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Biologics Price Competition & Innovation Act (BPCIA): Litigation Considerations

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A Practice Note discussing strategic considerations when litigating a biosimilars case under the Biologics Price Competition & Innovation Act (BPCIA). It explains biologics, discusses the history and intent behind the BPCIA, the Food & Drug Administration's (FDA)'s Purple Book, biosimilar FDA regulatory approval and exclusivities, strategic pre-litigation and litigation considerations for both reference product sponsors and biosimilar applicants, and antitrust considerations in BPCIA settlements.

The Biologics Price Competition & Innovation Act (BPCIA) was enacted on March 23, 2010 as part of the Patient Protection and Affordable Care Act (ACA) (Pub. L. No. 111-148) and encoded under 42 U.S.C. § 262. Modeled after the Hatch-Waxman Act, which governs the approval process of generic, small-molecule pharmaceuticals, the BPCIA seeks to both encourage competition and promote innovation in the field of biologics. It facilitates the approval and market entry of lower-cost versions of previously approved biologic medicines, biosimilars, while also providing exclusivity incentives for the research and development of pioneer medicines.

This Note discusses:

- The BPCIA's relevant background.
- The Food & Drug Administration's (FDA) "Purple Book."
- FDA approval of abbreviated biologics license applications (aBLA), including:
  - biosimilar safety and efficacy considerations;
  - regulatory exclusivities; and
  - FDA guidance highlights.
- Strategic pre-litigation strategies for:
  - reference product sponsors (RPS); and
  - biosimilar applicants (BA).
- The BPCIA's "patent dance" (first-wave patent litigation).
- Notice of commercial marketing (second-wave patent litigation).
- Declaratory judgment actions.
- BPCIA-specific litigation considerations.
- Antitrust considerations in BPCIA settlements.

For a full overview of the BPCIA, see Practice Note, Biosimilars and the Biologics Price Competition and Innovation Act (BPCIA): Overview.

BPCIA at A Glance

The BPCIA amends the Public Health Services Act (PHSA), which is the primary law regulating biologic drugs. Under the PHSA, a "biological product" means any of the following when it is used for the prevention, treatment, or cure of a disease or condition:

Virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound) (42 U.S.C. § 262(i)(1)).

The BPCIA's amendments to the PHSA:

- Create an abbreviated pathway for medicines that are biosimilar to, or interchangeable with, a previously-approved biologic medicine ("reference product" or "RP") to gain FDA approval through submission of an aBLA (42 U.S.C. § 262(k); see FDA Approval of aBLAs).
- Provide an exclusivity period for RPs under 42 U.S.C. § 262(k)(7), which states that approval of a biosimilar license application "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)" (see Regulatory Exclusivities for Biosimilars).

- Specify the process, commonly referred to as the "patent dance," through which patent disputes regarding biologics are resolved (42 U.S.C. § 262(l); see The Patent Dance and First Wave Patent Litigation).
- Expand the definition of "biological products" to include any "protein (except any chemically synthesized polypeptide)" (42 U.S.C. § 262(i)(1) (see 2019 Amendments)).

Biosimilar and Interchangeable Defined

The BPCIA provides that an aBLA can be submitted for either a "biosimilar" or an "interchangeable" product:

- **Biosimilar** products have no meaningful clinical differences in safety, purity, and potency from an RP. They are "highly similar to the reference product not withstanding minor differences in clinically inactive components" (42 U.S.C. § 262(i)(2)).
- **Interchangeable** products are not clinically the same as an RP but:
  - are expected to produce the same clinical result as the RP;
  - have a similar safety and efficacy profile to the RP; and
  - may be substituted for the RP without the intervention of the healthcare provider who prescribed the RP (42 U.S.C. § 262(i)(3)).

BPCIA Players

The BPCIA creates a roadmap for branded RP sponsors (RPSs) and biosimilar applicants (BAs) to navigate the regulatory and patent litigation landscape.

Reference Product Sponsor (RPS)

An RPS may file an original biologics license application (BLA) under PHSA § 351(a) (42 U.S.C. §262(a)). A Section 351(a) BLA is the traditional pathway for the approval of biologics and innovator biologics. The RPS must show that its product is safe, pure, and potent based on de novo data.

