
Health Law Daily Wrap Up

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This Strategic Perspective was originally published on August 5, 2015, and is now updated to include information regarding (1) a petition for a writ of certiorari filed by Sandoz, on February 16, 2016, in Amgen Inc. v. Sandoz Inc. (Fed. Cir., No. 2015-1499, July 21, 2015); (2) Amgen filing a conditional certiorari cross-petition after the Sandoz writ; and (3) the signing of the Trans-Pacific Partnership (TPP) trade agreement by the trade ministers of 12 nations on February 4, 2016.

Biosimilars have been the focus of both legal and regulatory action over the past year, domestically and internationally, highlighting potential impacts on these medical products. The Federal Circuit, on July 21, 2015, issued a divided decision regarding the “patent dance” and notice of commercial marketing under the abbreviated biologics pathway – the very same pathway that possibly may be a source of contention for industry and consumers of an international trade agreement in the final stages of negotiation. Subsequently, in a last minute legal maneuver, Sandoz, Inc. filed a petition for a writ of certiorari asking the Supreme Court to review the Federal Circuit’s interpretation of the Biologics Price Competition and Innovation Act’s (BPCIA) “notice of commercial marketing” provision. In its February 16, 2016, filing, Sandoz asked the Court to decide the validity of the Federal Circuit’s ruling in Amgen Inc. v. Sandoz Inc., which held that the 180-day notice of commercial marketing can only be given after a proposed biosimilar product receives FDA approval (see Court interprets biosimilar ‘enigma’ in favor of abbreviated biologic license applicant, July 22, 2015). In an unexpected counter, Amgen filed a conditional certiorari cross-petition on March 21, 2016, asking that, should the Court decide to review the commercial marketing ruling, it also review and overturn the Federal Circuit’s ruling that the patent dance information exchange procedures of the BPCIA are optional.

Domestically and in the near term, the Federal Circuit’s decision in Amgen v. Sandoz offers a view into a legal framework that is unsettled. In a matter of first impression, the appellate panel ruled in a manner evidencing the legal battles that lie ahead for the parties involved in the abbreviated biosimilars pathway. The panel was unable to come to a consensus regarding either the issue of the patent dance or notice of commercial marketing, as no two judges agreed on the same issue.

Additionally, in late June 2015, Congress passed The Bipartisan Congressional Trade Priorities and Accountability Act of 2015 (TPA) that would allow “fast-track” approval of large international trade bills. The TPA was a necessary grant of authority for President Obama to complete the TPP, a proposed trade agreement between the U.S. and 11 other countries, which the Administration views as a means of increasing U.S. influence in the Pacific Rim through economic policy. The 11 countries that are included in the agreement are Australia, Brunei Darussalam, Canada, Chile, Japan, Malaysia, Mexico, New Zealand, Peru, Singapore, and Vietnam. Trade ministers from the TPP countries met at the end of July to finalize negotiations on the TPP.

The Senate initially passed the TPA by a 62 to 37 vote in May, but the House made the status of the bill uncertain when it passed the bill by the slimmest of margins and stripped out the Trade Adjustment Assistance (TAA) provisions of the TPA, which would provide retraining and assistance to U.S. workers who lost jobs as a result of large international trade agreements. As a result, there was a brief moment of uncertainty for the Obama Administration as some Senate Democrats voiced reluctance for support of a TPA without the TAA. The Senate eventually passed the TPA without the TAA on a 60 to 37 vote in late June after reassurances from Republican congressional leaders to Democrats that the TAA provisions would be added and passed in a separate bill.
The President quickly signed the TPA and the separate bill (giving trade preferences to sub-Saharan African countries), with the TAA attached, into law giving him fast-track trade authority.

