



Biologics, Biosimilars and Patents:

A BEGINNER'S GUIDE

Introduction

Today, biologic drugs represent nearly half of the total sales for the United States pharmaceutical market. They treat a variety of conditions, including cancer and many immune-related diseases such as Crohn's Disease.

The Biologics Price Competition and Innovation Act (BPCIA) was signed into law as part of the Affordable Care Act of 2010, as an amendment to the Public Health Service (PHS) Act. This created an abbreviated pathway for FDA approval of biologic products shown to be biosimilar or interchangeable with other biologics (reference products) already approved by the FDA. At its core, the BPCIA is intended to create competition and lower the price of biologic drugs. The BPCIA is similar to the Drug Price Competition and Patent term Restoration Act (Hatch-Waxman Act) that created the generic pharmaceutical industry.

Given the recent history of the BPCIA and the ongoing understanding of how the regulatory aspects are working in practice, including the multiple types of biologic products that are covered by the law, it can seem quite a complicated system for those not in the business. It is with this in mind that we created this beginners guide to provide an entry point for those who want to learn more about how the biologics regulatory system works for biosimilar drugs and its intersection with the patent system.



What are Biologic Drugs?

Also known as biologics or biologic medicines, biologic drugs consist mostly of proteins produced by human, animal, or microorganism cells. While definitions vary, the U.S. Food and Drug Administration (FDA) classifies “vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins” as biologics.¹

Insulin, which debuted in 1921, was the first biologic medicine and continues to be the best known and most widely used. Advances involving recombinant DNA expanded the possibilities for biologics. This breakthrough, which enables manufacturers to express therapeutic proteins by culturing bacterial, yeast, or mammalian cells in industrial-scale biotanks, remains at the core of this sphere of medicine.

Biologics are complex molecules containing up to 50,000 atoms, whereas chemical drugs typically contain 20-200 atoms—which is why they are often described as large-molecule and small-molecule drugs, respectively.

TABLE 1. MAJOR DIFFERENCES BETWEEN BIOLOGICS AND CHEMICAL DRUGS

 BIOLOGICAL DRUGS	 CHEMICAL DRUGS
Produced by living cell cultures	Produced by chemical processes
High molecular weight	Low molecular weight
Complex, heterogeneous structure	Well-defined structure
Strongly process-dependent	Mostly process-independent
Not entirely characterizable	Completely characterizable
Unstable	Stable
Injected or infused	Swallowed as pills

Biologic Drugs and How They Work

Biologics are used for the treatment of an ever-expanding range of conditions. In addition to diabetes, these include autoimmune disorders, cancer and genetic conditions. Many biologics help regulate overactive or misfiring immune systems to disrupt processes that cause inflammation as a result of autoimmune diseases or trigger cancer cells to divide and grow, while other biologics activate the immune system to better attack cancer cells.

Whereas most chemical or small-molecule drugs like aspirin or atorvastatin (Lipitor®) are administered orally through tablets or capsules, biologic or large-molecule drugs are most often administered intravenously or subcutaneously because, if swallowed, stomach acids would break them down. Usually a medical professional administers the drugs in a hospital or clinic, but some can be self-administered in the home.

Non-Patent Exclusivities for Branded Biologics

The BPCIA provides a 12-year FDA market exclusivity period for a reference branded biologic (the original biologic drug). This means that the FDA is prevented from approving a biosimilar until 12 years have passed from the date of first approval of the reference product.² This FDA market exclusivity is designed to incentivize research and development of novel biologics by providing an incontestable period of time without competition to recoup a return on investment and is entirely separate from any patent protection related to the reference product.

A new 12-year period of market exclusivity is *not* available for a subsequent application to the FDA for a change that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength. It is also *not* available for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. In other words, the 12-year market exclusivity period is only available for novel biologics as determined by a different safety, purity, or potency profile, including drug combinations.³

Other regulatory incentives include orphan drug exclusivity and pediatric exclusivity. The US Orphan Drug Act (1984) defines an orphan drug as one with “*efficacy against a disease affecting fewer than 200,000 people...or one that...will not be profitable for seven years.*” The exclusivity granted to orphan drugs provides seven years without generic or biosimilar competition for the approved orphan designation. This seven year period does not prevent competition for other approved uses of the medicine where the 12 year FDA market exclusivity and any relevant patent protection has expired or has been resolved through patent litigation.⁴

Pediatric exclusivity is designed to incentivize research and development into drugs to treat childhood diseases, which typically have a smaller population of patients and are less profitable than drugs that treat adult diseases. After completion of FDA requested clinical trials in a pediatric population, a 6-month extension is added to any existing 12 year market exclusivity and patent exclusivity, even if the pediatric study is not successful. Once pediatric exclusivity is obtained for a branded drug, it applies to all other FDA marketing or patent exclusivities covering drugs from the applicant containing the same active ingredient.

