

***COMMENTS SUBMITTED ON BEHALF OF THE
FOOD, DRUG AND COSMETIC LAW SECTION***

on

U.S. Food and Drug Administration Guidance

***Entitled “Implementation of the ‘Deemed to be a License’ Provision of the Biologics
Price Competition and Innovation Act of 2009”***

Docket No. FDA-2015-D-4750

Food, Drug and Cosmetic #5

May 13, 2016

As members of the New York State Bar Association Food, Drug and Cosmetic Law Section, we are pleased to offer these comments on the U.S. Food and Drug Administration’s (“FDA” or “Agency”) Guidance entitled “Implementation of the ‘Deemed to be a License’ Provision of the Biologics Price Competition and Innovation Act of 2009” issued on March 14, 2016 (“Guidance”).

A. Overarching Public Policy Concerns and Legislative Intent

We recognize and appreciate the challenges with implementing the “deemed to be a license” provision of the Biologics Price Competition and Innovation Act of 2009 (“BPCI Act”). However, we are concerned that FDA’s current interpretation of the BPCI Act, as set forth in the Guidance, may inadvertently discourage certain biosimilar product development by taking the path of administrative convenience. Congress has stated that the BPCI Act was intended to establish a biosimilar pathway that balances innovation and consumer interests.¹ We find it reasonable to deduce from this statement that Congress intended the BPCI Act to be interpreted to facilitate rather than stall biosimilar applications for reference products previously approved as new drug applications (“NDAs”) and now deemed to be biologics.

Notwithstanding the above, it is clear that Congress also intended to permanently change the means by which biological products gain approval for marketing. By amending the definition of “biological product” under the Public Health Service Act (“PHS Act”) to include “proteins (except any chemically synthesized polypeptide)” the legislature has unequivocally established that after March 23, 2020 such products would be required to submit a biologics license application (“BLA”) under section 351 of the PHS Act. However, as FDA has itself acknowledged, (i) some biological protein products have traditionally been approved under section 505 of the Food, Drug, and Cosmetic Act

¹ See BPCI Act section 7001(b).

(“FD&C Act”)², and (ii) Congress has authorized the continued submission of such applications for qualifying biological products up until March 23, 2020.³ The language of the BPCI Act, or rather lack thereof, gives FDA considerable discretion in implementing this new regulatory framework, and we believe that an alternative interpretation of the “deemed to be a license” provision of the BPCI Act would more effectively promote the public health.

B. Automatic Rejection of Biological Product Applications Filed under Section 505 of the FD&C Act on March 23, 2020

We believe that FDA construes the BPCI Act too narrowly in the Guidance by adopting the position that applications for biological products submitted under section 505 of the FD&C Act “will not be able to be approved” if they are still pending as of March 23, 2020, and will subsequently have to be withdrawn and resubmitted under section 351 of the PHS Act.⁴ The language of the BPCI Act is ambiguous and lacks any express provision that forces FDA to categorically reject all A/NDAs for biological products still pending as of March 23, 2020. We believe that the BPCI Act provides FDA with the authority to continue evaluating and approving, pending A/NDAs beyond March 23, 2020, as long as those applications were filed before such date, and that nothing in the FD&C Act, BPCI Act, or the PHS Act precludes the Agency from doing so. As mentioned above in section A, Congress has authorized qualifying biological products to continue submitting A/NDAs up until March 23, 2020.⁵ We do not believe that it was Congress’s intent to allow an A/NDA for a biological product to be submitted, for example, on March 20, 2020, as permitted under the BPCI Act, and then to be automatically rejected just several days later.

Allowing biological products to seek marketing approval under section 505 of the FD&C Act would encourage both biological and biosimilar product development because the 505 pathway of the FD&C Act may be less expensive and more predictable or faster than the 351 pathway of the PHS Act.⁶ FDA’s Guidance, on the other hand, encourages companies to either develop full BLAs (submitted as 351(a) applications under the PHS Act) or stall submission of biosimilars (submitted as 351(k) applications under the PHS Act) until after March 23, 2020. With respect to biosimilars in particular, FDA’s current interpretation leaves a potential biosimilar product with little choice as to which approval

² Applications submitted under section 505 of the FD&C Act are new drug applications and abbreviated new drug applications, which may be referred to throughout this document as “NDAs”, “ANDAs,” or collectively as “A/NDAs”.

³ See Guidance at 1 and 5, respectively.

⁴ See Guidance at 5:162 – 6:169.

⁵ See BPCI Act section 7002(e)(2).

⁶ For example, there are no pre-application user fees for A/NDAs as with 351(k) BLAs, and the section 505 pathway of the FD&C Act is better known to industry.

pathway to pursue. Any biosimilar product that does not have a reference product approved under section 351(a) of the PHS Act is forced to either (i) undertake the process of developing their own 351(a) BLA,⁷ or (ii) file an A/NDA application and run the risk of losing that investment on March 23, 2020, if their application has not been approved by such date. We believe that this dilemma will incentivize potential biosimilar product developers to hold off on submitting applications until after the March 23, 2020 date, so that they may take advantage of the 351(k) pathway under the PHS Act.

Since Congress wants to encourage the development of biosimilar products and not forestall them, we think that FDA should allow the approval of A/NDA applications for biological products beyond March 23, 2020, *so long as* such applications were submitted prior to such date. FDA's current interpretation may lead to lost investments (with the possible effect of raising biological product costs) and a delay in the availability of biosimilar options and competition. We believe this may have a short-term detrimental effect on the public health and may be inconsistent with Congress's intentions.