In February 2016, the TPP was signed by the trade ministers of U.S. and the other 11 countries above, and thus, the world’s largest trade deal is now waiting for ratification of the treaty’s text in each nation. Here in the United States, President Obama has called upon Congress to vote on and pass the TPP before he leaves office in early 2017. At the core of the debate over the TPP are concerns regarding its application and impact on countries’ regulations—in particular the TPP’s key feature of regulatory coherence for the promotion of trade.

This Strategic Perspective will provide a brief overview about the potential legal and regulatory impacts on biosimilars in the U.S. and how they are being addressed by U.S. courts and the TPP.

**The science behind biosimilars**

The BPCIA was enacted as Sections 7001 through 7003 of the Patient Protection and Affordable Care Act (ACA) (P.L. 111-148). The BPCIA required the FDA to develop an expedited process for the approval of biosimilars, modeled after the abbreviated pathway used for the approval of generic small-molecule drugs, when the agency finds that standards for safety, risk mitigation, and clinical effectiveness have been met.

Unlike generic small-molecule drugs, i.e. where the active ingredient is required to be identical to the original, branded reference drug, biosimilars (also referred to as follow-on biologics) are similar to but not identical copies of the originator biologic because of manufacturing processes. Due to the complex structure and the process involved in production, biosimilars must be determined on the basis of analytical, nonclinical, and clinical data to be similar to an original biologic in terms of structural characteristics, and safety and efficacy. The active ingredient of a biosimilar is expected to closely resemble that of the original biologic. As a result, differences in clinical outcomes tend to restrict the use of the innovator’s original safety and efficacy data for evaluation and approval of the biosimilar (see *The challenge of the FDA’s biosimilars regulation*, August 14, 2014).

Biologics can include any therapy derived from a biological source; this group is broad, including vaccines, antitoxins, proteins, and monoclonal antibodies. In general, DNA technology is often used to insert desirable genes or remove undesirable ones within a living cell or via a vector such as a virus, prompting a specific function to be activated – for example, the production of a protein to treat disease. Because biologics are typically much larger and more structurally complex than traditional small-molecule drugs, which are made through chemical processes in a lab, biologics are also more difficult and much more costly to develop and manufacture.

**High cost of biologics.** As noted, biologics are also among the most expensive drugs on the market, at an average cost of 22 times more than small-molecule drugs. According to pharmacy benefits manager Express Scripts, even though only 2 percent of the population uses biologic drugs, biologics account for 40 percent of prescription drug spending in the U.S. For instance, Soliris®, used to treat rare causes of anemia and kidney ailments, costs $440K to $570K per patient per year, while Avastin®, a cancer drug, can cost more than $50,000 a year. There are nine biologics expected to get FDA approval in 2015 and each will likely carry a massive price tag.

With these prohibitive costs there is substantial interest in encouraging the development of biosimilars via the BPCIA's abbreviated approval pathway. As discussed below, the abbreviated approval pathway’s complex litigation requirements are problematic for the biopharmaceutical industry domestically, although the biopharmaceutical industry could benefit in an international trade agreement such as the TPP.

**Biosimilars and the patent dance**

Under the BPCIA, new biologic products are eligible for 12 years of market-based exclusivity during which time the FDA cannot approve any biosimilar products for the same indication as the innovator product (the product of which the biosimilar will be a “generic” derivative). The BPCIA’s provision mirrors the five years of market-based exclusivity for small-molecule drugs, which is meant to promote the development of new drugs. Because a drug molecule and its potential uses are often patented at the time of discovery, that period of patent protection can often expire before (or soon after) a drug has a chance to be brought to market. Market-based exclusivity
is meant to ensure that a company that has worked to bring a new drug to market will have a predictable period during which time it will face no competition from FDA-approved generics.