Regulatory Approval of Biosimilars and Interchangeable Biosimilars

The BPCIA provides a two-tier regulatory pathway for biosimilar drugs to gain FDA approval through submission of an abbreviated Biologics License Application (aBLA).⁵

Biosimilars are a type of biologic drug. Just as copies of branded chemical drugs are known as generic drugs, copies of branded biologics are known as biosimilars. The FDA defines a biosimilar as a biological product that is “highly similar” and has no clinically meaningful differences from an existing FDA approved reference product with respect to its safety, purity and potency.⁶

How does a biosimilar product meet the “highly similar” regulatory standard? As biologics are produced by living cells and are very complex in structure, each batch of branded biological drug varies slightly from the next. This is known as microheterogeneity. For example, there may be microheterogeneity in the charge profile, purity or structural properties between different batches of the same drug. One important factor responsible for microheterogeneity is the variability of the glycosylation pattern. Another factor is variable substitution of different amino acids at specific points in the protein chain. These patterns of microheterogeneity are affected by cell culture conditions and methods of drug purification. The acceptable limits of microheterogeneity of the branded biologic define the limits of similarity that the biosimilar must fall into. If batches of the branded drug range from having 7% to 12% of glycosylation, the biosimilar batches should also fall within this percentage range. In other words, a biosimilar must be as similar to the branded biologic as the branded biologic is to itself.

In contrast to small molecule drugs, which only require human studies to demonstrate bioequivalence (equivalent blood levels of drug), biosimilar manufacturers must require clinical trials for its proposed product. Once clinical studies have been completed, the biosimilar manufacturer compiles the study results together with the analytical data package into an aBLA for submission to the FDA. The FDA review process takes 12 months and results in either approval of the aBLA or rejection in the form of a complete response letter.

An aBLA contains evidence that the potential drug is biosimilar to a reference product already approved by the FDA. The biosimilar aBLA cannot be filed with the FDA until at least four years has passed since the FDA reference product obtained approval.⁷ Given that it takes approximately eight years to develop a biosimilar and biosimilar development cannot start until after the FDA approval of the reference product,

this four-year period is unlikely to cause a delay.⁸ The reason is that biosimilar development requires samples of the FDA reference product to be available on the public market for analytical testing. Moreover, the FDA may not approve a biosimilar until 12 years after the reference product is first approved.⁹

An interchangeable biologic is also a biosimilar, but which meets the additional regulatory challenge of producing the same clinical result as the reference product in any given patient. To gain interchangeable status, biosimilar manufacturers are required to require additional clinical studies that investigate the effect of switching patients back and forth between the biosimilar and the reference branded biologic. Switching studies cost tens of millions of dollars, and many biosimilar manufacturers have opted not to conduct them. An interchangeable biosimilar may be substituted for the respected branded biologic without consulting the prescriber, much like how generic drugs are routinely substituted for brand name drugs. This is commonly called pharmacy-level substitution and is subject to state pharmacy laws. A biosimilar product that receives the first interchangeable designation has exclusivity for a full year.¹⁰ It is possible for multiple interchangeable biosimilars to share a period of interchangeable exclusivity if they are approved on the same day. In the case of gene therapy products and vaccines, interchangeability cannot be demonstrated in practice.

In contrast, in the U.K., Europe, Canada and other industrialized countries, biosimilars are deemed interchangeable with their reference branded biologic upon receiving regulatory approval and without the additional studies required in the U.S. An interchangeable biosimilar may be substituted for the respective branded biologic without consulting the prescriber. While the interchangeability designation in the U.S requires the *automatic* substitution of biosimilars at the pharmacy level, it has led to confusion in the U.S health care community that “ordinary” biosimilars may not be suitable for interchanging by the prescriber. The interchangeability designation is a key reason for the slow biosimilar uptake in the U.S market as compared to Europe.¹¹

KEY TAKEAWAYS

- Biosimilars are the equivalent of generics for small molecule drugs.
- Some, but not most biologics, have an added ‘interchangeability’ designation which means they can be substituted for the original biologic product without consulting the prescriber, much like generic drugs.
- Interchangeability designation is unique to biosimilars in the U.S.

