent is invalid, unenforceable, or will not be infringed by the

commercial marketing of the biological product that is the subject of the subsection (k) application; or

"(II) a statement that the subsection (k) applicant does not intend to begin commercial marketing of the biological product before the date that such patent expires; and

"(iii) shall provide to the reference product sponsor a response regarding each patent identified by the reference product sponsor under subparagraph (A)(ii).

"(C) DESCRIPTION BY REFERENCE PRODUCT SPONSOR.—Not later than 60 days after receipt of the list and statement under subparagraph (B), the reference product sponsor shall provide to the subsection (k) applicant a detailed statement that describes, with respect to each patent described in subparagraph (B)(ii)(I), on a claim by claim basis, the factual and legal basis of the opinion of the reference product sponsor that such patent will be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application and a response to the statement concerning validity and enforceability provided under subparagraph (B)(ii)(I).

"(4) PATENT RESOLUTION NEGOTIATIONS.—

"(A) IN GENERAL.—After receipt by the subsection (k) applicant of the statement under paragraph (3)(C), the reference product sponsor and the subsection (k) applicant shall engage in good faith negotiations to agree on which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product

sponsor shall be the subject of an action for patent infringement under paragraph (6).

"(B) FAILURE TO REACH AGREEMENT.—If, within 15 days of beginning negotiations under subparagraph (A), the subsection (k) applicant and the reference product sponsor fail to agree on a final and complete list of which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6), the provisions of paragraph (5) shall apply to the parties.

"(5) PATENT RESOLUTION IF NO AGREEMENT.—

"(A) NUMBER OF PATENTS.—The subsection (k) applicant shall notify the reference product sponsor of the number of patents that such applicant will provide to the reference product sponsor under subparagraph (B)(i)(I).

"(B) EXCHANGE OF PATENT LISTS.—

"(i) IN GENERAL.—On a date agreed to by the subsection (k) applicant and the reference product sponsor, but in no case later than 5 days after the subsection (k) applicant notifies the reference product sponsor under subparagraph (A), the subsection (k) applicant and the reference product sponsor shall simultaneously exchange—

"(I) the list of patents that the subsection (k) applicant believes should be the subject of an action for patent infringement under paragraph (6); and

"(II) the list of patents, in accordance with clause (ii), that the reference product sponsor

believes should be the subject of an action for patent infringement under paragraph (6).

"(ii) NUMBER OF PATENTS LISTED BY REFERENCE PRODUCT SPONSOR.—

"(I) IN GENERAL.—Subject to subclause (II), the number of patents listed by the reference product sponsor under clause (i)(II) may not exceed the number of patents listed by the subsection (k) applicant under clause (i)(I).

"(II) EXCEPTION.—If a subsection (k) applicant does not list any patent under clause (i)(I), the reference product sponsor may list 1 patent under clause (i)(II).

"(6) IMMEDIATE PATENT INFRINGEMENT ACTION.—

"(A) ACTION IF AGREEMENT ON PATENT LIST.—If the subsection (k) applicant and the reference product sponsor agree on patents as described in paragraph (4), not later than 30 days after such agreement, the reference product sponsor shall bring an action for patent infringement with respect to each such patent.

"(B) ACTION IF NO AGREEMENT ON PATENT LIST.—If the provisions of paragraph (5) apply to the parties as described in paragraph (4)(B), not later than 30 days after the exchange of lists under paragraph (5)(B), the reference product sponsor shall bring an action for patent infringement with respect to each patent that is included on such lists.

"(C) NOTIFICATION AND PUBLICATION OF COMPLAINT.—

"(i) NOTIFICATION TO SECRETARY.—Not later than 30 days after a complaint is served to a subsection (k) applicant in an action for patent

infringement described under this paragraph, the subsection (k) applicant shall provide the Secretary with notice and a copy of such complaint.

"(ii) PUBLICATION BY SECRETARY.—The Secretary shall publish in the Federal Register notice of a complaint received under clause (i).

"(7) NEWLY ISSUED OR LICENSED PATENTS.—In the case of a patent that—

"(A) is issued to, or exclusively licensed by, the reference product sponsor after the date that the reference product sponsor provided the list to the subsection (k) applicant under paragraph (3)(A); and

"(B) the reference product sponsor reasonably believes that, due to the issuance of such patent, a claim of patent infringement could reasonably be asserted by the reference product sponsor if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application,

not later than 30 days after such issuance or licensing, the reference product sponsor shall provide to the subsection (k) applicant a supplement to the list provided by the reference product sponsor under paragraph (3)(A) that includes such patent, not later than 30 days after such supplement is provided, the subsection (k) applicant shall provide a statement to the reference product sponsor in accordance with paragraph (3)(B), and such patent shall be subject to paragraph (8).

"(8) NOTICE OF COMMERCIAL MARKETING AND PRELIMINARY INJUNCTION.—

"(A) NOTICE OF COMMERCIAL MARKETING.—The subsection (k) applicant shall provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k).

"(B) PRELIMINARY INJUNCTION.—After receiving the notice under subparagraph (A) and before such date of the first commercial marketing of such biological product, the reference product sponsor may seek a preliminary injunction prohibiting the subsection (k) applicant from engaging in the commercial manufacture or sale of such biological product until the court decides the issue of patent validity, enforcement, and infringement with respect to any patent that is—

"(i) included in the list provided by the reference product sponsor under paragraph (3)(A) or in the list provided by the subsection (k) applicant under paragraph (3)(B); and

"(ii) not included, as applicable, on—

"(I) the list of patents described in paragraph (4); or

"(II) the lists of patents described in paragraph (5)(B).

"(C) REASONABLE COOPERATION.—If the reference product sponsor has sought a preliminary injunction under subparagraph (B), the reference product sponsor and the subsection (k) applicant shall reasonably cooperate to expedite such further discovery as is needed in connection with the preliminary injunction motion.