In general, innovator biologics may retain their 12-year market exclusivity, but also allow use of relevant quality and nonclinical/clinical data for development or evaluation of biosimilars. Although innovator drug product manufacturers are given procedural rights to litigate drug patents prior to generic launch under both the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act) (P.L. 98-417) (small-molecule drugs) and the BPCIA (biologics), small-molecule drug innovators are required to list all patents that claim the drug or method of using the drug in the FDA's “Orange Book.” Although the FDA has established an analogous “Purple Book,” which lists all biological products, including any biosimilar and interchangeable biological products, most significantly, it will not list patents for biologic products for biosimilar applicants to search. The Purple Book does track approval of biosimilars and interchangeables as well as when a product may be approved. Yet, without any patent information, it will not provide all of the information that manufacturers may use to determine if and when a competitor will or could enter the market.

Under the brand and generic small-molecule drug approval process, the first generic drug applicant to certify under Paragraph IV (challenging the pioneer’s patents listed in the Orange Book) receives six months of generic small-molecule drug exclusivity. In contrast, for the abbreviated biologics license application (aBLA) process, BPCIA provides broader exclusivity incentives to the first approved biosimilar. The law grants one-year of market exclusivity to the first biosimilar demonstrated to be interchangeable with its reference biologic, per Public Health Service Act Sec. 351(k) (as codified, 42 U.S.C. §262(k)(6)), and the timetable can be extended in the event of litigation against the first licensee.

The patent dance. As part of the aBLA process under the BPCIA, biosimilar applicants seeking to enter the market prior to expiration are required to notify the innovator and provide a detailed analysis as to why each challenged patent is invalid or will not be infringed. If the innovator biologic manufacturer files suit within 45 days of the biosimilar applicant's notice, the FDA is required to suspend review and approval of the abbreviated new drug application for 30 months unless shortened or lengthened by court order.

A biosimilar applicant can only discover the patents that protect the innovator biologic after providing the innovator manufacturer with access to the aBLA application and related manufacturing process because, as noted, the FDA’s Purple Book does not provide patent information. This is the first step in the “patent dance.” The biosimilar applicant and innovator then undertake a limited duration, complex exchange of patent information compiling a list of patents that will be subject to an initial pre-launch litigation. Once the list has been "agreed" upon, the innovator has 30 days to file suit concerning those patents to enjoin the biosimilar's launch or else forfeit all monies but royalties in subsequent litigation on those patents.

Under the BPCIA, an additional round of pre-launch litigation can begin once the biosimilar applicant notifies the innovator a second time at least 180 days prior to launch – the notice of commercial marketing. In this second step disclosed patents that were not on the initial pre-launch litigation list are eligible for possible injunctive relief, and applicants can file declaratory judgments during this time regarding patents that the innovator elected not to pursue. The FDA has noted that determining the “date of first licensure” is not as apparent as determining which date a product obtained FDA approval through, “in most instances,” it will be because “not every licensure of a biological product under 351(a) is considered a ‘first licensure’ that gives rise to its own exclusivity period.”

A new legal framework

Amgen brought suit against Sandoz in federal court asserting violations of California’s unfair competition law, conversion, and wrongful use of Amgen’s approved license for its cancer-fighting biologic Neupogen® (filgrastim), and infringement of Amgen’s patent for a particular method of using filgrastim. The FDA previously accepted Sandoz’s application for the filgrastim biosimilar Zarxio in July 2014 and approved the application earlier this year (see FDA enters new era with approval of first biosimilar; March 6, 2015).

Amgen alleged that Sandoz violated BPCIA Sec. 262(l) by not providing Amgen with the patent information required and by providing premature and ineffective notice of commercial marketing of Zarxio because the notice
was given prior to the FDA’s approval of Zarxio. Sandoz filed a counterclaim alleging that it complied with the BPCIA and Amgen’s filgrastim patent was invalid and, therefore, could not have been infringed.

