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Client Alert

Life Sciences and Healthcare

APRIL 7, 2021

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# "Purple Book" Patent Listing Under Biological Product Patent Transparency Act: What is Required, and What to Expect?

The Biological Product Patent Transparency Act ("BPPT")[1] – tucked into Congress's omnibus spending bill ("Consolidated Appropriations Act," H.R. 133, Pub. L. No. 116-260) signed into law on December 27, 2020 – is the first-ever provision requiring public listing in the FDA's "Purple Book" of certain patents associated with biologic drug products (*e.g.*, monoclonal antibody products and other protein drug products). See the text of the BPPT here.

The BPPT sidestepped some of the more controversial approaches to biologics patent listing, by piggybacking off of the patent lists that reference product sponsors (*i.e.*, biologics innovators) are already required to exchange with biosimilar applicants[2] under the "patent dance" provisions of the Biologics Price Competition and Innovation Act ("BPCIA").[3] But, we still expect that the publication of such patent lists – which were previously maintained under strict confidentiality[4] – may impact litigation, regulatory and commercial strategy for reference product sponsors and biosimilars alike.

Read on for our analysis and insights, and please stay tuned as we keep track of future developments.

## RECENT HISTORY OF BIOLOGICS PATENT LISTING PROPOSALS

In contrast to small molecule drugs, for which applicants are required to submit patent information with their New Drug Applications ("NDAs") and certain supplements,[5] as well as within 30 days following FDA approval[6] and/or new patent issuance,[7] an applicant seeking licensure of a biological product[8] need not submit any patent information in its original Biologics License Application ("BLA") or subsequent submissions (*i.e.*, supplements).[9] Also, unlike small molecule drugs, for which the approvability of Abbreviated New Drug Applications ("ANDAs") and "§ 505(b)(2)" NDAs is impacted by the status of listed patents for the

reference NDA drug product,[10] the approvability of abbreviated BLAs ("aBLAs") for biosimilar products is presently delinked from the various processes for resolving patent disputes. Biosimilar applicants have a choice whether to engage in the so-called "patent dance" to identify and litigate a defined list of patents[11]; and there had not been a process for including patents in the FDA's "Purple Book" database[12] of licensed biological products (such as there is for small molecule reference listed drugs in the FDA's "Orange Book"[13]).

Much has been made of the role played by patents in the development of biological products, and in the development and marketing of biosimilar and interchangeable products particularly. Regulators and others have commented that intellectual property considerations can affect biosimilar development and launch and can alter the BPCIA's balance between innovation and competition.[14] FDA has gone to considerable lengths to accommodate changes to labeling sought by applicants in light of patent litigation.[15] FTC also has said that it intends to review patent settlement agreements involving biosimilars for potential antitrust violations.[16]

Over the last few years, there have been several legislative proposals aimed at enhancing public disclosure of patents related to biologic reference products, with stated goals including encouraging use of the "patent dance" and stimulating biosimilar development and market competition overall. Some proposals have been more aggressive than others: threatening antitrust enforcement for "patent thickets,"[17] limiting the numbers of patents that could be asserted against biosimilar applicants in the BPCIA "patent dance,"[18] penalizing untimely disclosure of biologic patents by strictly limiting enforcement,[19] or even creating a presumption of patent invalidity for subsequent patents (*e.g.*, "formulation" or "method of treatment" patents claiming innovations beyond the biological product itself).[20]

## "PURPLE BOOK" PATENT LISTING UNDER THE BIOLOGICAL PRODUCT PATENT TRANSPARENCY ACT

Ultimately, from among these various proposals, Congress in December 2020 passed the BPPT, which added section 351(k)(9) to the Public Health Service ("PHS") Act (42 U.S.C. § 262(k)(9)).

Prior to the BPPT, reference product sponsors and biosimilars would exchange patent lists confidentially, under strict limitations on disclosure, as an early step in the patent dance[21] (assuming the biosimilar elected to initiate the patent dance by disclosing its aBLA and other information specified by statute).[22] Now, however, the BPPT sets up a framework for FDA to receive and publish at least the reference product sponsor's lists of patents in the Purple Book.