C. New Chemical Entity and New Clinical Data Exclusivity Rights

For the reasons described in section B above, we believe that FDA does not have to extinguish unexpired NDA-related exclusivity rights, as proposed in the Guidance.⁸ We do not recognize any potential conflicts if these A/NDA rights are allowed to co-exist with the rights granted to BLAs. Consistent with our comments in section B above, extinguishing these rights would create an incentive for industry to adopt product development programs suited for approval under the 351(k) pathway of the PHS Act, which may stall current biosimilar development programs and lead to increased costs and delays.

D. No Section 351 Innovator Exclusivity Rights to be Granted to A/NDAs

We believe that FDA has correctly decided to deny a new period of innovator exclusivity rights *beginning on* March 23, 2020 (otherwise known as the 12-year exclusivity period under section 351 of the PHS Act) to biological products that were originally approved as NDAs.⁹ We agree with FDA that some of these products have been on the market for decades and that nothing in the BPCI Act suggests that Congress intended to impede biosimilar or interchangeable product competition in several product classes until the year 2032.¹⁰ To provide such products an additional round of exclusivity

⁷ In order to take advantage of the abbreviated pathway provided for under section 351(k) of the PHS Act, a potential biosimilar product must have a "reference product" that was licensed under section 351(a) of the PHS Act. See section 351(i)(4) of the PHS Act for definition of "reference product." (42 U.S.C. § 262(i)(4)).

⁸ See Guidance at 6:182 – 6:192.

⁹ See Guidance at 6:201 – 7:218.

¹⁰ See Guidance at 7:210 – 7:214.

appears to be a windfall without purpose. We further believe that denying companies a new period of innovator exclusivity rights as of March 23, 2020 has the desirable effect of removing barriers to subsequent 351(k) applications, which would promote the public health via increased treatment options and price competition.

Nevertheless, we would like to present an alternative exclusivity interpretation that may help achieve public policy goals. Beginning the 12-year exclusivity countdown for biological products as of the date of NDA approval should be an option for FDA to consider, especially if the Agency ultimately chooses not to honor unexpired NDA-related exclusivity rights to biological products approved as NDAs as of March 23, 2020. In the case of biosimilars that currently do not have the 351(k) pathway under the PHS Act as an option for market approval, the potential chilling effect on product development is particularly acute as these product sponsors will either have to undertake the risk of filing an A/NDA that may not gain approval by March 23, 2020, and yet will not have any upside after such date since FDA's interpretation would remove both NDA and BLA-related exclusivity rights for this class of products, except for any orphan product exclusivity.¹¹ Providing for a more balanced set of incentives may encourage companies to submit their marketing applications under the lower cost and more familiar NDA route during the transition period, which will result in quicker product availability and less expense to be passed down to end users.

**E. Classification of 505(b)(2) and 505(j) Biologics as of March 23, 2020:
Biosimilar or Interchangeable?**

We have given some thought to how biological products approved under sections 505(b)(2) and 505(j) of the FD&C Act would be treated once they are “deemed to be” licensed under section 351 of the PHS Act on March 23, 2020. Specifically, the question has been raised as to whether FDA would consider these products to be biosimilars, or be granted the higher status of interchangeable.¹² FDA has indicated that the Agency will provide additional guidance regarding this matter,¹³ and perhaps an issue with this level of complexity deserves to be treated separately, but, nonetheless, we would like to take this opportunity to bring to FDA's attention our concern for market disruptions.

We are concerned that FDA may choose to not *automatically* grant interchangeable status to even previously-approved AB-rated NDA products deemed to be biologics.

¹¹ Again, as discussed in section B above, biosimilar product developers are being strongly incentivized to either develop a full BLA under section 351(a) of the PHS Act (along with the increased costs), or forestall development until after March 23, 2020 when the 351(k) pathway under the PHS Act becomes a legally permissible option.

¹² Interchangeable biologics may be substituted for innovator/reference products without the intervention of the health care provider who prescribed the innovator/reference product under section 351(i)(3) of the PHS Act.

¹³ See Guidance at footnote 7.

Products with the AB-rating are considered therapeutic equivalents and require a showing of “bioequivalence,” as defined under 21 C.F.R. § 320.1(e), in order to be granted this designation. The standard for “interchangeability” goes beyond the standard for AB-rating bioequivalence, because it requires the additional showing that switching between the biosimilar and the referenced product does not pose any increased risk in safety/diminished efficacy, as compared to using the referenced product without such alteration or switch.¹⁴ We think that FDA should consider adopting an incremental mechanism that would allow biologics approved under 505(b)(2) or 505(j), and possessing an AB-rating as of March 23, 2020, to submit additional data (perhaps from existing clinical studies), so that they can be further deemed “interchangeable” at the end of the transition period. We make this recommendation, because we believe that it would be in the best interest of the public health to avoid any period of time in which an AB-rated NDA-type biological product, formerly subject to automatic substitution (i.e., without physician intervention), to revert back to a status that would require intervention on behalf of the health care provider. The subsequent market disruptions that could occur after March 23, 2020 may create confusion and inefficiencies that would be detrimental to the public health.

We thank you for the opportunity to submit these comments and look forward to a continued discussion.

Submission by the New York State Bar Association Food, Drug and Cosmetic Law Section (Chair, Brian Malkin), Committee on Biologics Law (Committee Co-Chairs, Brian Malkin and Karl Williams).

¹⁴ Section 351(k)(4)(B) of the BPCI Act states that in order to be granted the status of interchangeable the sponsor must demonstrate that “for a biological product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.”