Biosimilar Applicant (BA)

The BA files a Section 351(k) aBLA for a biosimilar or interchangeable product (42 U.S.C. §262(k)). The aBLA must demonstrate biosimilarity (or interchangeability) to an RP (42 U.S.C. § 262(i)(2)).

An aBLA for a biosimilar may include fewer than all the RP's licensed indications, but an aBLA for an interchangeable must demonstrate that the interchangeable product is expected to produce the same clinical results as the RP for all licensed indications.

Once the BA files the aBLA, it may provide a copy of the aBLA and information about the biosimilar's manufacturing process to the RPS to initiate the BPCIA's resolution mechanism for patent disputes (see The Patent Dance and First Wave Patent Litigation). Regardless of whether it chooses to initiate the patent dance, the BA must provide a notice of commercial marketing (NCM) to the RPS at least 180 days prior to the first commercial marketing of its biosimilar product (see Notice of Commercial Marketing and Second-Wave Patent Litigation).

The Purple Book

The FDA publishes a list of biological products licensed under the PHSA. This publication is formally titled *Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluation*, but is commonly known as the Purple Book. The Purple Book:

- Contains information on FDA-licensed RPs, biosimilars, and interchangeables.
- Lists RP exclusivities and evaluations of biosimilarity or interchangeability.
- Provides information about the patents that RPSs consider potentially infringed by biosimilar or interchangeable products for which aBLAs have been filed.

For more on the Purple Book and its listings, see Practice Note, Biosimilars and the Biologics Price Competition and Innovation Act (BPCIA): Overview: Purple Book.

History of the Purple Book

The Purple Book combines information from two previous lists:

- A list of drugs approved by the Center for Drug Evaluation and Research (CDER).
- A list of biological products approved by the Center for Biologics Evaluation and Research (CBER).

On February 24, 2020, the FDA released the searchable-online Purple Book database replacing both the CDER and CBER lists. Before then, some biological products were approved through the New Drug Application (NDA) process, and the FDA listed information related to those approved products (including patents claimed to covering the products) in its Orange Book.

On March 23, 2020, the FDA removed products it deemed biological products approved through the NDA process from the Orange Book database and transitioned those listings to the Purple Book database.

On December 27, 2020, the Biological Product Patent Transparency Act was enacted, requiring RPSs to submit any patent list disclosed to BAs pursuant to the patent dance (see The Patent Dance and First Wave Patent Litigation), along with the patent expiration dates, to the FDA within 30 days of providing that list to the BA (42 U.S.C. § 262(k), (l)(3)(A), and (l)(7)).

Scope of the Purple Book

Unlike the Orange Book's limited categories of patents that can be listed for drugs approved through the NDA process, the categories of patents subject to the patent dance and listed in the Purple Book are not limited. The Purple Book may include patents that claim methods of manufacture or purification, starting materials, and expression vectors, for example.

The FDA is required to:

- List the patent information it receives from RPSs in the Purple Book.
- Update Purple Book listings every 30 days.

(See 42 U.S.C. § 262(k), (l)(3)(A), and (l)(7).)

In June 2021, the FDA began making publicly available the patent lists it received from RPSs under the Biological Product Patent Transparency Act.

FDA Approval of aBLAs

FDA approval of an aBLA for a **biosimilar** product is contingent on the BA demonstrating that the product:

- Acts through the same mechanism for the condition for which the RP is approved (to the extent such a mechanism is known for the RP).
- The condition or conditions of use for which the aBLA seeks approval have been previously approved for the RP.
- The route of administration, dosage form, and strength of the biosimilar are the same as those of the RP.
- The facility in which the biosimilar is manufactured and handled meets standards designed to assure its continued safety, purity, and potency.

(42 U.S.C. § 262(k)(2)(A)(i).)

FDA approval of an aBLA for an **interchangeable** product is contingent on the BA demonstrating that the product:

- Meets all the criteria for a biosimilar product.
- Is expected to produce the same clinical result as the RP.
- Presents no increased safety risk or diminished efficacy if a patient alternates or switches between it and the RP compared to using the RP alone.

(42 U.S.C. § 262(k)(4).)

Biosimilar Safety and Efficacy Considerations for FDA Approval

Biologics are typically produced in bacteria, yeast, or mammalian cells. Therefore, small changes to the manufacturing process (such as changes in cell culture media or modifications to the purification process) may alter the function or immunogenicity of the product. When an RPS submits a Section 351(a) BLA, it must include extensive data and information regarding the product's safety, purity, and potency, including its method of manufacture (see Clinical and Non-Clinical Data).