"(9) LIMITATION ON DECLARATORY JUDGMENT ACTION.—

"(A) SUBSECTION (k) APPLICATION PROVIDED.—If a subsection (k) applicant provides the application and information required under paragraph (2)(A), neither the reference product sponsor nor the subsection (k) applicant may, prior to the date notice is received under paragraph (8)(A), bring any action under section 2201 of title 28, United States Code, for a declaration of infringement, validity, or enforceability of any patent that is described in clauses (i) and (ii) of paragraph (8)(B).

"(B) SUBSEQUENT FAILURE TO ACT BY SUBSECTION (k) APPLICANT.—If a subsection (k) applicant fails to complete an action required of the subsection (k) applicant under paragraph (3)(B)(ii), paragraph (5), paragraph (6)(C)(i), paragraph (7), or paragraph (8)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28, United States Code, for a declaration of infringement, validity, or enforceability of any patent included in the list described in paragraph (3)(A), including as provided under paragraph (7).

"(C) SUBSECTION (k) APPLICATION NOT PROVIDED.—If a subsection (k) applicant fails to provide the application and information required under paragraph (2)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28, United States Code, for a declaration of infringement, validity, or enforceability of any

patent that claims the biological product or a use of the biological product.".

(b) DEFINITIONS.—Section 351(i) of the Public Health Service Act (42 U.S.C. 262(i)) is amended—

(1) by striking "In this section, the term 'biological product' means" and inserting the following: "In this section:

"(1) The term 'biological product' means";

(2) in paragraph (1), as so designated, by inserting "protein (except any chemically synthesized polypeptide)," after "allergenic product,"; and

(3) by adding at the end the following:

"(2) The term 'biosimilar' or 'biosimilarity', in reference to a biological product that is the subject of an application under subsection (k), means—

"(A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and

"(B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.

"(3) The term 'interchangeable' or 'interchangeability', in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

"(4) The term 'reference product' means the single biological product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k).".

(c) CONFORMING AMENDMENTS RELATING TO PATENTS.—

(1) PATENTS.—Section 271(e) of title 35, United States Code, is amended—

(A) in paragraph (2)—

(i) in subparagraph (A), by striking "or" at the end;

(ii) in subparagraph (B), by adding "or" at the end; and

(iii) by inserting after subparagraph (B) the following:

"(C)(i) with respect to a patent that is identified in the list of patents described in section 351(*l*)(3) of the Public Health Service Act (including as provided under section 351(*l*)(7) of such Act), an application seeking approval of a biological product, or

"(ii) if the applicant for the application fails to provide the application and information required under section 351(*l*)(2)(A) of such Act, an application seeking approval of a biological product for a patent that could be identified pursuant to section 351(*l*)(3)(A)(i) of such Act,"; and

(iv) in the matter following subparagraph (C) (as added by clause (iii)), by striking "or veterinary biological product" and inserting ", veterinary biological product, or biological product";

(B) in paragraph (4)—

(i) in subparagraph (B), by—

(I) striking "or veterinary biological product" and inserting ", veterinary biological product, or biological product"; and

(II) striking "and" at the end;

(ii) in subparagraph (C), by—

(I) striking "or veterinary biological product" and inserting ", veterinary biological product, or biological product"; and

(II) striking the period and inserting ", and";

(iii) by inserting after subparagraph (C) the following:

"(D) the court shall order a permanent injunction prohibiting any infringement of the patent by the biological product involved in the infringement until a date which is not earlier than the date of the expiration of the patent that has been infringed under paragraph (2)(C), provided the patent is the subject of a final court decision, as defined in section 351(k)(6) of the Public Health Service Act, in an action for infringement of the patent under section 351(*l*)(6) of such Act, and the biological product has not yet been approved because of section 351(k)(7) of such Act."; and

(iv) in the matter following subparagraph (D) (as added by clause (iii)), by striking "and (C)" and inserting "(C), and (D)"; and

(C) by adding at the end the following:

"(6)(A) Subparagraph (B) Applies, in lieu of paragraph (4), in the case of a patent—

"(i) that is identified, as applicable, in the list of patents described in section 351(*l*)(4) of the Public Health Service Act or the lists of patents described in section 351(*l*)(5)(B) of such Act with respect to a biological product; and

"(ii) for which an action for infringement of the patent with respect to the biological product—

"(I) was brought after the expiration of the 30-day period described in subparagraph (A) or (B), as applicable, of section 351(*l*)(6) of such Act; or

"(II) was brought before the expiration of the 30-day period described in subclause (I), but which was dismissed without prejudice or was not prosecuted to judgment in good faith.

"(B) In an action for infringement of a patent described in subparagraph (A), the sole and exclusive remedy that may be granted by a court, upon a finding that the making, using, offering to sell, selling, or importation into the United States of the biological product that is the subject of the action infringed the patent, shall be a reasonable royalty.

"(C) The owner of a patent that should have been included in the list described in section 351(*l*)(3)(A) of the Public Health Service Act, including as provided under section 351(*l*)(7) of such Act for a biological product, but was not timely included in such list, may not bring an action under this section for infringement of the patent with respect to the biological product.".

(2) CONFORMING AMENDMENT UNDER TITLE 28.—Section 2201(b) of title 28, United States Code, is amended by inserting before the period the following: ", or section 351 of the Public Health Service Act".

(d) CONFORMING AMENDMENTS UNDER THE FEDERAL FOOD, DRUG, AND COSMETIC ACT.—

(1) CONTENT AND REVIEW OF APPLICATIONS.—Section 505(b)(5)(B) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)(5)(B)) is amended by inserting before the period at the end of the first sentence the following: "or, with respect to an

applicant for approval of a biological product under section 351(k) of the Public Health Service Act, any necessary clinical study or studies".

(2) NEW ACTIVE INGREDIENT.—Section 505B of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355c) is amended by adding at the end the following:

"(n) NEW ACTIVE INGREDIENT.—

"(1) NON-INTERCHANGEABLE BIOSIMILAR BIOLOGICAL PRODUCT.—A biological product that is biosimilar to a reference product under section 351 of the Public Health Service Act, and that the Secretary has not determined to meet the standards described in subsection (k)(4) of such section for interchangeability with the reference product, shall be considered to have a new active ingredient under this section.