Under the BPCIA, if a biosimilar sponsor chooses to engage in the "patent dance," the reference product sponsor will provide an "initial list" ("(*l*)(3)(A)" or "3A" list) to that biosimilar applicant,[23] along with a "supplemental list" ("(*l*)(7)" list) of any additional patents that issued after the time for the "(*l*)(3)(A)" list. These lists identify the specific patents that the reference product sponsor believes may be infringed by the biosimilar, should that biosimilar's aBLA be approved and its product marketed.

In section 351(k)(9) of the PHS Act, added by the BPPT and presently in effect, a reference product sponsor that provides a biosimilar applicant with an (*l*)(3)(A) initial patent list or (*l*)(7) supplemental patent list must now submit those lists to FDA, within 30 days after exchange with the biosimilar applicant.[24] In addition, beginning on June 25, 2021, FDA is required to make those lists (along with any revisions or updates) public on the Purple Book website.

FDA has published some practical information regarding submission of patent lists on its Purple Book "FAQs" website.[25]

## POTENTIAL STRATEGIC IMPLICATIONS FOR BIOLOGICS INNOVATORS AND BIOSIMILARS

It remains to be seen how the new requirements of the BPPT will impact the strategic approach of reference product sponsors and biosimilars. But, as follows, it is possible that these patent publication requirements will add new strategic considerations for both regarding product development, the "patent dance" and litigation, and commercial strategies.

**Potential Impact on Reference Product Sponsor Strategy?** Reference product sponsors will need to consider the strategic implications of an early public disclosure of their full "3A" list of patents for potential assertion against the first biosimilar applicant to engage in the "patent dance."

For example, reference product sponsors might consider whether the public disclosure of their "3A" patent list for a first biosimilar applicant may cause certain future biosimilar applicants to withhold their "2A" disclosures of aBLAs and other manufacturing information – if such future biosimilars are satisfied with the patent list information in the Purple Book, and do not otherwise wish to participate in the "patent dance." Reference product sponsors will also have to consider the possibility that an early public disclosure of a "3A" patent list might enable second or subsequent biosimilars (at earlier stages of development) to "design around" certain patents listed in the Purple Book, or to bring early challenges against such patents before the Patent Trial and Appeal Board ("PTAB").

Accordingly, while reference product sponsors might have previously included the broadest possible set of patents in each "3A" list, they might now think about strategically omitting certain patents that might be challenging to assert against the first biosimilar applicant, but potentially could provide stronger protection against future biosimilar applicants. Because the BPCIA limits the enforcement of patents not included on a reference product sponsor's "3A" list,[26] however, a reference product sponsor strategy of providing circumscribed "3A" lists would have to be used cautiously.

**Potential Impact on Biosimilar Applicant Strategy?** As with reference product sponsors, biosimilar applicants may engage in strategic maneuvering around the early publication of the first "3A" list in the Purple Book. First biosimilar applicants (*i.e.*, those developing biosimilar versions of previously-unchallenged reference products) now might choose not to engage in the patent dance at all, as they face the burden of developing their biosimilar products without access to the "3A" list (which comes late in the regulatory process under the patent dance and after that biosimilar's product development is essentially complete), and they may consider publication of the first "3A" list to create a "free-riding" advantage for second or subsequent biosimilar applicants relying on the same reference product.

If a first biosimilar applicant does engage in the patent dance, resulting in a "3A" list that is published in the Purple Book, some second or subsequent biosimilar applicants also might now choose not to participate in the "patent dance" at all, if their primary incentive to do so was to obtain the reference product sponsor's patent list. But that strategy could be a risky one, since there may be certain patents (*e.g.*, manufacturing process; formulation patents) that were not previously listed, *e.g.*, because a first biosimilar applicant that had squarely designed around them, or for strategic reasons on the part of the reference product sponsor (as described above); whereas a subsequent applicant might infringe those unlisted patents. And, there are other reasons a biosimilar applicant, whether first or later, might want to engage in part or all of the "patent dance," versus ceding control of litigation to the reference product sponsor.

Some biosimilar applicants might also consider whether there is strategic benefit from "waiting in the wings," and letting a first biosimilar applicant draw the reference product sponsor's "3A" list out into the Purple Book. Such public patent information might guide later biosimilar product development (*e.g.*, efforts to "design around" listed patents); and, as noted above, might in some cases lessen the litigation burden by avoiding the "patent dance." On the other hand, there can be substantial commercial advantages to being the first FDA-approved biosimilar to enter the market in competition with the reference product sponsor – and so a strategy of waiting comes with some business risk.