Patent Thickets and Biosimilar Entry

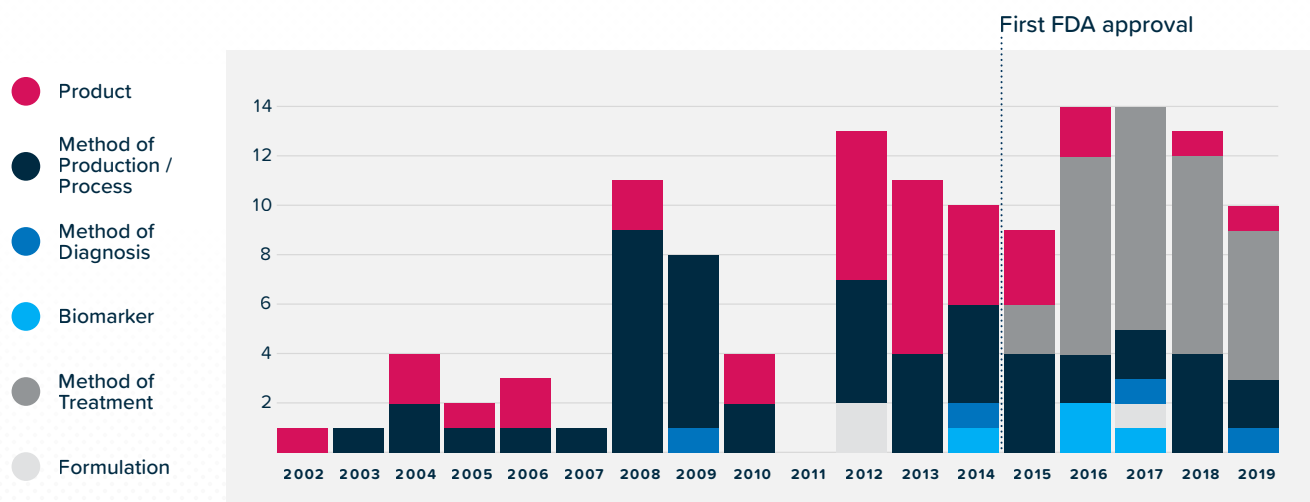
Patents and patent litigation have a significant role to play in determining when biosimilar competition is able to enter the market under the BPCIA. A strategy commonly used by branded drugmakers of a reference biologic is to develop a patent thicket around their product in order to maintain a market monopoly for as long as possible.

Patent thickets¹² include two key aspects of patenting activity in relation to a reference biologic product: 1) dozens or even hundreds of patent applications that drugmakers file with the U.S. Patent and Trademark

Office (USPTO), and 2) patents that are actually granted and which can be enforced in litigation.¹³ The high volume of both filed patent applications and granted patents creates a complex web of both actual and potential or likely barriers that biosimilar competitors must avoid to stay in compliance with the law. This creates a great deal of uncertainty that can deter biosimilar competitors from entering the market, and creates ambiguity for Americans regarding the availability of more affordable medications.¹⁴

Current policy discussions and legislative efforts around patent thickets focus on how many patents are eventually asserted during litigation and when a biosimilar version of a product is allowed to enter the market.¹⁵ However, this narrow scope of assessing the problem fails to capture the bigger picture of how patent thickets impact biosimilar competition. In addition to the standard development work, biosimilar manufacturers are often challenged to design around patents belonging to the branded company. The patents may cover specific steps in the manufacturing process, for example media used to feed the living cells that produce the drug, or specific steps and technologies used to purify the drug. Patents that cover manufacturing steps often expire after the primary active ingredient patents. Branded drug companies typically own extensive portfolios of manufacturing process patents, many of which are filed and granted after a drug is approved by the FDA (see Figure 1) and which are not used in relation to the reference product.¹⁶ Even if these manufacturing process patents are not used for the approved reference product, biosimilar manufacturers still have to design around them all to avoid any claim of infringement, which is often not possible. This adds to the development costs of biosimilar manufacturers and can delay or even deter them from deciding to enter the market even before any litigation commences.

FIGURE 1: THE TYPES OF PATENT APPLICATIONS FILED ON KEYTRUDA OVER TIME.