"(2) INTERCHANGEABLE BIOSIMILAR BIOLOGICAL PRODUCT.—A biological product that is interchangeable with a reference product under section 351 of the Public Health Service Act shall not be considered to have a new active ingredient under this section.".

(e) PRODUCTS PREVIOUSLY APPROVED UNDER SECTION 505.—

(1) REQUIREMENT TO FOLLOW SECTION 351.—Except as provided in paragraph (2), an application for a biological product shall be submitted under section 351 of the Public Health Service Act (42 U.S.C. 262) (as amended by this Act).

(2) EXCEPTION.—An application for a biological product may be submitted under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) if—

(A) such biological product is in a product class for which a biological product in such product

class is the subject of an application approved under such section 505 not later than the date of enactment of this Act; and

(B) such application—

(i) has been submitted to the Secretary of Health and Human Services (referred to in this subtitle as the "Secretary") before the date of enactment of this Act; or

(ii) is submitted to the Secretary not later than the date that is 10 years after the date of enactment of this Act.

(3) LIMITATION.—Notwithstanding paragraph (2), an application for a biological product may not be submitted under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) if there is another biological product approved under subsection (a) of section 351 of the Public Health Service Act that could be a reference product with respect to such application (within the meaning of such section 351) if such application were submitted under subsection (k) of such section 351.

(4) DEEMED APPROVED UNDER SECTION 351.—An approved application for a biological product under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) shall be deemed to be a license for the biological product under such section 351 on the date that is 10 years after the date of enactment of this Act.

(5) DEFINITIONS.—For purposes of this subsection, the term "biological product" has the meaning given such term under section 351 of the Public Health Service Act (42 U.S.C. 262) (as amended by this Act).

(f) FOLLOW-ON BIOLOGICS USER FEES.—

(1) DEVELOPMENT OF USER FEES FOR BIOSIMILAR BIOLOGICAL PRODUCTS.—

(A) IN GENERAL.—Beginning not later than October 1, 2010, the Secretary shall develop recommendations to present to Congress with respect to the goals, and plans for meeting the goals, for the process for the review of biosimilar biological product applications submitted under section 351(k) of the Public Health Service Act (as added by this Act) for the first 5 fiscal years after fiscal year 2012. In developing such recommendations, the Secretary shall consult with—

(i) the Committee on Health, Education, Labor, and Pensions of the Senate;

(ii) the Committee on Energy and Commerce of the House of Representatives;

(iii) scientific and academic experts;

(iv) health care professionals;

(v) representatives of patient and consumer advocacy groups; and

(vi) the regulated industry.

(B) PUBLIC REVIEW OF RECOMMENDATIONS.—After negotiations with the regulated industry, the Secretary shall—

(i) present the recommendations developed under subparagraph (A) to the Congressional committees specified in such subparagraph;

(ii) publish such recommendations in the Federal Register;

(iii) provide for a period of 30 days for the public to provide written comments on such recommendations;

(iv) hold a meeting at which the public may present its views on such recommendations; and

(v) after consideration of such public views and comments, revise such recommendations as necessary.

(C) TRANSMITTAL OF RECOMMENDATIONS.—Not later than January 15, 2012, the Secretary shall transmit to Congress the revised recommendations under subparagraph (B), a summary of the views and comments received under such subparagraph, and any changes made to the recommendations in response to such views and comments.

(2) ESTABLISHMENT OF USER FEE PROGRAM.—It is the sense of the Senate that, based on the recommendations transmitted to Congress by the Secretary pursuant to paragraph (1)(C), Congress should authorize a program, effective on October 1, 2012, for the collection of user fees relating to the submission of biosimilar biological product applications under section 351(k) of the Public Health Service Act (as added by this Act).

(3) TRANSITIONAL PROVISIONS FOR USER FEES FOR BIOSIMILAR BIOLOGICAL PRODUCTS.—

(A) APPLICATION OF THE PRESCRIPTION DRUG USER FEE PROVISIONS.—Section 735(1)(B) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379g(1)(B)) is amended by striking "section 351" and inserting "subsection (a) or (k) of section 351".

(B) EVALUATION OF COSTS OF REVIEWING BIOSIMILAR BIOLOGICAL PRODUCT APPLICATIONS.—During the period beginning on the date of enactment of this Act and ending on October 1, 2010, the Secretary shall collect and evaluate data regarding the costs of reviewing applications for biological products submitted under section 351(k) of the Public Health Service Act (as added by this Act) during such period.

(C) AUDIT.—

(i) IN GENERAL.—On the date that is 2 years after first receiving a user fee applicable to an application for a biological product under section 351(k) of the Public Health Service Act (as added by this Act), and on a biennial basis thereafter until October 1, 2013, the Secretary shall perform an audit of the costs of reviewing such applications under such section 351(k). Such an audit shall compare—

(I) the costs of reviewing such applications under such section 351(k) to the amount of the user fee applicable to such applications; and

(II)(aa) such ratio determined under subclause (I); to

(bb) the ratio of the costs of reviewing applications for biological products under section 351(a) of such Act (as amended by this Act) to the amount of the user fee applicable to such applications under such section 351(a).

(ii) ALTERATION OF USER FEE.—If the audit performed under clause (i) indicates that the ratios compared under subclause (II) of such

clause differ by more than 5 percent, then the Secretary shall alter the user fee applicable to applications submitted under such section 351(k) to more appropriately account for the costs of reviewing such applications.

(iii) ACCOUNTING STANDARDS.—The Secretary shall perform an audit under clause (i) in conformance with the accounting principles, standards, and requirements prescribed by the Comptroller General of the United States under section 3511 of title 31, United States Code, to ensure the validity of any potential variability.

(4) AUTHORIZATION OF APPROPRIATIONS.—There is authorized to be appropriated to carry out this subsection such sums as may be necessary for each of fiscal years 2010 through 2012.

(g) PEDIATRIC STUDIES OF BIOLOGICAL PRODUCTS.—

(1) IN GENERAL.—Section 351 of the Public Health Service Act (42 U.S.C. 262) is amended by adding at the end the following:

"(m) PEDIATRIC STUDIES.—

"(1) APPLICATION OF CERTAIN PROVISIONS.—The provisions of subsections (a), (d), (e), (f), (i), (j), (k), (*l*), (p), and (q) of section 505A of the Federal Food, Drug, and Cosmetic Act shall apply with respect to the extension of a period under paragraphs (2) and (3) to the same extent and in the same manner as such provisions apply with respect to the extension of a period under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act.