Likewise, as noted above, the Purple Book will not capture patents that, *e.g.*, the reference product sponsor did not include on the "3A" list for the first biosimilar applicant, but might use against later challengers.

## POTENTIAL IMPACT OF ADDITIONAL PROVISIONS IN THE BPPT?

In addition to its primary function of bringing patent listing into the Purple Book, the BPPT also added two provisions to the PHS Act that may impact strategic thinking for both reference product sponsors and biosimilar applicants.

First, the BPPT requires FDA to publish ongoing periods of reference product exclusivity (under section 351(k)(7) of the PHS Act, 42 U.S.C. § 262(k)(7)) and first interchangeable exclusivity (under section 351(k)(6) of the PHS Act, 42 U.S.C. § 262(k)(6)) – but only if "the Secretary has determined such biological product to be eligible."[27] Reference product sponsors that believe they are eligible for such periods of exclusivity, as well as potential biosimilar applicants who believe reference products are no longer protected by exclusivity, might begin to petition FDA to make such determinations so that the relevant periods of exclusivity will be required to be included in the Purple Book, forestalling confusion about availability of reference products for biosimilar competition. This is particularly true in the context of potential applicability of "umbrella exclusivity," under which a biological product that would not be eligible for a new period of exclusivity (*e.g.*, a new strength of a previously-approved product)[28] may nevertheless be protected for the duration of an ongoing period of exclusivity for the original reference product. To date, FDA has been silent on the topic of umbrella exclusivity for biological products, but perhaps the BPPT requirement will result in some light being shed on the subject.

Second, the BPPT instructs FDA to exclude or remove from the Purple Book any biological product for which the license has been revoked or suspended for reasons of safety, purity, or potency (safety or effectiveness).[29] FDA will have to grapple with a process for making such determinations for biological products. Until then, this provision may raise questions regarding the availability of such products to be relied on as reference products, as well as when, and for what stated reason, a license-holder may wish to initiate revocation of its license.[30]

## CONCLUSION

At the end of the day, it remains to be seen whether and how the new regime of "Purple Book" patent listing under the BPPT will impact the strategic approaches of biologics innovators and biosimilars to litigation and regulatory and commercial strategy. Given the tight listing timelines under the BPPT, though, we should start to see data points pertaining to these questions in relatively short order.

Reference product sponsors and biosimilars alike should also keep an eye out for the FDA's forthcoming solicitation of public comments "regarding the type of information, if any, that should be added to or removed from the list required"[31] under the BPPT by new section 351(k)(9)(A) of the PHS Act.

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[1] Biological Product Patent Transparency Act ("BPPT"), Pub. L. No. 116-260 (H.R. 133, 116th Congress), Div. BB, Section 325. The core language of the BPPT was originally introduced to the House in March 2019 as the "Purple Book Continuity Act" (H.R. 1520, 116th Congress), before it was placed in the year-end omnibus bill.

[2] "Biosimilar," as used throughout, includes "interchangeable" biosimilars. *See* Public Health Service ("PHS") Act § 351(k)(4) (42 U.S.C. § 262(k)(4)).

[3] *See* Biologics Price Competition and Innovation Act ("BPCIA"), Pub. L. No. 111-148, §§ 7001 *et seq*., adding sections 351(k), (*l*) of the PHS Act (42 U.S.C. §§ 262(k), (*l*)).

[4] *See* PHS Act § 351(*l*)(1) (42 U.S.C. § 262(*l*)(1)).

[5] 21 U.S.C. § 355(b)(1)(A)(viii); 21 C.F.R. § 314.53.

[6] 21 U.S.C. § 355(c)(2); 21 C.F.R. § 314.53(c)(2)(ii).

[7] 21 U.S.C. § 355(c)(2); 21 C.F.R. § 314.53(d)(3).

[8] Section 351(i)(1) of the PHS Act (42 U.S.C. § 262(i)(1)) defines "biological product" to mean "a 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), applicable to the prevention, treatment, or cure of a disease or condition of human beings." FDA regulations further define the term "protein" as "any alpha amino acid polymer with a specific, defined sequence that is greater than 40 amino acids in size." 21 C.F.R. § 600.3(h)(6). Notably, as of March 23, 2020, insulins and other biologic products that historically had been approved using NDAs were "transitioned" to licensure as BLAs. *See* BPCIA § 7002(e)(4).