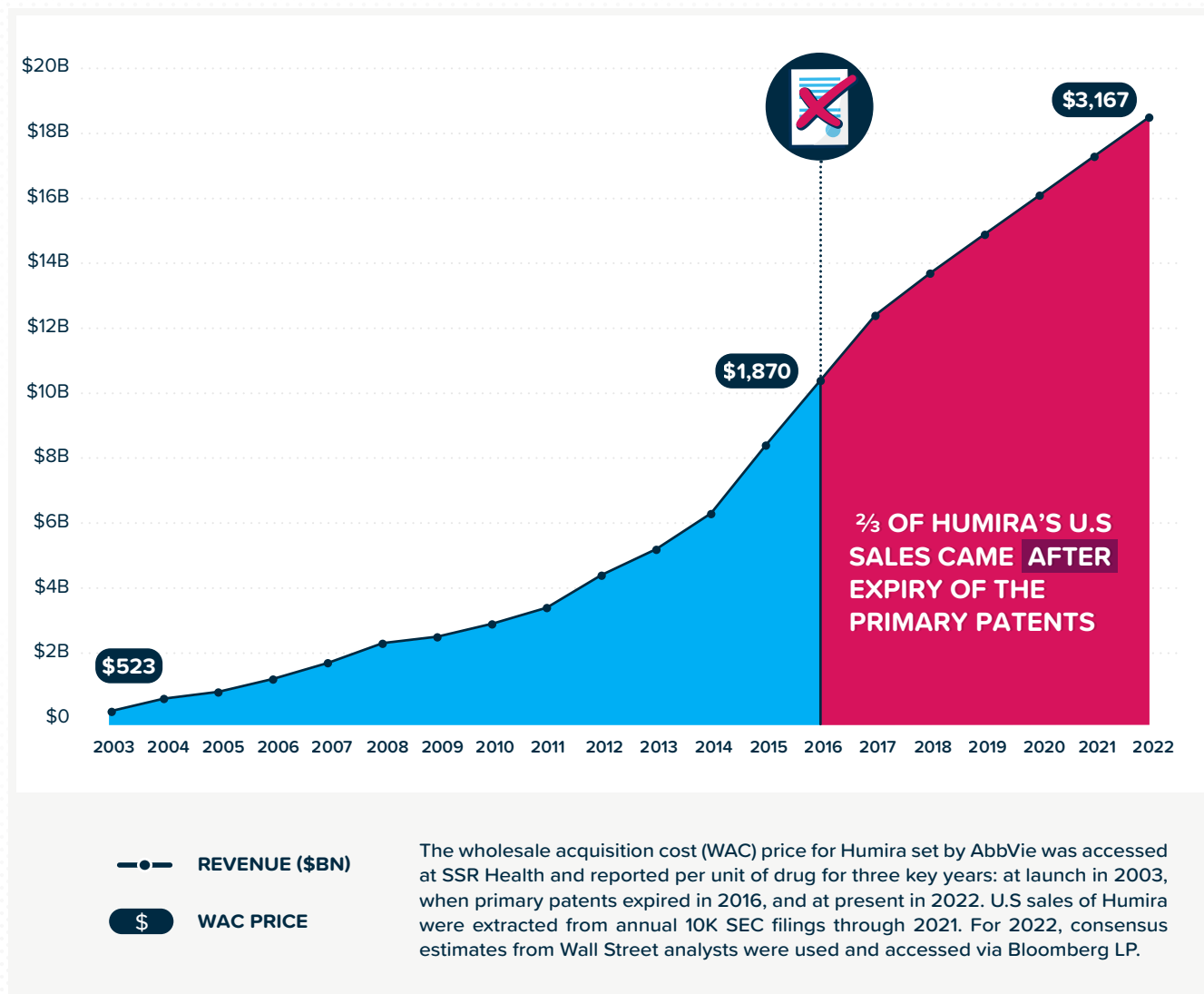


SOURCE: I-MAK, OVERPATENTED, OVERPRICED, KEYTRUDA'S PATENT WALL, MAY 2021¹⁷

In addition to manufacturing process patents, another common strategy branded drug companies use to build a patent thicket is to accumulate as many patents as possible covering different formulations. Patents for formulations can include a combination of excipients, such as buffers, stabilizers, detergents and tonicity agents, that perform different functions in order to stabilize the active ingredient for long-term storage and rendering the drug suitable for delivery into the patient. Patents that cover formulations often expire after the active ingredient patent expires. An example of this strategy is Abbvie's drug Humira, which is used to treat a variety of inflammatory diseases. The original active ingredient patents covering the adalimumab (Humira[®]) antibody were filed on February 9, 1996¹⁸ and the formulation patents were filed six years later. Abbvie obtained at least 20 granted U.S patents covering different

formulations of Humira, effectively fencing off biosimilar manufacturers' ability to design around them.¹⁹ Many of the formulation patent claims are extremely broad and capture the alternative formulations developed by the biosimilar manufacturers, even though these formulations have not been exemplified in practice by AbbVie and were not used in relation to its product. The result was that Humira's U.S. market exclusivity lasted many years after the patent protection on the active ingredient expired, allowing it to maximize its revenue and profits while increasing its prices at the expense of Americans (see Figure 2).²⁰ Moreover, these additional patents were then used to extract settlements from biosimilars that were unable to litigate through the patent thicket, resulting in these competitors having to license and pay royalties to AbbVie on some of these patents.²¹