"(2) MARKET EXCLUSIVITY FOR NEW BIOLOGICAL PRODUCTS.—If, prior to approval of an application that is submitted under subsection (a), the Secretary

determines that information relating to the use of a new biological product in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act—

"(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

"(B) if the biological product is designated under section 526 for a rare disease or condition, the period for such biological product referred to in section 527(a) is deemed to be 7 years and 6 months rather than 7 years.

"(3) MARKET EXCLUSIVITY FOR ALREADY-MARKETED BIOLOGICAL PRODUCTS.—If the Secretary determines that information relating to the use of a licensed biological product in the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under subsection (a) for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with

section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act—

"(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

"(B) if the biological product is designated under section 526 for a rare disease or condition, the period for such biological product referred to in section 527(a) is deemed to be 7 years and 6 months rather than 7 years.

"(4) EXCEPTION.—The Secretary shall not extend a period referred to in paragraph (2)(A), (2)(B), (3)(A), or (3)(B) if the determination under section 505A(d)(3) is made later than 9 months prior to the expiration of such period.".

(2) STUDIES REGARDING PEDIATRIC RESEARCH.—

(A) PROGRAM FOR PEDIATRIC STUDY OF DRUGS.—Subsection (a)(1) of section 409I of the Public Health Service Act (42 U.S.C. 284m) is amended by inserting ", biological products," after "including drugs".

(B) INSTITUTE OF MEDICINE STUDY.—Section 505A(p) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355b(p)) is amended by striking paragraphs (4) and (5) and inserting the following:

"(4) review and assess the number and importance of biological products for children that are being tested as a result of the amendments made by the Biologics Price Competition and Innovation Act of 2009 and the importance for children, health care providers, parents, and others of labeling changes made as a result of such testing;

"(5) review and assess the number, importance, and prioritization of any biological products that are not being tested for pediatric use; and

"(6) offer recommendations for ensuring pediatric testing of biological products, including consideration of any incentives, such as those provided under this section or section 351(m) of the Public Health Service Act.".

(h) ORPHAN PRODUCTS.—If a reference product, as defined in section 351 of the Public Health Service Act (42 U.S.C. 262) (as amended by this Act) has been designated under section 526 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bb) for a rare disease or condition, a biological product seeking approval for such disease or condition under subsection (k) of such section 351 as biosimilar to, or interchangeable with, such reference product may be licensed by the Secretary only after the expiration for such reference product of the later of—

(1) the 7-year period described in section 527(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360cc(a)); and

(2) the 12-year period described in subsection (k)(7) of such section 351.

SEC. 7003. SAVINGS.

(a) DETERMINATION.—The Secretary of the Treasury, in consultation with the Secretary of Health and Human Services, shall for each fiscal year determine the amount of savings to the Federal Government as a result of the enactment of this subtitle.

(b) USE.—Notwithstanding any other provision of this subtitle (or an amendment made by this subtitle), the savings to the Federal Government

generated as a result of the enactment of this subtitle shall be used for deficit reduction.

TITLE 28—JUDICIARY AND JUDICIAL PROCEDURE

PART VI—PARTICULAR PROCEEDINGS

CHAPTER 151—DECLARATORY JUDGMENTS

§ 2201. Creation of remedy

(a) In a case of actual controversy within its jurisdiction, except with respect to Federal taxes other than actions brought under section 7428 of the Internal Revenue Code of 1986, a proceeding under section 505 or 1146 of title 11, or in any civil action involving an antidumping or countervailing duty proceeding regarding a class or kind of merchandise of a free trade area country (as defined in section 516A(f)(10) of the Tariff Act of 1930), as determined by the administering authority, any court of the United States, upon the filing of an appropriate pleading, may declare the rights and other legal relations of any interested party seeking such declaration, whether or not further relief is or could be sought. Any such declaration shall have the force and effect of a final judgment or decree and shall be reviewable as such.

(b) For limitations on actions brought with respect to drug patents see section 505 or 512 of the Federal Food, Drug, and Cosmetic Act, or section 351 of the Public Health Service Act.

TITLE 35—PATENTS
PART III—PATENTS AND PROTECTION OF PATENT RIGHTS
CHAPTER 28—INFRINGEMENT OF PATENTS

§ 271. Infringement of patent

(a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.

* * *

(e)(1) It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

(2) It shall be an act of infringement to submit—

(A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent,

(B) an application under section 512 of such Act or under the Act of March 4, 1913 (21 U.S.C. 151-158) for a drug or veterinary biological product which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques and which is claimed in a patent or the use of which is claimed in a patent, or

(C)(i) with respect to a patent that is identified in the list of patents described in section 351(*l*)(3) of the Public Health Service Act (including as provided under section 351(*l*)(7) of such Act), an application seeking approval of a biological product, or

(ii) if the applicant for the application fails to provide the application and information required under section 351(*l*)(2)(A) of such Act, an application seeking approval of a biological product for a patent that could be identified pursuant to section 351(*l*)(3)(A)(i) of such Act,

if the purpose of such submission is to obtain approval under such Act to engage in the commercial manufacture, use, or sale of a drug, veterinary biological product, or biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent.

(3) In any action for patent infringement brought under this section, no injunctive or other relief may be granted which would prohibit the making, using, offering to sell, or selling within the United States or importing into the United States of a patented invention under paragraph (1).

(4) For an act of infringement described in paragraph (2)—

(A) the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed,

(B) injunctive relief may be granted against an infringer to prevent the commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product,

(C) damages or other monetary relief may be awarded against an infringer only if there has been commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of an approved drug, veterinary biological product, or biological product, and

(D) the court shall order a permanent injunction prohibiting any infringement of the patent by the biological product involved in the infringement until a date which is not earlier than the date of the expiration of the patent that has been infringed under paragraph (2)(C), provided the patent is the subject of a final court decision, as defined in section 351(k)(6) of the Public Health Service Act, in an action for infringement of the patent under section 351(*l*)(6) of such Act, and the biological product has not yet been approved because of section 351(k)(7) of such Act.