**District court’s findings.** The lower court granted partial judgment in favor of Sandoz reasoning: (1) the BPCIA allows an aBLA applicant not to disclose its aBLA and manufacturing information to a reference product sponsor (RPS), subject only to a lawsuit on the infringement, validity, or enforceability of a patent; (2) a decision not to disclose that information does not authorize an RPS to obtain injunctive relief, restitution, or damages against the applicant; and (3) an applicant can give valid commercial marketing notice prior to FDA approval. As a result, the court dismissed Amgen’s unfair competition and conversion claims. The court also denied Amgen’s state law request for an injunction to bar Sandoz from marketing Zarxio. The patent claims remain pending in the district court (see *Drug company’s request for preemptive non-infringement judgment of biosimilar drug in development fails*, November 14, 2013). Amgen appealed.

Upon reviewing the lower court’s decision, the Federal Circuit decided that an aBLA applicant did not need to engage in the patent dance with the RPS, but did need to comply with the premarketing notice provision of 42 U.S.C. §262(l)(8). Specifically to the latter, the appellate panel held that notice of commercial marketing, to be effective under the BPCIA, must be given only after the product is licensed by the FDA. In a dissent from this portion of the decision, Judge Chen wrote that the majority’s position extra-statutorily extended RPS’ 12-year market exclusivity as established in the BPCIA by an additional six months.

**Patent dance—“shall” means “may.”** Upon review by the Federal Circuit, the panel considered whether the BPCIA permitted an aBLA applicant to choose not engage in the patent dance by failing to disclose its aBLA or providing the manufacturing information to the reference product sponsor. Amgen asserted that language stating that the applicant “shall provide” the information to the reference product sponsor rendered the information disclosure mandatory and not voluntary. Sandoz disagreed and argued that it was permissive and the result of not disclosing the information was to give Amgen, as the reference product sponsor, the right to file an infringement suit and obtain the undisclosed information in discovery—a right that Amgen invoked with the litigation at hand. In essence, Sandoz maintained that the use of the term “shall” did not mean that a biosimilar applicant must provide a copy of its application in every instance, rather, a copy of its application is required only if it wished to partake in the benefits of the patent dance.

The appellate court agreed with Sandoz and held that the statute expressly contemplated the actions that Sandoz took (see *Court interprets biosimilar ‘enigma’ in favor of abbreviated biologic license applicant*, July 22, 2015). Specifically, the appellate panel noted that while the statute sought to promote the patent dance’s information disclosure, it did not mandate it, which was made apparent by the statutory consequence of a patent infringement lawsuit—the very consequence that Amgen pursued.

Christopher B. Ferenc*, associate in the Pharmaceutical and Life Sciences Litigation group at Katten Muchin Rosenman LLP, told Wolters Kluwer that it was “interesting” that each judge on the Federal Circuit panel deciding *Amgen* issued individual opinions regarding the patent dance and notice of commercial marketing, but it was “indicative of the first impression nature of the issue.”

“For biosimilar applicants a voluntary patent dance is important,” said Ferenc, as these applicants now have the added benefit of whether to disclose patent information in the aBLA to the innovator “outside of a court setting.” Disclosure in court, rather than outside, affords the biosimilar applicant an important advantage—fewer patents may be litigated during the entire process. Ferenc noted however, that biosimilar applicants should “continue with due diligence” during the aBLA process. Without a comparable Orange Book to rely upon, biosimilar applicants do not have a complete view of the patents held by the innovator biologic, which could be problematic once litigation commences.

**Commercial marketing—“shall” means “must.”** Amgen also argued that Sandoz violated the BPCIA’s requirement that an aBLA 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).” Amgen asserted that the notice was insufficient because it was given prior to the licensure of Sandoz’s product. Sandoz countered that the plain language of the requirement permitted notice prior to FDA approval and that
Amgen’s reading would create an automatic 180-day bar on marketing of any aBLA-approved product following approval.

The appellate panel agreed with Amgen and held that the statutory language compelled a finding that “notice, to be effective under this statute, must be given only after the product is licensed by the FDA.” The court reached its conclusion by taking note of other provisions that referred to the status of a product not as licensed but as the biological product that is the subject of an application. The court recognized that its holding established an additional 180 days, or 6 months, of market exclusivity for reference product sponsors, but reasoned that the extension was consistent with the four- and 12-year exclusivity periods in the BPCIA.