When submitting an aBLA, a BA must demonstrate that its biosimilar or interchangeable product has no clinically meaningful differences in safety, purity, and potency from the FDA-approved RP. In practice, BAs submit comparative data and bridging studies to demonstrate the high degree of similarity between their product and the RP, and aBLAs must include comparative clinical and non-clinical data for approval. For an FDA presentation on biosimilar and interchangeable approval, see Overview of the Regulatory Framework and FDA's Guidance for the Development and Approval of Biosimilar and Interchangeable Products in the US.

Clinical and Non-Clinical Data

Clinical data includes:

- Immunogenicity.
- Pharmacokinetics.
- Pharmacodynamics.

Non-clinical data includes:

- Structural and functional analyses.
- In vitro comparisons of reference product and biosimilar characteristics.

The nature and scope of clinical trials depends on the residual uncertainty about biosimilarity that remains after the biosimilar product undergoes structural and functional analyses. Therefore, the FDA recommends that BAs use a "stepwise approach." At each step, the

BA and the FDA evaluate the residual uncertainty about biosimilarity and determine the necessary additional data that the BA should collect and submit for aBLA approval.

In addition to meeting all the criteria for a biosimilar (see FDA Approval of aBLAs), an aBLA for an interchangeable product must also demonstrate that:

- The product is expected to produce the same clinical result as the RP.
- Switching between it and the RP will not increase safety concerns or decrease efficacy.

The FDA expects an aBLA for an interchangeable product to include analyses that compare the mechanism of action of the interchangeable product with the mechanism of action of the RP as well as data from one or more clinical switching studies.

Regulatory Exclusivities for Biosimilars

The BPCIA provides exclusivity incentives for BAs to receive approval for the first interchangeable for an RP.

Under 42 U.S.C. § 262(k)(6), when the first interchangeable aBLA is approved for an RP, the FDA will not approve subsequent interchangeable products until the earliest of:

- One year after the commercial marketing of the first interchangeable product.
- 18 months after a district court's final judgement, or dismissal, in a patent dance litigation.
- 42 months after the approval of the first interchangeable product if there is patent dance litigation, or 18 months after approval if there is no patent dance litigation.

FDA Guidance Highlights

The FDA's guidance on approval of aBLAs for biosimilar and interchangeable products continues to evolve. In Questions and Answers on Biosimilar Development and the BPCIA Act Guidance for Industry (Rev. 2, September 2021), the FDA provides guidance on:

- **Formulation differences.** A proposed biosimilar may have a different formulation than the RP (such as where the RP contains human serum albumin but the biosimilar does not).
- **Drug delivery device or container differences.** Some design differences may be acceptable (such as when the biosimilar is dosed in a prefilled syringe or autoinjector while the RP is dosed in a vial). The BA cannot, however, seek approval for a biosimilar with a route of administration, dosage form, strength, or indication that has not been previously approved for the RP.
- **Label differences.** The proposed biosimilar may obtain licensure for fewer than all indications for which the RP is authorized (a so-called carve-out label).

RPS Considerations: How to Prepare for aBLAs

Once a Section 351(a) BLA for an RP is approved, the RPS should assume that the RP will face biosimilar competition and assess asserting any patents covering its RP in litigation.

Strategic Assessment of the RPS's Patent Portfolio

There are several types of patent claims that may be asserted against aBLA filers. The RPS should strategically assess and develop a patent portfolio comprising a variety of patent claims, such as:

- Therapeutic agents.
- Methods of use.
- Formulations.
- Cell lines.
- Cell culture medium.
- Drug delivery systems.
- Methods of manufacture.
- Purification methods.
- Starting materials.
- Expression vectors.
- Technology platforms.
- Delivery devices.
- Packaging.

The strategic assessment of this patent portfolio must take into account not only the likelihood that the claims will read on a biosimilar product but the strength of each patent to withstand a challenge to its validity and enforceability through both:

- Federal court patent infringement litigation.
- Proceedings at the U.S. Patent and Trademark Office (USPTO) through, for example, an *inter partes* review

(IPR). For more on IPR and other PTAB proceedings, see PTAB Proceedings Toolkit.