The remedies prescribed by subparagraphs (A), (B), (C), and (D) are the only remedies which may be granted by a court for an act of infringement described in paragraph (2), except that a court may award attorney fees under section 285.

(5) Where a person has filed an application described in paragraph (2) that includes a certification under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), and neither the owner of the patent that is the subject of the certification nor the holder of the approved application under subsection (b) of such section for the drug that is claimed by the patent or a use of which is claimed by the patent brought an action for infringement of such patent before the expiration of 45 days after the date on which the notice given under subsection (b)(3) or (j)(2)(B) of such section was received, the courts of the United States shall, to the extent consistent with the Constitution, have subject matter jurisdiction in any action brought by such person under section 2201 of title 28 for a declaratory judgment that such patent is invalid or not infringed.

(6)(A) Subparagraph (B) applies, in lieu of paragraph (4), in the case of a patent—

(i) that is identified, as applicable, in the list of patents described in section 351(*l*)(4) of the Public Health Service Act or the lists of patents described in section 351(*l*)(5)(B) of such Act with respect to a biological product; and

(ii) for which an action for infringement of the patent with respect to the biological product—

(I) was brought after the expiration of the 30-day period described in subparagraph (A) or (B), as applicable, of section 351(*l*)(6) of such Act; or

(II) was brought before the expiration of the 30-day period described in subclause (I), but which was dismissed without prejudice or was not prosecuted to judgment in good faith.

(B) In an action for infringement of a patent described in subparagraph (A), the sole and exclusive remedy that may be granted by a court, upon a finding that the making, using, offering to sell, selling, or importation into the United States of the biological product that is the subject of the action infringed the patent, shall be a reasonable royalty.

(C) The owner of a patent that should have been included in the list described in section 351(*l*)(3)(A) of the Public Health Service Act, including as provided under section 351(*l*)(7) of such Act for a biological product, but was not timely included in such list, may not bring an action under this section for infringement of the patent with respect to the biological product.

* * * *

TITLE 42—THE PUBLIC HEALTH AND WELFARE

CHAPTER 6A—PUBLIC HEALTH SERVICE

SUBCHAPTER II—GENERAL POWERS AND DUTIES

PART F—LICENSING OF BIOLOGICAL PRODUCTS AND CLINICAL LABORATORIES

SUBPART 1—BIOLOGICAL PRODUCTS

§ 262. Regulation of biological products

(a) Biologics license

(1) No person shall introduce or deliver for introduction into interstate commerce any biological product unless—

(A) a biologics license under this subsection or subsection (k) is in effect for the biological product; and

(B) each package of the biological product is plainly marked with—

(i) the proper name of the biological product contained in the package;

(ii) the name, address, and applicable license number of the manufacturer of the biological product; and

(iii) the expiration date of the biological product.

(2)(A) The Secretary shall establish, by regulation, requirements for the approval, suspension, and revocation of biologics licenses.

(B) PEDIATRIC STUDIES—A person that submits an application for a license under this paragraph shall submit to the Secretary as part of the application any assessments required under section 505B

of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355c].

(C) The Secretary shall approve a biologics license application—

(i) on the basis of a demonstration that—

(I) the biological product that is the subject of the application is safe, pure, and potent; and

(II) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent; and

(ii) if the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c) of this section.

(D) POSTMARKET STUDIES AND CLINICAL TRIALS; LABELING; RISK EVALUATION AND MITIGATION STRATEGY—A person that submits an application for a license under this paragraph is subject to sections 505(*o*), 505(p), and 505-1 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355(*o*), (p), 355-1].

(3) The Secretary shall prescribe requirements under which a biological product undergoing investigation shall be exempt from the requirements of paragraph (1).

* * *

(i) "Biological product" defined

In this section:

(1) The term "biological product" means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product,

protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

(2) The term "biosimilar" or "biosimilarity", in reference to a biological product that is the subject of an application under subsection (k), means—

(A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and

(B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.

(3) The term "interchangeable" or "interchangeability", in reference to a biological product that is shown to meet the standards described in subsection (k)(4), means that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product.

(4) The term "reference product" means the single biological product licensed under subsection (a) against which a biological product is evaluated in an application submitted under subsection (k).

* * *

(k) Licensure of biological products as biosimilar or interchangeable

(1) In general

Any person may submit an application for licensure of a biological product under this subsection.

(2) Content

(A) In general

(i) Required information

An application submitted under this subsection shall include information demonstrating that—

(I) the biological product is biosimilar to a reference product based upon data derived from—

(aa) analytical studies that demonstrate that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components;

(bb) animal studies (including the assessment of toxicity); and

(cc) a clinical study or studies (including the assessment of immunogenicity and pharmacokinetics or pharmacodynamics) that are sufficient to demonstrate 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;

(II) the biological product and reference product utilize the same mechanism or mechanisms of action for the condition or conditions of use prescribed, recommended, or suggested in the proposed labeling, but only to the extent the mechanism or mechanisms of action are known for the reference product;

(III) the condition or conditions of use prescribed, recommended, or suggested in the labeling proposed for the biological product

have been previously approved for the reference product;

(IV) the route of administration, the dosage form, and the strength of the biological product are the same as those of the reference product; and

(V) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

(ii) Determination by Secretary

The Secretary may determine, in the Secretary's discretion, that an element described in clause (i)(I) is unnecessary in an application submitted under this subsection.

(iii) Additional information

An application submitted under this subsection—

(I) shall include publicly-available information regarding the Secretary's previous determination that the reference product is safe, pure, and potent; and

(II) may include any additional information in support of the application, including publicly-available information with respect to the reference product or another biological product.

(B) Interchangeability

An application (or a supplement to an application) submitted under this subsection may include information demonstrating that the biological product meets the standards described in paragraph (4).