FIGURE 2: HUMIRA U.S SALES BEFORE AND AFTER EXPIRY OF THE PRIMARY PATENTS



SOURCE: I-MAK, OVERPATENTED, OVERPRICED, CURBING PATENT ABUSE: TACKLING THE ROOT OF THE DRUG PRICING CRISIS, SEPTEMBER, 2022

The ability of branded drugmakers to build patent thickets, such as the Humira example described above, is further enabled by what is a special type of patent application unique to the U.S patent system called a *continuation*. Continuation patents can typically cover minor follow-on tweaks of an existing patent for an invention, such as new methods of treatment or modified formulations. Many continuation patents are initially rejected by the patent office for being “non-patentably distinct”, being obvious variants over

other patents in the same patent family belonging to the same patent owner. However, the patent owner can overcome these rejections by linking its continuation patents together with a common expiry date, called a terminal disclaimer. Therefore, the USPTO permits parties to patent the same invention (such as the same dosing regimen or the same formulation) over and over again provided that the applicant uses slightly different wording in its claims. The U.S is the only country that allows parties to duplicate their patents using this terminal disclaimer maneuver. In other countries, this duplicative patent strategy is known as “double patenting” and is not permitted.

These duplicative patent thickets create uncertainty for biosimilar manufacturers who must invalidate every claim of every patent to enter the market, which becomes a cost-prohibitive proposition as the number of patents increases. Biosimilar companies work to identify follow-on patents that should be considered invalid to challenge as a means to come to the market sooner. However, the existence of so many duplicative patents, in addition to the various secondary and tertiary patents, can often be an insurmountable barrier. While each patent may cost as little as \$25,000 to obtain, on average it costs \$774,000 to challenge a patent in an *inter partes* review or post-grant review at the USPTO.²² Federal court litigation is even more expensive. Branded drug companies are aware that it is a numbers game that most biosimilar competitors cannot win. The result is delayed biosimilar launches which keep patients and payers, including Medicare, paying higher drug costs for longer than anywhere else in the world.

Delayed Legal Standing and Settlements

The patent thicket problem is exacerbated by the issue of delayed “standing.” Biosimilar competitors do not have legal standing to challenge patents in Federal Court until its dossier for the biosimilar version of a reference product is on file with the FDA. Patent litigation takes approximately three to four years to reach a final non-appealable decision, whereas FDA review takes only 12 months. Therefore, biosimilars obtain FDA approval at a time when the court litigation is commencing. Under the current system, biosimilar companies are faced with the choice of either putting their product on hold while waiting for a final resolution from the court, or launching “at risk” in the face of claims of patent infringement. Given the typical shelf-life of biosimilar drugs, which is usually 3 years or less, storing product manufactured for launch, while litigation is ongoing, is not an option. As a result, this places biosimilar competitors in a difficult predicament, because the consequence of being found to infringe a valid patent includes an injunction or an order to pay the lost profits of the branded drug company, which can run into hundreds of millions of dollars.

The issue of delayed standing is more harmful to biosimilars than to small molecule generic drugs. Generic competitors typically target to launch upon expiry of the primary patent, which is usually considered to be the strongest patent in the portfolio and is typically the first patent to expire. The court litigation serves to resolve the validity and infringement of the follow-on patents that expire later than the basic product patent. Given the development of a generic drug takes approximately three years, generic drug companies can submit their dossier to the FDA and obtain standing to litigate the patents in ample time before the primary patent expires. In other words, generic companies have sufficient time to litigate the follow-on secondary patents to a final resolution prior to their target launch date. In contrast, as mentioned above, the development of a biosimilar takes approximately eight years,²³ meaning that access to a legal resolution on the patents is also delayed. The long development time for biosimilars provides time for branded drug companies to build up their patent portfolios and grow excessively large patent thickets, which go unchecked until a competitor completes its biosimilar development.

As of today, no biosimilar company has been able to litigate their case to a final decision prior to product patent expiry, the ideal target launch date.