As to the determination that notice to commercial marketing could only occur after FDA-approval of the biosimilar, Ferenc said that Judge Chen’s characterization of the majority’s holding (in his dissent) as an “extra-statutory exclusivity windfall” is likely to frame the biosimilar applicant arguments as the appeal moves forward. The applicant is bound to a “trigger event” unless the FDA revises its current approval process to issue approvals in a different manner with the BPCIA in mind. The innovator biologic thus receives an extra 180 days of exclusivity and commensurately higher measures of profitability for the manufacturer.

In a per curiam order in October 2015, the Federal Circuit declined to rehear the matter en banc, which came as something of a surprise, as the panel decision was fractured, and neither party disputed that it raised important issues of first impression. Indeed, both Amgen and Sandoz had sought en banc review, albeit on different issues. Unless the Supreme Court (or a later en banc court) chooses to intervene, as discussed below, the panel’s decision will stand as the Federal Circuit’s authoritative statement on the issues presented.

Biosimilars and the Supreme Court

In January 2016, Amgen declined to file its own free-standing cert petition. As its own filing deadline approached, Sandoz chose to file a petition for a writ of certiorari, asking the Supreme Court to review the Federal Circuit’s interpretation of the BPCIA’s notice of commercial marketing provision. In its February 16, 2016, filing, Sandoz asked the Court to decide the validity of the Federal Circuit’s holding that the 180-day notice of commercial marketing can only be given after a proposed biosimilar product receives FDA approval. On March 21, 2016, Amgen filed an opposition brief to the Sandoz petition, and in an unexpected move filed a conditional cross-petition, requesting that if the Court chooses to take up Sandoz’s petition on commercial marketing, it would address the issue Amgen lost before the Federal Circuit, specifically whether the BPCIA’s patent dance was mandatory.

Will cert be granted? Courtenay C. Brinckerhoff, a partner with Foley & Lardner and editor of Foley’s PharmaPatents blog, told Wolters Kluwer that the Supreme Court may be inclined to hear the case because (1) Sandoz presented an issue of statutory construction of an important provision of the BPCIA; and (2) district courts are already applying the Federal Circuit’s interpretation of the BPCIA in other biosimilar cases.

The appellate panel’s decision in Amgen v. Sandoz acknowledged that its ruling could establish additional six months exclusivity for the RPS, but found that it was consistent within the four- and 12-year exclusivity periods in the BPCIA. Under the Federal Circuit’s interpretation of 42 U.S.C. §262(l)(8)(A), actions authorized by §262(l)(8)(B) cannot be commenced until the biosimilar product has been approved. Sandoz’s argument is that this interpretation is not supported by either the BPCIA’s language or purpose. According to Brinckerhoff, the majority’s rationale seems to rest on the assumption that, if a biosimilar application is filed during the 12-year exclusivity period, the FDA will “license” the biosimilar product before the 12-year period has run, in which case the pre-marketing notice could be given before the 12-year period has run. However, the 12-year period is embodied in 42 U.S.C. §262(k)(7)(A), which states that “[a]pproval of [a biosimilar application] may not be made effective” until the 12-year period has run. Thus, Brinckerhoff said, it is not clear that the FDA has the statutory authority to “license” a product before the 12-year period has run.

Ferenc added that given the number of biosimilar applications that have and will be filed, the Supreme Court would likely grant cert on the commercial marketing provision. However, given the vacancy on the Court, any
decision would not likely come until 2017. Further complicating the issue, according to Ferenc, is whether Amgen will file a cross-petition for review of the “optional patent dance” holding from the appellate court.