(3) Evaluation by Secretary

Upon review of an application (or a supplement to an application) submitted under this subsection, the Secretary shall license the biological product under this subsection if—

(A) the Secretary determines that the information submitted in the application (or the supplement) is sufficient to show that the biological product—

(i) is biosimilar to the reference product; or

(ii) meets the standards described in paragraph (4), and therefore is interchangeable with the reference product; and

(B) the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).

(4) Safety standards for determining interchangeability

Upon review of an application submitted under this subsection or any supplement to such application, the Secretary shall determine the biological product to be interchangeable with the reference product if the Secretary determines that the information submitted in the application (or a supplement to such application) is sufficient to show that—

(A) the biological product—

(i) is biosimilar to the reference product; and

(ii) can be expected to produce the same clinical result as the reference product in any given patient; and

(B) for a biological 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 without such alternation or switch.

(5) General rules

(A) One reference product per application

A biological product, in an application submitted under this subsection, may not be evaluated against more than 1 reference product.

(B) Review

An application submitted under this subsection shall be reviewed by the division within the Food and Drug Administration that is responsible for the review and approval of the application under which the reference product is licensed.

(C) Risk evaluation and mitigation strategies

The authority of the Secretary with respect to risk evaluation and mitigation strategies under the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.] shall apply to biological products licensed under this subsection in the same manner as such authority applies to biological products licensed under subsection (a).

(6) Exclusivity for first interchangeable biological product

Upon review of an application submitted under this subsection relying on the same reference product for which a prior biological product has received a determination of interchangeability for any condition of use, the Secretary shall not make a determination under paragraph (4) that the second or subsequent biological product is interchangeable for any condition of use until the earlier of—

(A) 1 year after the first commercial marketing of the first interchangeable biosimilar biological product to be approved as interchangeable for that reference product;

(B) 18 months after—

(i) a final court decision on all patents in suit in an action instituted under subsection (*l*)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(ii) the dismissal with or without prejudice of an action instituted under subsection (*l*)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(C)(i) 42 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has been sued under subsection (*l*)(6) and such litigation is still ongoing within such 42-month period; or

(ii) 18 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has not been sued under subsection (*l*)(6).

For purposes of this paragraph, the term "final court decision" means a final decision of a court from which no appeal (other than a petition to the United States Supreme Court for a writ of certiorari) has been or can be taken.

(7) Exclusivity for reference product

(A) Effective date of biosimilar application approval

Approval of an application under this subsection may not be made effective by the Secretary until

the date that is 12 years after the date on which the reference product was first licensed under subsection (a).

(B) Filing period

An application under this subsection may not be submitted to the Secretary until the date that is 4 years after the date on which the reference product was first licensed under subsection (a).

(C) First licensure

Subparagraphs (A) and (B) shall not apply to a license for or approval of—

(i) a supplement for the biological product that is the reference product; or

(ii) a subsequent application filed by the same sponsor or manufacturer of the biological product that is the reference product (or a licensor, predecessor in interest, or other related entity) for—

(I) a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength; or

(II) a modification to the structure of the biological product that does not result in a change in safety, purity, or potency.

(8) Guidance documents

(A) In general

The Secretary may, after opportunity for public comment, issue guidance in accordance, except as provided in subparagraph (B)(i), with section 701(h) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 371(h)] with respect to the licensure of a

biological product under this subsection. Any such guidance may be general or specific.

(B) Public comment

(i) In general

The Secretary shall provide the public an opportunity to comment on any proposed guidance issued under subparagraph (A) before issuing final guidance.

(ii) Input regarding most valuable guidance

The Secretary shall establish a process through which the public may provide the Secretary with input regarding priorities for issuing guidance.

(C) No requirement for application consideration

The issuance (or non-issuance) of guidance under subparagraph (A) shall not preclude the review of, or action on, an application submitted under this subsection.

(D) Requirement for product class-specific guidance

If the Secretary issues product class-specific guidance under subparagraph (A), such guidance shall include a description of—

(i) the criteria that the Secretary will use to determine whether a biological product is highly similar to a reference product in such product class; and

(ii) the criteria, if available, that the Secretary will use to determine whether a biological product meets the standards described in paragraph (4).

(E) Certain product classes

(i) Guidance

The Secretary may indicate in a guidance document that the science and experience, as of the date of such guidance, with respect to a product or product class (not including any recombinant protein) does not allow approval of an application for a license as provided under this subsection for such product or product class.

(ii) Modification or reversal

The Secretary may issue a subsequent guidance document under subparagraph (A) to modify or reverse a guidance document under clause (i).

(iii) No effect on ability to deny license

Clause (i) shall not be construed to require the Secretary to approve a product with respect to which the Secretary has not indicated in a guidance document that the science and experience, as described in clause (i), does not allow approval of such an application.

(*l*) Patents

(1) Confidential access to subsection (k) application

(A) Application of paragraph

Unless otherwise agreed to by a person that submits an application under subsection (k) (referred to in this subsection as the "subsection (k) applicant") and the sponsor of the application for the reference product (referred to in this subsection as the "reference product sponsor"), the provisions of this paragraph shall apply to the exchange of information described in this subsection.

(B) In general

(i) Provision of confidential information

When a subsection (k) applicant submits an application under subsection (k), such applicant shall provide to the persons described in clause (ii), subject to the terms of this paragraph, confidential access to the information required to be produced pursuant to paragraph (2) and any other information that the subsection (k) applicant determines, in its sole discretion, to be appropriate (referred to in this subsection as the "confidential information").

(ii) Recipients of information

The persons described in this clause are the following:

(I) Outside counsel

One or more attorneys designated by the reference product sponsor who are employees of an entity other than the reference product sponsor (referred to in this paragraph as the "outside counsel"), provided that such attorneys do not engage, formally or informally, in patent prosecution relevant or related to the reference product.

(II) In-house counsel

One attorney that represents the reference product sponsor who is an employee of the reference product sponsor, provided that such attorney does not engage, formally or informally, in patent prosecution relevant or related to the reference product.

(iii) Patent owner access

A representative of the owner of a patent exclusively licensed to a reference product

sponsor with respect to the reference product and who has retained a right to assert the patent or participate in litigation concerning the patent may be provided the confidential information, provided that the representative informs the reference product sponsor and the subsection (k) applicant of his or her agreement to be subject to the confidentiality provisions set forth in this paragraph, including those under clause (ii).