Once the applicable patents are identified, the RPS should create an internal Purple Book listing, which will require the calculation of expiration dates, including any patent term adjustments and potential patent term extensions.

Exclusively Licensed Third-Party Patents

If the RP is covered by exclusively licensed third-party patents, the RPS must review the licenses for:

- Notification provisions.
- Licensee obligations to enforce the licensed patents against potential infringers.
- Licensor obligations to participate and cooperate in litigation.
- Any confidentiality issues that may be raised by listing the licensed patents in the Purple Book pursuant to the patent dance.
- Any confidentiality issues that may be raised by providing access to the 351(a) BLA to a BA.

Designating a Point Person

BPCIA cases are often complex, expensive, and lengthy. A key step in managing them effectively is identifying in-house counsel familiar with the patent portfolio for the RP, who will act as the point person for managing the substantive and the procedural aspects of the patent dance and any resulting litigation.

The point person should be familiar with:

- The information needed to assess possible infringement by biosimilar products.
- The invention story behind the key patents covering the RP as well as any discussions with the inventors of key patents.
- The prosecution history of the key patents, including any concerns regarding validity and enforceability.

BA Considerations: Preparing for Patent Assertion by the RPS

To successfully launch a biosimilar or interchangeable product, BAs must assume that there may be competition from other such products and that the RPS will assert patents protecting its RP. Early investigation and analysis of the patents likely to be asserted against the biosimilar product are a key step in preparing for a BPCIA litigation. This analysis should include:

- Freedom-to-operate and landscape searches for patents owned by or licensed to the RPS.
- Assessment of the strengths and weaknesses of any invalidity, enforceability, and non-infringement positions.
- Identification of any design-around options for process claims.

The BA should also assess its potential to:

- **Be first to market**, by assessing if it is feasible to:
  - seek exclusivity for a first-approved interchangeable product; and
  - produce all information required by the FDA for approval ahead of competitors to gain greater market share by being first to market.
- **Avoid an injunction.** Permanent injunctions are mandatory, under certain limited conditions, including that they apply only to proposed biosimilar products that have not yet been approved due to the RP's statutory 12-year exclusivity period (35 U.S.C. § 271(e)(4)(D)). Permanent injunctions are also available under 35 U.S.C. § 283 if the RPS demonstrates that the four *eBay* factors warrant injunctive relief:
  - the RPS has suffered or will suffer irreparable injury or harm;
  - legal remedies are insufficient to compensate the RPS's injury;
  - the balance of hardships favors the RPS; and
  - the public would not be hurt by an injunction.

  (See *eBay Inc. v. MercExchange L.L.C.*, 547 U.S. 388, 391 (2006).)
- **Avoid multiple waves of litigation.** The BA can potentially:
  - force all listed patents to be litigated at the same time by providing the notice of commercial marketing (NCM) required under § 262(l)(8)(B) to the RPS early in the patent dance (see Notice of Commercial Marketing and Second-Wave Patent Litigation); and
  - limit litigation by submitting an aBLA for fewer than all of the RP's licensed indications.

The Patent Dance and First-Wave Patent Litigation

The BPCIA provides a detailed process for RPSs and BAs to resolve patent disputes. It involves a stepwise exchange

of information, commonly referred to as the patent dance. By engaging in the patent dance, the parties:

- Identify all the patents to be asserted in infringement litigation.
- Create an artificial act of infringement by the BA filing an aBLA, similar to the artificial act of infringement by the submission of an abbreviated NDA under the Hatch-Waxman Act (see Practice Note, Patent Litigation: Hatch-Waxman Infringement).
- Provide public notice of the patents that the RPS is likely to assert against BAs by listing the identified patents in the Purple Book.

Patent Dance Timeline

Once the FDA accepts the aBLA:

- Within 20 days after receiving the notice of acceptance, the BA, if participating in the patent dance, provides a copy of the aBLA and manufacturing information to the RPS (42 U.S.C. § 262(l)(2)(A)).
- Within 60 days after receiving a copy of the aBLA, the RPS must provide the BA with a list of potentially infringed patents (Section 3(A) List) (42 U.S.C. § 262(l)(3)(A)(i)).
- The RPS must supplement its Section 3(A) List with relevant newly issued or licensed patents within 30 days of issuance or licensing. Any newly issued licensed patents listed on the RPS's supplement will be subject to the second wave of patent litigation (42 U.S.C. § 262(l)(7) (see Notice of Commercial Marketing and Second-Wave Patent Litigation).
- The RPS cannot assert patents that it does not include in its Section 3(A) List and it cannot later seek discovery to determine whether other patents should be asserted. The RPS should therefore list all patents that it believes that it may reasonably assert against the biosimilar or interchangeable product (see *Amgen Inc. v. Hospira, Inc.*, 866 F.3d 1355, 1362-63 (Fed. Cir. 2017)).

