DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Ave
Building 51
Silver Spring, MD 20993

MAR 2 5 2015

Jeffrey Kushan
Sidley Austin LLP
1501 K Street NW
Washington, DC 20005

Re: Docket No. 2014-P-1771

Dear Mr. Kushan:

This letter responds to your citizen petition dated October 29, 2014 (Petition), requesting that the Food and Drug Administration (FDA or Agency) take action to ensure that biosimilar applicants will comply with section 351(l)(2)(A) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(l)(2)(A)). Specifically, the Petition requests that before accepting an application for review under section 351(k) of the PHS Act, FDA should require the application to include a certification that the applicant will timely comply with section 351(l)(2)(A) "by providing the reference product sponsor with a copy of the biosimilar application and information that describes the process(es) used to manufacture the biosimilar product that is the subject of that application."[1]

The Petition urges that this certification should be required for all future section 351(k) applications (biosimilar applications) that have not been accepted for review by FDA.[2] We have considered the requests in the Petition, as well as a November 25, 2014, comment submitted to the docket by Momenta (Momenta Comment). For the reasons described below, the Petition is denied.

I. BACKGROUND AND SUMMARY OF THE PETITION

The Biologics Price Competition and Innovation Act (BPCI Act) amended section 351(k) of the PHS Act to create an abbreviated licensure pathway for biological products shown to be biosimilar to an FDA-licensed biological reference product. Section 351(k) describes the requirements for a biosimilar application. Section 351(i) defines *biosimilarity* to mean "that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components" and that

[1] Petition at 1.
[2] Id.

"there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product." A biosimilar application must contain, among other things, information demonstrating that the biological product is biosimilar to a reference product based upon data derived from analytical, animal, and clinical studies, unless FDA determines that certain of those studies are unnecessary.[3]

Section 351(l) of the PHS Act, also added by the BPCI Act, describes certain procedures for exchanging patent information and identifying and resolving patent disputes involving biosimilar applications prior to licensure by FDA. According to section 351(l)(2)(A) of the PHS Act, a biosimilar applicant "shall provide to the reference product sponsor a copy of the application submitted [to FDA] under subsection (k), and such other information that describes the process or processes used to manufacture the biological product" not later than 20 days after receiving notice that the application was accepted for review by FDA. When the applicant provides a copy of its application to the reference product sponsor under section 351(l)(2)(A), a series of information exchanges and negotiations are triggered. These procedures, described in section 351(l)(3)-(l)(7), identify the patents that may be the subject of patent disputes between the two parties.

The Petition contends that the biosimilar application and manufacturing process disclosures described in section 351(l)(2)(A) are mandatory and urges FDA to require biosimilar applicants to certify that they will comply with these provisions. Specifically, the Petition points to language in section 351(l)(2)(A) that states that the applicant "*shall provide* to the reference product sponsor a copy of the application" and other information that describes the manufacturing process.[4] The Petition compares this language to the following paragraph in section 351(1)(2)(B) stating that the applicant "*may provide* to the reference product sponsor additional information requested by or on behalf of the reference product sponsor."[5] The Petition concludes that the use of "shall" indicates that disclosure of the application and manufacturing process is mandatory, in contrast to the "additional information" that "may" be provided.[6]

According to the Petition, the legislative history and policy goals of the BPCI Act support this "mandatory" interpretation.[7] The Petition asserts that Congress intended section 351(l) to enable the "timely identification of patent disputes" and resolution of those disputes before the "first commercialization of the approved biosimilar product."[8] The Petition contends that noncompliance with section 351(l)(2)(A) "vitiates the entire scheme that Congress intended" because, without disclosure, the reference product

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[3] See draft guidance for industry, *Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009*, available at: http://www.fda.gov/downloads/Drugs/Guidances/UCM273001.pdf.
[4] Petition at 2 and 7.
[5] Petition at 15 (comparing section 351(l)(2)(A) and (2)(B) of the PHS Act).
[6] Id.
[7] Petition at 9-10.
[8] Id. at 6.

sponsor may not know that a biosimilar application that relies on its product has been submitted, and as a result, the resolution of patent disputes will be thwarted or delayed.[9]

In contrast, the Momenta Comment contends that the patent exchange provisions in section 351(l) are not mandatory and that "there is no statutory basis for the requested FDA role via certification or enforcement with respect to the private patent exchange process under Section 351(l)."[10] According to Momenta, granting the Petition would be contrary to congressional intent. Specifically, Momenta contends that Congress intended the process described in 351(l):