(C) Limitation on disclosure

No person that receives confidential information pursuant to subparagraph (B) shall disclose any confidential information to any other person or entity, including the reference product sponsor employees, outside scientific consultants, or other outside counsel retained by the reference product sponsor, without the prior written consent of the subsection (k) applicant, which shall not be unreasonably withheld.

(D) Use of confidential information

Confidential information shall be used for the sole and exclusive purpose of determining, with respect to each patent assigned to or exclusively licensed by the reference product sponsor, whether a claim of patent infringement could reasonably be asserted if the subsection (k) applicant engaged in the manufacture, use, offering for sale, sale, or importation into the United States of the biological product that is the subject of the application under subsection (k).

(E) Ownership of confidential information

The confidential information disclosed under this paragraph is, and shall remain, the property

of the subsection (k) applicant. By providing the confidential information pursuant to this paragraph, the subsection (k) applicant does not provide the reference product sponsor or the outside counsel any interest in or license to use the confidential information, for purposes other than those specified in subparagraph (D).

(F) Effect of infringement action

In the event that the reference product sponsor files a patent infringement suit, the use of confidential information shall continue to be governed by the terms of this paragraph until such time as a court enters a protective order regarding the information. Upon entry of such order, the subsection (k) applicant may redesignate confidential information in accordance with the terms of that order. No confidential information shall be included in any publicly-available complaint or other pleading. In the event that the reference product sponsor does not file an infringement action by the date specified in paragraph (6), the reference product sponsor shall return or destroy all confidential information received under this paragraph, provided that if the reference product sponsor opts to destroy such information, it will confirm destruction in writing to the subsection (k) applicant.

(G) Rule of construction

Nothing in this paragraph shall be construed—

(i) as an admission by the subsection (k) applicant regarding the validity, enforceability, or infringement of any patent; or

(ii) as an agreement or admission by the subsection (k) applicant with respect to the

competency, relevance, or materiality of any confidential information.

(H) Effect of violation

The disclosure of any confidential information in violation of this paragraph shall be deemed to cause the subsection (k) applicant to suffer irreparable harm for which there is no adequate legal remedy and the court shall consider immediate injunctive relief to be an appropriate and necessary remedy for any violation or threatened violation of this paragraph.

(2) Subsection (k) application information

Not later than 20 days after the Secretary notifies the subsection (k) applicant that the application has been accepted for review, the subsection (k) applicant—

(A) shall provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k), and such other information that describes the process or processes used to manufacture the biological product that is the subject of such application; and

(B) may provide to the reference product sponsor additional information requested by or on behalf of the reference product sponsor.

(3) List and description of patents

(A) List by reference product sponsor

Not later than 60 days after the receipt of the application and information under paragraph (2), the reference product sponsor shall provide to the subsection (k) applicant—

(i) a list of patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted by

the reference product sponsor, or by a patent owner that has granted an exclusive license to the reference product sponsor with respect to the reference product, if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application; and

(ii) an identification of the patents on such list that the reference product sponsor would be prepared to license to the subsection (k) applicant.

(B) List and description by subsection (k) applicant

Not later than 60 days after receipt of the list under subparagraph (A), the subsection (k) applicant—

(i) may provide to the reference product sponsor a list of patents to which the subsection (k) applicant believes a claim of patent infringement could reasonably be asserted by the reference product sponsor if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application;

(ii) shall provide to the reference product sponsor, with respect to each patent listed by the reference product sponsor under subparagraph (A) or listed by the subsection (k) applicant under clause (i)—

(I) a detailed statement that describes, on a claim by claim basis, the factual and legal basis of the opinion of the subsection (k) applicant that such patent is invalid, unenforceable, or will not be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application; or

(II) a statement that the subsection (k) applicant does not intend to begin commercial marketing of the biological product before the date that such patent expires; and

(iii) shall provide to the reference product sponsor a response regarding each patent identified by the reference product sponsor under subparagraph (A)(ii).

(C) Description by reference product sponsor

Not later than 60 days after receipt of the list and statement under subparagraph (B), the reference product sponsor shall provide to the subsection (k) applicant a detailed statement that describes, with respect to each patent described in subparagraph (B)(ii)(I), on a claim by claim basis, the factual and legal basis of the opinion of the reference product sponsor that such patent will be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application and a response to the statement concerning validity and enforceability provided under subparagraph (B)(ii)(I).

(4) Patent resolution negotiations

(A) In general

After receipt by the subsection (k) applicant of the statement under paragraph (3)(C), the reference product sponsor and the subsection (k) applicant shall engage in good faith negotiations to agree on which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6).

(B) Failure to reach agreement

If, within 15 days of beginning negotiations under subparagraph (A), the subsection (k) applicant and the reference product sponsor fail to agree on a final and complete list of which, if any, patents listed under paragraph (3) by the subsection (k) applicant or the reference product sponsor shall be the subject of an action for patent infringement under paragraph (6), the provisions of paragraph (5) shall apply to the parties.

(5) Patent resolution if no agreement

(A) Number of patents

The subsection (k) applicant shall notify the reference product sponsor of the number of patents that such applicant will provide to the reference product sponsor under subparagraph (B)(i)(I).

(B) Exchange of patent lists

(i) In general

On a date agreed to by the subsection (k) applicant and the reference product sponsor, but in no case later than 5 days after the subsection (k) applicant notifies the reference

product sponsor under subparagraph (A), the subsection (k) applicant and the reference product sponsor shall simultaneously exchange—

(I) the list of patents that the subsection (k) applicant believes should be the subject of an action for patent infringement under paragraph (6); and

(II) the list of patents, in accordance with clause (ii), that the reference product sponsor believes should be the subject of an action for patent infringement under paragraph (6).

(ii) Number of patents listed by reference product sponsor

(I) In general

Subject to subclause (II), the number of patents listed by the reference product sponsor under clause (i)(II) may not exceed the number of patents listed by the subsection (k) applicant under clause (i)(I).