  The RPS must identify any patents on the Section 3(A) List that it is willing to license to the BA (42 U.S.C. § 262(l)(3)(A)(ii)).

Within 60 days after receiving the RPS's Section 3(A) List, the BA:

- May provide its own list of patents that the BA believes that the RPS could reasonably assert against the biosimilar or interchangeable product (42 U.S.C. § 262(l)(3)(B)(i)).
- Must provide a response to each patent on the RPS's list that includes:
  - a detailed statement of invalidity, unenforceability, or non-infringement for each relevant claim; or
  - a statement that the BA will not commercially market its product before patent expiration (42 U.S.C. § 262(l)(3)(B)(ii)(I)-(II)).
- Must respond to the RPS's licensing offer, if any (42 U.S.C. § 262(l)(3)(B)(iii)).

Within 60 days after receiving the information detailed in § 262(l)(3)(B) from the BA, the RPS must respond to each of the BA's invalidity, unenforceability, and non-infringement assertions (42 U.S.C. § 262(l)(3)(C)). It is unclear whether the BA may waive its right to receive a detailed statement, for example to accelerate the patent dance (see *Amgen v. Sandoz*, 877 F.3d 1315 (Fed. Cir. 2017); Notice of Commercial Marketing and Second-Wave Patent Litigation).

Immediately after the BA receives the §262(l)(3)(C) Statement, the parties should begin to negotiate the patents to be litigated. If within **15 days** after the BA receives the §262(l)(3)(C) detailed statement from the RPS, the parties:

- **Agree** on the patents to litigate:
  - the RPS must file its patent infringement complaint and initiate the first-wave litigation within 30 days (42 U.S.C. § 262(l)(6)(A)-(B)); and
  - the BA must then notify the FDA that a suit has been filed within 30 days of litigation being initiated (42 U.S.C. § 262(l)(6)(C)).
- **Do not agree** on the patents to be litigated:
  - the BA must notify the RPS of the number of patents that the BA believes should be litigated (42 U.S.C. § 262(l)(5)(A));
  - within 5 days, the parties must simultaneously exchange the lists of patents to be litigated (42 U.S.C. § 262(l)(5)(B)(i)). The number of patents on the RPS's list cannot exceed the number of patents on the BA's list unless the BA has zero patents on its list, in which case the RPS may list one patent (42 U.S.C. § 262(l)(5)(B)(ii)); and
  - the BA must notify the FDA that a suit has been filed within 30 days of litigation being initiated (42 U.S.C. § 262(l)(6)(C)).

If the RPS does not sue the BA within 30 days after the scope of the litigation has been negotiated under § 262(l)(4) or § 262(l)(6), the RPS can no longer sue for an injunction and its sole and exclusive remedy for infringement of a listed patent is a reasonable royalty.

Whether or Not to Dance

The BA may find it advantageous not to engage in the patent dance, especially because the RPS's remedies are rather limited if a BA refuses to initiate or fully participate in this process. The RPS cannot seek an injunction to force compliance with § 262(l) disclosure requirements, nor are state law remedies likely available due to preemption. The RPS's only remedy is bringing a declaratory judgment action pursuant to § 262(l)(9)(C), which entitles the RPS to immediately seek a "declaration of infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product" if a BA does not comply with the patent dance disclosure requirements (see Declaratory Judgment Actions).

It is unclear whether an RPS has the right to bring a declaratory judgment action in the event that a BA produces an aBLA without providing additional manufacturing information (see *Genentech, Inc. v. Amgen Inc*, No. 17-165 (GMS), D.I. 16, (D. Del. Mar. 1, 2017)).

Discovery and Confidentiality Advantages

If a BA produces a partial aBLA (or does not produce manufacturing information other than the information contained in the aBLA) and, as a result, the RPS does not include patents in its Section 3(A) List, the RPS cannot seek discovery during subsequent BPCIA litigation about the possibility of these other patents being infringed. It also cannot assert unlisted patents in the second-wave litigation. (See *Amgen v. Hospira*, 866 F.3d at 1362-63.)