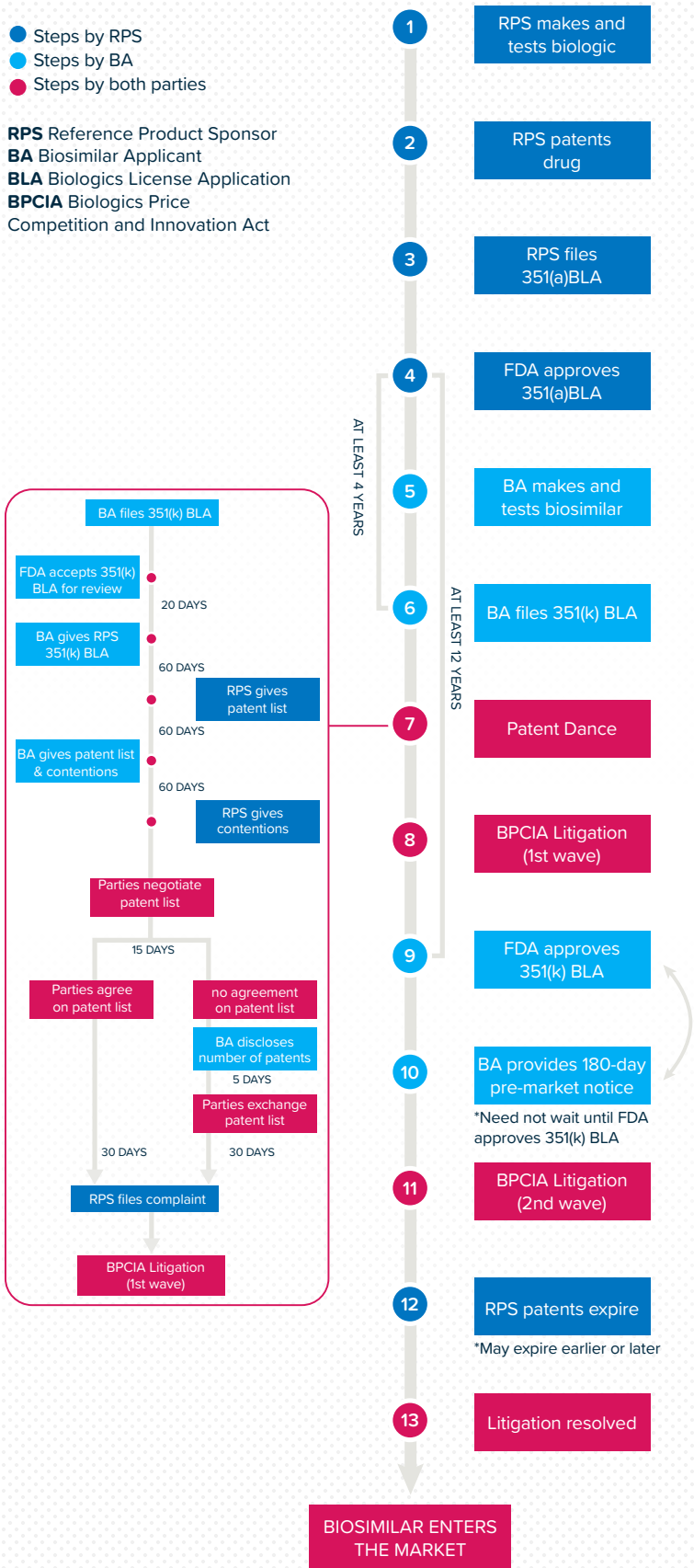
The time it takes to obtain a court resolution due to delayed standing and having to navigate a dense thicket of patents often leads to patent settlements. A settlement is an agreement between the branded drug company and the biosimilar company that provides the biosimilar with a license to market the product. This overcomes the issue of patents that have been too costly or uncertain to litigate. The larger the patent thicket, the greater the uncertainty, and the greater the leverage that the branded drug company has over the biosimilar company in settlement negotiations to insist on later market entry dates or other concessions.

The Patent Dance

The BPCIA provides a pre-litigation framework, which is colloquially referred to as the “patent dance.” The goal of the patent dance is to guide the reference product sponsor (the branded biologic manufacturer) and the biosimilar applicant to agree upon a list of patents that will be subject to patent litigation. The patent dance takes place before court action is initiated and consists of correspondence between the reference product sponsor and the biosimilar applicant. The procedure also includes fixed deadlines for the parties to share and respond to certain information. If the patent dance is carried out to completion, the process takes approximately eight months (Figure 3).