(II) Exception

If a subsection (k) applicant does not list any patent under clause (i)(I), the reference product sponsor may list 1 patent under clause (i)(II).

(6) Immediate patent infringement action

(A) Action if agreement on patent list

If the subsection (k) applicant and the reference product sponsor agree on patents as described in paragraph (4), not later than 30 days after such agreement, the reference product sponsor shall bring an action for patent infringement with respect to each such patent.

(B) Action if no agreement on patent list

If the provisions of paragraph (5) apply to the parties as described in paragraph (4)(B), not later than 30 days after the exchange of lists under paragraph (5)(B), the reference product sponsor shall bring an action for patent infringement with respect to each patent that is included on such lists.

(C) Notification and publication of complaint

(i) Notification to Secretary

Not later than 30 days after a complaint is served to a subsection (k) applicant in an action for patent infringement described under this paragraph, the subsection (k) applicant shall provide the Secretary with notice and a copy of such complaint.

(ii) Publication by Secretary

The Secretary shall publish in the Federal Register notice of a complaint received under clause (i).

(7) Newly issued or licensed patents

In the case of a patent that—

(A) is issued to, or exclusively licensed by, the reference product sponsor after the date that the reference product sponsor provided the list to the subsection (k) applicant under paragraph (3)(A); and

(B) the reference product sponsor reasonably believes that, due to the issuance of such patent, a claim of patent infringement could reasonably be asserted by the reference product sponsor if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell,

selling, or importing into the United States of the biological product that is the subject of the subsection (k) application,

not later than 30 days after such issuance or licensing, the reference product sponsor shall provide to the subsection (k) applicant a supplement to the list provided by the reference product sponsor under paragraph (3)(A) that includes such patent, not later than 30 days after such supplement is provided, the subsection (k) applicant shall provide a statement to the reference product sponsor in accordance with paragraph (3)(B), and such patent shall be subject to paragraph (8).

(8) Notice of commercial marketing and preliminary injunction

(A) Notice of commercial marketing

The subsection (k) applicant shall provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k).

(B) Preliminary injunction

After receiving the notice under subparagraph (A) and before such date of the first commercial marketing of such biological product, the reference product sponsor may seek a preliminary injunction prohibiting the subsection (k) applicant from engaging in the commercial manufacture or sale of such biological product until the court decides the issue of patent validity, enforcement, and infringement with respect to any patent that is—

(i) included in the list provided by the reference product sponsor under paragraph (3)(A) or

in the list provided by the subsection (k) applicant under paragraph (3)(B); and

(ii) not included, as applicable, on—

(I) the list of patents described in paragraph (4); or

(II) the lists of patents described in paragraph (5)(B).

(C) Reasonable cooperation

If the reference product sponsor has sought a preliminary injunction under subparagraph (B), the reference product sponsor and the subsection (k) applicant shall reasonably cooperate to expedite such further discovery as is needed in connection with the preliminary injunction motion.

(9) Limitation on declaratory judgment action

(A) Subsection (k) application provided

If a subsection (k) applicant provides the application and information required under paragraph (2)(A), neither the reference product sponsor nor the subsection (k) applicant may, prior to the date notice is received under paragraph (8)(A), bring any action under section 2201 of title 28, for a declaration of infringement, validity, or enforceability of any patent that is described in clauses (i) and (ii) of paragraph (8)(B).

(B) Subsequent failure to act by subsection (k) applicant

If a subsection (k) applicant fails to complete an action required of the subsection (k) applicant under paragraph (3)(B)(ii), paragraph (5), paragraph (6)(C)(i), paragraph (7), or paragraph (8)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under

section 2201 of title 28, for a declaration of infringement, validity, or enforceability of any patent included in the list described in paragraph (3)(A), including as provided under paragraph (7).

(C) Subsection (k) application not provided

If a subsection (k) applicant fails to provide the application and information required under paragraph (2)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of title 28, for a declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product.

(m) Pediatric studies

(1) Application of certain provisions

The provisions of subsections (a), (d), (e), (f), (h), (i), (j), (k), (*l*), (n), and (p) of section 505A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a(a), (d), (e), (f), (h), (i), (j), (k), (*l*), (n), (p)] shall apply with respect to the extension of a period under paragraphs (2) and (3) to the same extent and in the same manner as such provisions apply with respect to the extension of a period under subsection (b) or (c) of section 505A of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a(b), (c)].

(2) Market exclusivity for new biological products

If, prior to approval of an application that is submitted under subsection (a), the Secretary determines that information relating to the use of a new biological product in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for

completing such studies), the applicant agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a(d)(3)]—

(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

(B) if the biological product is designated under section 526[footnote omitted] [21 U.S.C. 360bb] for a rare disease or condition, the period for such biological product referred to in section 527(a)[footnote omitted] [21 U.S.C. 360cc(a)] is deemed to be 7 years and 6 months rather than 7 years.

(3) Market exclusivity for already-marketed biological products

If the Secretary determines that information relating to the use of a licensed biological product in the pediatric population may produce health benefits in that population and makes a written request to the holder of an approved application under subsection (a) for pediatric studies (which shall include a timeframe for completing such studies), the holder agrees to the request, such studies are completed using appropriate formulations for each age group for which the study is requested within any such timeframe, and the reports thereof are submitted and accepted in accordance with section 505A(d)(3) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355a(d)(3)]—

(A) the periods for such biological product referred to in subsection (k)(7) are deemed to be 4 years and 6 months rather than 4 years and 12 years and 6 months rather than 12 years; and

(B) if the biological product is designated under section 526[footnote omitted] [21 U.S.C. 360bb] for a rare disease or condition, the period for such biological product referred to in section 527(a)[footnote omitted] [21 U.S.C. 360cc(a)] is deemed to be 7 years and 6 months rather than 7 years.

(4) Exception

The Secretary shall not extend a period referred to in paragraph (2)(A), (2)(B), (3)(A), or (3)(B) if the determination under section 505A(d)(3)[footnote omitted] [21 U.S.C. 355a(d)(3)] is made later than 9 months prior to the expiration of such period.