By not participating in the patent dance, the BA avoids the requirement of providing a detailed statement pursuant to § 262(l)(3)(B), and the BA may decide that it prefers to keep its noninfringement, invalidity, and unenforceability positions confidential until they must be disclosed during litigation. Although these positions are not binding and can be amended in litigation, they are considered party admissions.

A BA must also consider that its aBLA and manufacturing information may be discoverable to other BAs who are in litigation with the RPS relating to the same RP or overlapping patents. Although protective orders can limit the use of this information and the individuals to whom it is made available, some BAs may object to disclosing such sensitive information earlier than necessary.

Notice of Commercial Marketing and Second-Wave Patent Litigation

An RPS may decide to assert only a subset of its applicable patents during the first wave and keep the rest for when a second-wave litigation is triggered by the BA's provision of an NCM.

The BA must provide to the RPS an NCM at least 180 days before the date of the first commercial marketing of its biosimilar product (§ 262(l)(8)(A)). Immediately after the receipt of a NCM, the RPS may seek a preliminary injunction prohibiting the commercial launch of the BA's product until the court rules on any patents disclosed by the RPS or the BA in their §262(l)(3) lists or in the RPS's §262(l)(7) supplement that were not the subject of first-wave litigation (§262(l)(8)(B)).

Notably, a BA:

- Must provide an NCM pursuant to §262(l)(8)(A) regardless of whether it provides the RPS with a copy of its aBLA and manufacturing information pursuant to §262(l)(2)(A) (*Amgen Inc. v. Apotex Inc.*, 827 F.3d 1052, 1061 (Fed. Cir. 2016), cert. denied, 137 S. Ct. 591 (2016)).
- Need not wait until FDA approval to provide NCM. Rather, the BA "may provide notice either before or after receiving FDA approval" (*Sandoz v. Amgen Inc.*, 137 S. Ct. 1664, 1668 (2017)).
- Who provided an NCM "need not provide another notice for each supplemental application concerning the same biological product" (*Genentech, Inc. v. Immunex Rhode Island Corp.*, No. 2019-2155, D.I. 91 Fed. Cir. Jul. 6, 2020)).

A declaratory judgment action is not an exclusive remedy for failure to provide an NCM in violation of the §262(l)(8)(A). The Federal Circuit found that Section "(9)(B) does not make declaratory judgments exclusive and thereby wipes out the remedies expressly provided for in 35 U.S.C. 271(e)(4)." (*Amgen Inc. v. Apotex Inc.*, 827 F.3d 1052, 1065, n4 (Fed. Cir. 2016).)

Declaratory Judgment Actions

The BPCIA expressly limits the ability of the parties to seek declaratory judgment during the patent dance (§ 262(l)(9)).

If the BA:

- Timely produces the aBLA and additional manufacturing information pursuant to § 262(l)(2)(A), neither party can file a declaratory judgment action before the NCM is provided.
- Abandons the patent dance after the RPS discloses its Section 3(A) List, only the RPS can file a declaratory judgment action on any of the listed patents.
- Does not initiate the patent dance, only the RPS can file a declaratory judgment action for "any patent that

claims the biological product or use of the biological product."

BPCIA-Specific Litigation Considerations

BPCIA litigation is similar to Hatch-Waxman litigation in many respects. However, although the BPCIA's conforming amendments to 35 U.S.C. § 271(e)(4) have brought the remedies available through this litigation in line with remedies available for infringement in other patent cases, there are several elements that distinguish BPCIA cases.

Notable differences between BPCIA and Hatch-Waxman litigation include, for example:

- **A large number of asserted patents.** RPSs may assert more patents against the biosimilar product than typically asserted in Hatch-Waxman litigation. Some courts have therefore ordered RPSs to limit the number of asserted claims, but RPSs often challenge the constitutionality of these orders (see, for example, *Genentech, Inc. v. Amgen Inc.*, Nos. 17-1407-GMS, 17-1471-GMS (Scheduling Order) (D. Del. Apr. 13, 2018); *Genentech, Inc. v. Pfizer, Inc.*, No. 17-1672-CFC (Scheduling Order) (D. Del. Nov. 1, 2018)).
- **Parallel litigations.** Multiple parallel litigations involving the same RP or the same patents are frequent and may lead to the production of competitors' patent dance disclosures (*AbbVie Inc. v. Boehringer Ingelheim Int'l GmbH*, 17-01065-MSG (D. Del.)).
- **Preliminary injunction expedited discovery.** The BA's NCM may trigger an RPS's motion for a preliminary injunction and the need for expedited discovery in view of the fast-track schedule that these motions entail. Section 262(l)(8)(C) directs the parties to "reasonably cooperate" on any expedited discovery necessary for the preliminary injunction motion. Through this expedited process, parties may only be entitled to discovery that is directly related to the motion (see, for example, *Genentech, Inc. v. Celltrion, Inc.*, 18-cv-00574, D.I. 128 (D.N.J. Sep. 10, 2018)).
- **More limited safe harbor protections.** The safe harbor provision in 35 U.S.C. § 271(e)(1) protects a BA from liability for activities that may be considered infringing if carried out in order to gain FDA approval. The safe harbor provision is not a blanket protection for the BA's activities, however, and is to be analyzed on a batch-by-batch basis. The parties may need to engage in discovery regarding the intent and the reasons for the BA's manufacture and use of each batch of the biosimilar or interchangeable product. If a BA's activity is found not to be protected by the safe harbor provision, the BA may be liable for monetary damages, most likely in the form of reasonable royalties. (*Amgen*, 944 F.3d at 1337.)
- **Patent eligibility issues.** Patent claims directed to products of nature or diagnostic methods may be at issue in the litigation because BPCIA litigation involves biologic products. The validity of these claims may be challenged for covering unpatentable subject matter under 35 U.S.C. § 101.
- **Discovery issues.** BPCIA litigation often involves methods of manufacture patents, which may present unique discovery considerations. BAs may contract all or part of the manufacturing process with third parties, including foreign manufacturers, which may potentially carry infringement liability under 35 U.S.C. § 271(g) for a product manufactured abroad by a process patented in the United States. Fact discovery directed specifically at the BA's manufacturing process may be required and may involve foreign discovery.
- **Infringement proofs challenges.** Infringement proof can be challenging because it is often possible to design around the claimed process in whole or in part.
- **Section 112 validity challenges.** Claims directed to a protein's functional characteristics, including its method of action in the body, may be susceptible to invalidity challenges under 35 U.S.C. § 112 for lack of sufficient written description or enablement or for indefiniteness.

Antitrust Considerations in BPCIA Settlements

The pharmaceutical industry has been subject to a growing number of antitrust investigations that scrutinize settlements between branded and generic pharmaceutical companies. Similar scrutiny can be expected for BPCIA settlements involving RPSs and BAs. For example, a February 2020 Joint Statement of the FDA and the Federal Trade Commission (FTC) Regarding a Collaboration to Advance Competition in the Biologic Marketplace notes that the FTC will review patent settlement agreements involving biologics, including biosimilars, for antitrust violations pursuant to the Patient Right to Know Drug Prices Act, Public Law No. 115-263 (Oct. 10, 2018), codified at 21 U.S.C. § 355.

Also, under the Medicare Modernization Act, as amended in 2018, an RSP-BA agreement must be filed with the FTC and the U.S. Department of Justice if it pertains

the manufacture, marketing, or sale of either an RP or a biosimilar product.

So-called "pay for delay" or "reverse payment" settlements have drawn significant antitrust scrutiny in the Hatch-Waxman context and they are likely to be treated with suspicion in the BPCIA context as well. In these settlements, the branded pharmaceutical company pays the generic pharmaceutical company for delaying the entry of the generic product into the market. These settlements have been accused of being anticompetitive because they can prolong the branded company's monopoly, increase the profits of both the branded and the generic companies, and potentially harm consumers by maintaining high prices. In *FTC v. Actavis*, the Supreme Court found that reverse payments were unusual and created a "reason for concern that settlements taking this form tend to have significant adverse effects on competition." Although the Court declined to find reverse payment settlements to be unlawful per se, the Actavis decision paved the way to multiple successful court challenges of these settlements and these decisions are likely to hold sway in cases where BPCIA settlements are challenged.

For more information regarding antitrust concerns with settlements, see Practice Note, Reverse Payment Settlement Agreements and Actavis Case Tracker.