**Biosimilar availability.** Sandoz also noted in its petition that the Federal Circuit’s ruling would create a delay in availability for all biosimilars. Brinckerhoff stated that whether the post-approval notice requirement itself would keep a biosimilar product off the market in another case would depend on the circumstances, including whether the RPS had obtained a preliminary injunction based on any patents being litigated. She noted that it was possible that in other cases the notice requirement would be the only factor keeping the biosimilar product off the market. Ferenc agreed, noting that if effective notice can only be given after the approval of the product by the FDA, the first eligible day for commercial marketing would be the 181st day after approval. An RPS suit during that time may cause additional delays.

**Optional partners.** While not addressed in Sandoz’s petition, the Federal Circuit also held that the patent dance was optional. A consequence of an optional patent dance is that the biosimilar applicant would be subject to patent infringement action. By not filing a petition, Amgen implied that it was content with an optional patent dance.

Under an optional patent dance scheme, Brinckerhoff said that the RPS can benefit because it can bring an immediate declaratory judgment action without having to go through the patent dance procedures. The RPS can litigate all patents that it believes should be litigated instead of being limited to the patents agreed upon after the exchange of patent lists. Ferenc added that he suspected that Amgen did not file a petition for cert because they were content with the commercial marketing notice provision. Outside of the notice of first commercial marketing, there are no real additional benefits to the RPS. Ferenc also noted that the statute was fairly clear on the optional aspect of the patent dance.

Conversely, for the aBLA applicant, the benefit of an optional patent dance is to let the RPS file suit (which the RPS would need a Rule 11 basis), rather than provide the RPS with additional pre-litigation access to its application. Brinckerhoff similarly noted this benefit for aBLA applicant, but cautioned that the strategy presented its own problems for the aBLA applicant. If the patents are not litigated until later in the approval process or after the product is approved, the biosimilar applicant may have to choose between delaying market entry until the patent litigation is resolved or launching at risk, e.g., entering the market at the risk of being held liable for willful patent infringement. Brinckerhoff said that given the costs of biologics and the risk of treble damages, a launch at risk could be associated with significant financial risk. Ferenc said that given the money at stake for parties involved, the patent dance was no longer a viable option for the foreseeable future.

**Amgen’s opposition brief and cross-petition.** Amgen’s opposition brief asserted that the Sandoz certiorari request be rejected for three reasons: (1) Sandoz was appealing the Federal Circuit’s unanimous and correct holding that notice of commercial marketing can only be given post-licensure; (2) Sandoz’s requests relating to a private right of action and the availability of injunctive relief were moot because the issues were not decided by the Federal Circuit; and (3) a Supreme Court review would be premature, as the BPCIA issues were currently being litigated in seven pending cases, including in a case before the Federal Circuit on April 4, 2016.

Amgen argued that there was no urgency for the Supreme Court to take up the matter, as only one biosimilar (Sandoz’s Zarxio) had been approved by FDA and that a minimal discount off of the wholesale price of the RDP (Amgen’s Neupogen) that Sandoz was offering demonstrated that waiting for the lower courts to resolve the differences would have a minimal impact on consumer costs.

In its cross-petition on the patent dance provisions, Amgen requested that the Court review the Federal Circuit’s ruling of an optional patent dance, should the Supreme Court decide to review the notice of commercial marketing issue. Amgen argued that the two issues were “inextricably intertwined” and that the Federal Circuit ruling is incorrect under Supreme Court precedent on statutory interpretation. In essence, Amgen contended that the word “shall” employed in the patent dance provisions of the BPCIA is a mandatory word, as it is in the notice of commercial marketing provisions.
Sandoz’s response to Amgen’s cross-petition is due in a matter of weeks. Aside from Amgen’s unsettled legal effect, the near future may see effects on domestic regulation of biosimilars resulting from international trade.

Regulatory impact on biosimilars

Advocates of the TPP highlight a trade agreement that accounts for one-third of the world’s total trade having a positive impact on the domestic market. Even as a matter of foreign policy, the TPP is touted as a means for the U.S. to influence Pacific Rim nation economies to the benefit of the domestic economy. The TPP has its share of critics from a diverse range of groups, including those groups concerned with drug safety and costs in the U.S.