FIGURE 3: PATENT DANCE TIMELINE

SOURCE: FISH LAW FIRM²⁴



After a biosimilar applicant submits its aBLA to the FDA, the FDA carries out formalities and checks on the dossier, which takes approximately 2 months. Upon successful completion of these checks, the FDA formally accepts the aBLA for review. This triggers the first step of the patent dance, which is for the biosimilar applicant to share, within 20 days, its aBLA with the reference product sponsor (the branded biologic company) and the process used to manufacture the biosimilar.²⁵ Sharing the aBLA allows the sponsor to assess which patents, if any, would be infringed by the biosimilar applicant.²⁶ The information the applicant provides is subject to strict confidentiality rules, enforceable by injunction.²⁷

Once the required information is provided by the biosimilar applicant, within 60 days the reference product sponsor “shall provide” to the applicant “a list of patents” for which it believes it could assert an infringement claim.²⁸ The reference product sponsor must also identify any patents on the list that it would be willing to license.²⁹ This raises the question of whether the “licensing option” of the patent dance system incentivizes branded drugmakers to actively develop patent thickets knowing that they can license any patents they may not be using for their product and which a biosimilar may not wish to litigate.

On receiving the sponsor’s patent list, the biosimilar applicant may provide a list of patents that the applicant believes are relevant, but that the sponsor omitted from its own list.³⁰ The applicant also provides to the sponsor reasons why it could not be held liable for infringing the relevant patents.³¹ The applicant may argue that the relevant patents are invalid, unenforceable, or not infringed, or the applicant may agree not to market the biosimilar until a particular patent has expired. At this point, the applicant must also respond to the sponsor’s offers to license particular patents.³² Then, within 60 days of receiving the applicant’s responses, the sponsor provides to the applicant its own arguments concerning infringement, enforceability, and validity as to each relevant patent.³³

Upon completion of the patent dance, the BPCIA channels the parties into two phases of patent litigation. In the first phase, the parties collaborate to identify patents that they would like to litigate immediately. The second phase is triggered by the applicant’s 180 day notice of commercial marketing and involves any patents that were included in the parties’ lists but not litigated in the first phase, plus any new patents that have been granted since.

In June 2017, the Supreme Court brought greater certainty to two key issues relating to the “patent dance” under BPCIA.³⁴ First, the Court held that where a biosimilar applicant declines to provide its aBLA to the reference product sponsor, the only remedy available to the patent owner is to bring a patent infringement lawsuit. In other words, the Court held that the patent dance is optional. Second, the Court held that a biosimilar applicant may provide its mandatory 180-day notice of commercial marketing at any time and need not wait until FDA has approved its application. This allows the biosimilar applicant to skip the dance and trigger commencement of litigation immediately, if desired.

One advantage of skipping the patent dance is to save time. As explained above, patent litigation takes approximately three to four years to reach a final non-appealable decision, whereas FDA review takes only 12 months. Therefore, biosimilars obtain FDA approval at a time when the court litigation is just getting started, which is further delayed by the addition of an eight month patent dance. If, on the rare occasion, there are only a few well-known patents, then the patent dance may not be particularly valuable to a biosimilar applicant and eliminating the patent dance could speed up the resolution of litigation.

On the other hand, there are several advantages for biosimilar applicants to comply with the patent dance, which is why many choose to do so. The advantages include the fact that once the list of patents

is received from the reference product sponsor, this becomes the universe of patents to be litigated. No additional patents may be added to the litigation unless new patents are granted after the list was shared. Having a concrete universe of patents provides some clarity for the biosimilar applicant and allows them to assess the prospects of their case and the risk of launching prior to resolution from the court. In practice, the patent dance tends to narrow the scope of the potential litigation prior to the initiation of the lawsuit. Another advantage of the patent dance is that it compels the reference product sponsor to bring suit within 30 days of completion of the patent dance; they cannot wait until the biosimilar launches at risk to sue them.

Some biosimilar applicants have opted for a so-called “abbreviated patent dance” where they cut the dance short after receiving the patent list from the reference product sponsor. However, one down-side to this is that it remains un-tested in court whether the patent list continues to be binding if the patent dance is not completed.

The Purple Book

The Purple Book, like the FDA Orange Book for small-molecule products, is a database that contains information about all the FDA approved (licensed) biological products, including approved biosimilar and interchangeable products.³⁵

Information included in the Purple Book includes:

- The date on which the biological product was licensed under the PHS Act;
- Whether the FDA has determined a biological product licensed under the PHS Act as a biosimilar or interchangeable with a reference biological product;
- The expiration date of any market exclusivity applicable for a biological product, including first interchangeable biologic product exclusivity;
- Patent information for certain licensed biological products required under the Purple Book Continuity Act 2020 (also known as the Biological Product Patent Transparency Act) of the Consolidated Appropriations Act of 2021. Under the Act, within 30 days of disclosing a patent list to a biosimilar applicant, the reference product sponsor must submit the list to the FDA for inclusion in the Purple Book.