- to separate FDA from the patent resolution process;
- to allow applicants to choose to engage in the patent exchange process at the time a 351(k) application is filed when appropriate;
- to provide reference biologic sponsors with procedural patent exchange protections should applicants elect to seek patent resolution early; and
- to allow for specific remedies should applicants elect not to seek patent resolution prior to commercial launch.[11]

II. DISCUSSION

The Petition urges FDA to require all future biosimilar applications to include a certification stating that the applicant will provide the reference product sponsor with "a copy of the application accepted for review and information that fully describes the manufacture of the proposed biosimilar product within 20 days after being informed by FDA that its biosimilar application has been accepted for review."[12]

Neither section 351(k) nor section 351(l) requires FDA to impose a certification requirement as part of the biosimilar review process. Section 351(l) describes procedures for information exchanges and the resolution of certain patent rights between the biosimilar applicant and the reference product sponsor. These procedures are parallel to, but separate from, the FDA review process. The BPCI Act generally does not describe any FDA involvement in monitoring or enforcing the information exchange by creating a certification process or otherwise.[13]

The lack of an explicit certification requirement in the BPCI Act is in contrast to provisions in the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) concerning patent certification for 505(b)(2) applications and abbreviated new drug applications (ANDAs). Section 505(b) requires new drug application sponsors to identify

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[9] Id. at 2-3.
[10] Momenta Comment at 2.
[11] Id. at 1.
[12] Petition at 5.
[13] The only express role for FDA described in section 351(l) of the PHS Act is in section 351(l)(6)(C). That subsection directs a biosimilar applicant to provide the Agency with notice and a copy of certain patent infringement complaints. It then directs FDA to publish notice that it received the complaint in the *Federal Register*.

certain patents for listing by FDA. Consistent with section 505(b)(1), FDA publishes these lists in its *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).[14] Sections 505(b)(2)(A) and 505(j)(2)(A)(vii) of the FD&C Act require 505(b)(2) and ANDA sponsors, respectively, to certify each patent submitted for the listed drug referenced in the Orange Book. Viewed against the explicit requirements under the FD&C Act, the Petition's contention that FDA "should" require a certification for biosimilar applications implicitly acknowledges that imposing such a requirement is a matter of regulatory discretion and not compelled under the PHS Act.[15]

Although the Petition contends[16] that the section 351(l)(2)(A) information exchange provisions are mandatory, another theory, described in the Momenta Comment, is that this information exchange is an optional method of resolving patent disputes that can be chosen by biosimilar applicants who seek patent certainty prior to launch.[17] These competing interpretations of section 351(l) are the subject of litigation that may clarify how section 351(l) should be interpreted.[18]

The Petition implicitly acknowledges that it seeks discretionary action from FDA based on one interpretation of a statutory provision that is the subject of litigation. In light of the ongoing litigation regarding interpretation of section 351(l) of the PHS Act, at this time, the Agency denies the request to exercise its discretion to require biosimilar applications to include a certification to FDA that the applicant will timely comply with section 351(l)(2)(A) of the PHS Act.[19]

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[14] The Orange Book is available on the Internet at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm.

[15] Petition at 19-22.

[16] Petition at 16.

[17] Momenta Comment at 2-3.

[18] See *Amgen, Inc. v. Sandoz, Inc.*, case no. 14-cv-04741 (N.D. Cal. Mar. 19, 2015) (order on cross motions for judgment on the pleadings and denying motion for a preliminary injunction) (finding that the BPCI Act "renders permissible a [biosimilar] applicant's decision not to provide its BLA and/or manufacturing information to the reference product sponsor, subject only to the consequences set forth in [section 351(l)(9)(C) of the PHS Act]"). At this time, it is unclear whether Amgen will appeal this decision. See also *Janssen BioTech, Inc. v. Celltrion Healthcare Co. Ltd.*, case no. 15-cv-10698 (D. Mass. filed Mar. 6, 2015).

[19] The Petition requests that FDA require a certification for all biosimilar applications that have not been accepted for review by FDA. FDA is generally prohibited from disclosing the filing status or other information concerning a pending BLA until the Agency has reached a final decision whether to approve or not approve the application. Therefore, our decision on the Petition does not address any specific biosimilar application. In addition, in light of our decision not to require a certification as a prerequisite to filing a biosimilar application at this time, we need not address the Petition's assertion that FDA can impose a certification requirement as a ministerial change, based on the Agency's interpretive or procedural authority (see Petition at 20-21).

III. CONCLUSION

For the reasons described in this response, the Petition is denied.

Sincerely,

Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research