The Trans-Pacific Partnership. In 2009 the U.S. began negotiating the TPP, seeking to boost U.S. economic growth with Canada, Mexico, and several Asian and Pacific counties considered key destinations for U.S. manufactured goods, agricultural products, and services suppliers. As a group, the TPP countries are the largest goods and services export market of the U.S., accounting for $698 billion in 2013, or 44 percent of total U.S. goods exports. U.S. exports of agricultural products to TPP countries totaled $58.8 billion in 2013, 85 percent of total U.S. agricultural exports.

The Office of the United States Trade Representative identified five features for the trade agreement:

1. comprehensive market access by eliminating tariffs and other barriers to goods and services trade and investment, so as to create new opportunities for our workers and businesses and immediate benefits for TPP consumers;
2. fully regional agreement facilitating the development of production and supply chains among TPP members, supporting the goal of creating jobs, raising living standards, improving welfare and promoting sustainable growth;
3. cross-cutting trade issues by building on work being done through the Asia-Pacific Economic Cooperation and other economic forums by incorporating in TPP four issues –
   a. regulatory coherence to promote seamless and efficient trade;
   b. competitiveness and business facilitation, including development of regional production and supply chains;
   c. commitment to address concerns of small- and medium-sized business about international trade; and
   d. development of comprehensive market liberalization, improvements in trade and investment enhancing disciplines, and other commitments.
4. new trade challenges to promote trade and investment in innovative products and services, including related to the digital economy and green technologies; and
5. flexibility in updating the TPP as appropriate to address trade issues that emerge in the future, as well as new issues that arise with the expansion of the TPP to include new countries.

The TPP was signed by the trade ministers of 12 nations on February 4, 2016, in New Zealand, and thus, the world’s largest trade deal is now waiting for ratification of the treaty’s text in each nation. Consumers of biologics would not immediately see positives or negatives to the TPP; those outcomes would be dependent upon the involvement of governments and industry. President Obama has called upon Congress to vote on and pass the TPP before he leaves office in early 2017.

However, there is strong opposition from many congressional Democrats and some Republicans, which could mean a vote on the TPP is unlikely before President Obama leaves office. These concerns and a myriad of others will still require years of tough negotiations before the TPP becomes a reality.

Exclusivity. At the core of the debate over the TPP, concerns have been raised about its application and impact on countries’ regulations – in particular the TPP’s key feature of regulatory coherence for the promotion of trade. Issues concerning intellectual property (IP) protection in the TPP have focused primarily on patents, but there are concerns that the patent protection schema is not as effective for biologics because biosimilars do not require exact identity with the reference product.
Specifically for life sciences and the pharmaceuticals industry, the ACA-established pathway for biologics employs a 12-year exclusivity period, in stark contrast to five years for generic small-molecule drugs. Supporters of the TPP argue that the greater cost and difficulties involved in research and development of biologics required a longer exclusivity period as incentive for innovation. Critics of the TPP counter that 12-year exclusivity would only result in keeping drug prices high, putting strains on the health care system and keeping life-saving drugs out of the reach of many patients.

Currently, the countries that would be signatories to the TPP have biologic exclusivity periods that range from zero years (Brunei) to eight years (Japan). Interestingly, in an effort to garner support for the TPP among biopharmaceuticals, the Obama Administration has touted that participating countries would increase exclusivity periods to match the U.S. Yet, this is in stark contrast to what the Administration has advocated domestically regarding patent exclusivity for biologics. After the ACA enactment, the Administration proposed to reduce biologic exclusivity from 12 to 7 years, arguing that Medicare would realize savings of up to $4.4 billion over the next 10 years.