Unlike the Orange Book, the posting requirements for patents on the Purple Book are only triggered when there is a first biosimilar applicant and the patent dance is initiated. Also, unlike the Orange Book, there is no obligation for the reference product sponsor to keep the patent information in the Purple Book current. It is important to note that despite the requirement to now provide the FDA with the patent listings exchanged as part of the patent dance, the patent data may not include every patent that the reference product sponsor has in its patent thicket. It is possible that the reference product sponsor could assert additional or different patents against another biosimilar competitor. Accordingly, subsequent biosimilar applicants should not solely rely on the Purple Book when assessing potential patent barriers.³⁶

Looking Ahead

Although the BPCIA is just over a decade old, the past 5 years in particular have highlighted the many flaws of the system. The current regulatory framework favors the drugmaker of the original reference product, especially when it comes to the issue of patents and interchangeability status. Despite the words “price competition” featuring in the title of the Act, the BPCIA, as designed and how it currently works in practice, is antithetical to competition and the early entry of more affordable biosimilars. The evidence to date shows that branded biologic drugmakers are using the patent system and patent thickets to stretch out their market monopoly without any competition to 20 years or more, which on average is six years more than for small molecule drugs.³⁷ Between the BPCIA framework and the patent system, the current regulatory environment is incentivizing the practice of patent thicketing around biologic drugs. As a result, there is a need for major policy fixes in order to ensure the entry of biosimilar competition can happen much earlier to reduce the ever growing price increases. Some of the solutions for addressing the patent thicket problem around biologic drugs can be found in our latest Blueprint.³⁸

About I-MAK

The Initiative for Medicines, Access and Knowledge (I-MAK) is a 501(c)(3) organization with a mission to build a more just and equitable medicines system. Our framework integrates deep analytical research to influence policy, education to activate change, and partnerships to drive solutions. We bring decades of private-sector expertise and an evidence-based approach to this mission. Our work spans 50 countries and we collaborate with patients, drug manufacturers, patent offices, community leaders, public health professionals, policymakers, scientists, economists, and more across the globe. I-MAK’s work on structural change in the patent system is featured regularly in the national and global press, as our data is cited in Congressional hearings and Committee reports. I-MAK is committed to evidence-based research and education that will benefit American families and help lower drug prices, and therefore have never taken funding from the pharmaceutical industry.

LEARN MORE ABOUT I-MAK’S WORK AT WWW.I-MAK.ORG



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Endnotes

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²¹ Fan C. Comparison of Humira biosimilars in the US and Europe. *Pharmaceutical Technology*. March 24, 2023. Accessed March 11, 2024. <https://www.pharmaceutical-technology.com/pricing-and-market-access/comparison-humira-biosimilars/>

²² 2021 report of the Economic Survey. American Intellectual Property Law Association. 2021. Accessed March 11, 2024. <https://www.aipla.org/detail/journal-issue/2021-report-of-the-economic-survey>

²³ Supra FN.8

²⁴ Wang C, McGlynn KE. How biosimilars are approved and litigated: Patent dance timeline. *Fish & Richardson*. August 12, 2020. Accessed March 11, 2024. <https://www.fr.com/insights/ip-law-essentials/how-biosimilars-approved-litigated-patent-dance-timeline/>

²⁵ 42 U.S.C. § 262(l)(2)(a)

²⁶ 42 U.S.C § 262(l)(1)(D)

²⁷ 42 U.S.C. § 262(l)(1)(H)

²⁸ 42 U.S.C. § 262(l)(3)(A)(i)

²⁹ 42 U.S.C. § 262(l)(3)(A)(ii).

³⁰ 42 U.S.C. § 262(l)(3)(B)(i)

³¹ 42 U.S.C. § 262(l)(3)(B)(ii)

³² 42 U.S.C. § 262(l)(3)(B)(iii)

³³ 42 U.S.C. § 262(l)(3)(C)

³⁴ Sandoz Inc. v. Amgen Inc., 773 F.3d 1274 (Fed. Cir. 2014)

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³⁶ Kalousi-Tatum M, Berman JR. Revamped purple book offers greater patent transparency for biologics. Morgan Lewis. May 18, 2021. Accessed March 11, 2024. <https://www.morganlewis.com/blogs/asprescribed/2021/05/revamped-purple-book-offers-greater-patent-transparency-for-biologics>.

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