[9] 21 C.F.R. § 601.2.

[10] *See generally* Sections 505(c) and 505(j) of the Federal Food, Drug & Cosmetic Act (21 U.S.C. §§ 355(c), (j)).

[11] *See Sandoz Inc.* v. *Amgen Inc.*, 137 S. Ct. 1664, 1674 (2017).

[12] FDA, Purple Book Database of Licensed Biological Products (*accessible at* https://purplebooksearch.fda.gov).

[13] FDA, Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations (*accessible at* https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm).

[14] *See* FDA's Biosimilars Action Plan at 1 ("After patents or other exclusivities expire on these novel products, prices can fall dramatically once follow-on products are available, potentially lowering costs for patients and payors and expanding access to these innovations.") (*available at* https://www.fda.gov/media/114574/download); *see also* Sean McGowan, *5 years of biosimilars in the US: what have we learned?*, PharmaPhorum (Jan. 29, 2020) (*available at* https://pharmaphorum.com/views-analysis-market-access/5-years-of-biosimilars-in-the-us-what-have-we-learned/).

[15] FDA, Draft Guidance for Industry, *Biosimilars and Interchangeable Biosimilars: Licensure for Fewer Than All Conditions of Use for Which the Reference Product Has Been Licensed* (February 2020) (*available at* https://www.fda.gov/media/134932/download).

[16] *See* Fostering Biologic Competition (opening remarks as prepared for delivery*), Remarks of Joe Simons, Chairman (March 9, 2020) (*available at* https://www.ftc.gov/system/files/documents/public_statements/1568645/simons_-_biosimilars_workshop_opening_remarks_3-9-20.pdf).

[17] The Affordable Prescriptions for Patients Act of 2019 (as introduced to the Senate on May 9, 2019) (*available at* https://www.congress.gov/bill/116th-congress/senate-bill/1416/text/is).

[18] The Affordable Prescriptions for Patients Act of 2019 (as reported to the Senate on June 28, 2019) (*available at* https://www.congress.gov/bill/116th-congress/senate-bill/1416/text/rs); Affordable Prescriptions for Patients Through Improvements to Patent Litigation Act (*available at* https://www.congress.gov/bill/116th-congress/house-bill/3991/text).

[19] Biologic Patent Transparency Act of 2019 (*available at* https://www.congress.gov/bill/116th-congress/senate-bill/659/text).

[20] Terminating the Extension of Rights Misappropriated (TERM) Act (*available at* https://www.congress.gov/bill/116th-congress/house-bill/3199/text); No Combination Drug Patents Act (*available at* https://www.ipwatchdog.com/wp-content/uploads/2019/06/DRAFT-Patent-Bill2.pdf).

[21] *See* PHS Act § 351(*l*)(1) (42 U.S.C. § 262(*l*)(1)).

[22] *See* PHS Act § 351(*l*)(2)(A) (42 U.S.C. § 262(*l*)(2)(A)); *supra* n.11.

[23] *See* PHS Act §§ 351(*l*)(3)(A), (*l*)(7) (42 U.S.C. §§ 262(*l*)(3)(A), (*l*)(7)).

[24] *See* PHS Act § 351(k)(9)(A)(iii) (42 U.S.C. § 262(k)(9)(A)(iii)).

[25] *See* FDA, Purple Book FAQs (*accessible at* https://purplebooksearch.fda.gov/faqs).

[26] *See, e.g.*, PHS Act § 351(*l*)(6) (42 U.S.C. § 262(*l*)(6)) (defining scope of "first-wave" suit); PHS Act § 351 (*l*)(9)(B) (42 U.S.C. § 262(*l*)(9)(B)) (defining scope of declaratory judgment action if biosimilar applicant only partially completes patent dance).

[27] *See* PHS Act § 351(k)(9)(A)(iv) (42 U.S.C. § 262(k)(9)(A)(iv)).

[28] *See* PHS Act § 351(k)(7)(C) (42 U.S.C. § 262(k)(7)(C)).

[29] See PHS Act § 351(k)(9)(B) (42 U.S.C. § 262(k)(9)(B)).

[30] *See id.*; *see also* 21 C.F.R. § 601.5(a).

[31] *See* BPPT, § 325(b)(1).