Not surprisingly, there is certainly debate both domestically and internationally on exclusivity. Advocacy group Médecins Sans Frontières (MSF, commonly known as Doctors Without Borders) considers the 12-year period of data exclusivity for biologics advocated by the U.S. as “devastating” and “unprecedented.” MSF claims these provisions will “limit access to medicines for at least half a billion people.” Conversely, pharmaceutical industry advocacy group Biotechnology Industry Organizations (BIO) stated that longer patent exclusivity was necessary to give biologics makers a level of protection from competition similar to what traditional drug makers enjoy for their innovative products. Given the inherent risk in developing biologics, the biopharmaceutical industry needed more than a “break even” approach in business terms. BIO has argued that until the BPCIA, innovator biologics did not have to worry about generic competitors eroding markets, a clearer incentive to offset the higher risk and costs in biologics development.

Thus, the difficult question to answer is whether an inventor of a new drug measures the cost of invention against the revenue that might be made in the “poor” world in calculating whether to undertake the research and development of the drug. Supporters of the TPP argue that the greater cost and difficulties involved in research and development of biologics required a longer exclusivity period as incentive for innovation. Critics look at the TPP as an attempt to use trade law and treaties to extend the “rich” world IP protections to the “poor” world.

Transparency. The impact of the TPP is difficult to ascertain, not only because the TPP is complex, nearly 30 chapters, but the draft text itself is not readily available for public review. As a result, several key chapters have raised concerns about the substantial effect on U.S. health care. For instance, the U.S. proposed in a 2011 annex to the TPP that all countries would use “competitive market-derived prices” to recognize the value of a drug when establishing the drug’s prices. Although a December 2014 draft annex, titled “Annex on Transparency and Procedural Fairness for Pharmaceutical Products and Medical Devices,” did strike some of this troublesome language, procedural hurdles are still in place and the TPP would be applicable to agencies such as CMS and the FDA. Specifically, a country’s health care authority that operates or maintains procedures for (1) listing new drugs or medical devices for reimbursement purposes, or (2) setting the amount of reimbursement under national health care programs must have procedures in place for reconsiderations of coverage determinations. Consumer policy groups are concerned that the annex could create an end-around in CMS or FDA decisions, i.e., rendering programs such as Medicare more vulnerable to corporate interference.

A different draft chapter, titled “Investment,” would permit foreign companies to sue TPP member countries for damages if they believe their expected future profits were undermined. Known as “investor-state dispute settlement,” (ISDS) these challenges would be heard by arbiters without independent review by domestic court systems. Although such provisions are found in trade agreements, critics argue the amount of trade involved in the proposed TPP would substantially increase the number of companies willing to challenge national laws. The Office of the United States Trade Representative disagreed, noting that it had more than two decades of experience with ISDS under separate U.S. trade agreements and providing a neutral international forum to resolve investment disputes under international law mitigated state-to-state conflict while protecting U.S. citizens.
Additionally, ISDS arbitration was vital because the potential for bias could be high in situations in which a foreign investor was seeking to redress injury in a domestic court, especially against the government itself.

**Conclusion**

While it is unlikely that concerns from industry and consumers will affect how the U.S. approaches TPP negotiations in these final stages, legal and regulatory issues surrounding biosimilars domestically will certainly continue for the near- and long-term future. In the U.S., ratification of the TPP could potentially bring to the forefront weaknesses in the current aBLA pathway, at least if domestic regulation clashes with international trade requirements. To achieve some sort of consensus with other TPP signatories, market exclusivity may be reduced. As a matter of domestic policy the reduction would potentially benefit the overall costs of health care in the U.S.; however, such a reduction would likely follow some form of concession or incentive to biologic innovators if the biologic market is to be preserved. Of the three entities involved, biologic sponsor, biosimilar applicant, and consumer, the latter may be the one to bear the biggest costs as the biosimilar process is refined.

As discussed, the small-molecule drug development process experienced numerous refinements, whether through enactment of Hatch-Waxman or years of convoluted jurisprudence. It should not be a surprise to those involved in the biologics and biosimilars market to deal with similar growing pains, both domestically and internationally.

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