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December 2, 2019

BY ELECTRONIC SUBMISSION

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD 20852

SUPPLEMENTAL CITIZEN PETITION – FDA 2019-P-5441

The undersigned ("Petitioner") submits this supplemental Citizen Petition pursuant to the Federal Food, Drug, and Cosmetic Act ("FDC Act") and in accordance with 21 C.F.R. §§ 10.25(a) and 10.30 with regard to the FDA-designated Reference Standard ("RS") for Polymyxin B Sulfate Injection, Eq 500,000 units base/vial. Though FDA has recently recognized an additional RS for Polymyxin B Sulfate Injection—ANDA 207322 held by Gland Pharma—Petitioner requests that the Food and Drug Administration ("FDA") designate an additional (or new) RS for Polymyxin B Sulfate Injection, EQ 500,000 units base/vial, to reflect FDA's policy of naming the "generic market leader" as the RS. Accordingly, Petitioner requests that FDA amend the *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book") to reflect ANDA 202766 as a RS for the drug.

I. ACTION REQUESTED

Petitioner requests that FDA designate ANDA 202766 (Polymyxin B Sulfate Injection, EQ 500,000 units base/vial) held by Xellia Pharmaceuticals APS as a RS for purposes of FDA evaluation of ANDAs for Polymyxin B Sulfate Injection, EQ 500,000 units base/vial.

II. STATEMENT OF GROUNDS

FDC Act § 505(j) allows the marketing of generic versions of previously approved drug products based on FDA approval of an ANDA. To obtain ANDA approval, the applicant must show, among other things, that with respect to a "listed drug" (i.e., a previously approved drug product), the generic drug product has the same active

ingredient(s) in the same strength, dosage form and route of administration, has essentially identical labeling, and is bioequivalent.

A "listed drug" includes a new drug product that has an effective approval under FDC Act § 505(j), that has not been withdrawn or suspended under FDC Act §§ 505(e)(1) through (5) or (j)(5), and that has not been withdrawn from sale for reasons of safety or effectiveness. See 21 C.F.R. § 314.3. Listed drugs are identified in FDA's Orange Book. An RLD is the listed drug identified by FDA as the drug product on which an ANDA applicant should rely in seeking approval of an application. Typically, the product designated by FDA as the "listed drug" also serves as the "reference standard," which must be used to conduct the in vivo bioequivalence testing required for FDA approval. However, where "FDA cannot select a drug product approved under section 505(c) of the FD&C Act as the reference standard," FDA may designate a different RS in the Orange Book. FDA, *Draft Guidance for Industry, Referencing Approved Drug Products in ANDA Submissions*, at 7-8 (Jan. 2017).

When a product designated as the RS is no longer marketed, FDA will select a new RS. *Id.* When FDA selects a new RS, it generally selects "the market leader based on units sold." FDA may also consider additional factors, such as RLD strengths. *Id.* As such, an ANDA applicant may request designation of a new RS when it "believes a reference standard other than the one selected by FDA is appropriate" through the submission of a citizen petition. *Id.* at 9. Indeed, FDA may designate a new RS in the Orange Book "when doing so will help to ensure that applications for generic drugs may be submitted and evaluated." *Id.* at 8.

At the time Petitioner submitted its original Citizen Petition, the designated RS—Polymyxin B Sulfate Injection, EQ 500,000 units base/vial (ANDA 060716)—was not commercially available. The sponsor of ANDA 060716 has since moved the product to the "Discontinued" section of the Orange Book. FDA subsequently designated ANDA 207322 held by Gland Pharma as the new RS for Polymyxin B Sulfate Injection, EQ 500,000 units base/vial. The selection of ANDA 207322, however, contravenes FDA's approach to selecting a new RS. As noted, a new RS is typically the market leader based on units sold or is selected on additional factors, such as available strengths. Based on our research, however, ***Gland ANDA 207322 is not the market leader nor is it available in strengths other than EQ 500,000 units base/vial.***

Instead, on information and belief, approximately 44% of the market for Polymyxin B Sulfate Injection, EQ 500,000 units base/vial, is filled with drug product marketed under Xellia ANDA 202766. As the market leader, Petitioner respectfully requests that FDA designate ANDA 202766 as an additional RS for Polymyxin B Sulfate Injection, EQ 500,000 units base/vial. Accordingly, the undersigned requests that FDA designate in the

Orange Book Polymyxin B Sulfate Injection, EQ 500,000 units base/vial, approved under ANDA 202766 as a new RS.

III. ENVIRONMENTAL IMPACT

An environmental assessment report on the action requested in this petition is not required under 21 C.F.R. § 25.31.

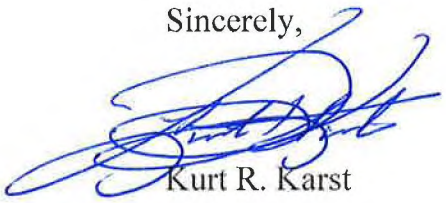
IV. ECONOMIC IMPACT

In accordance with 21 C.F.R. § 10.30(b), economic impact information is to be submitted only when requested by the Commissioner following review of the petition. Petitioner hereby commits to promptly provide this information, if so requested.

V. CERTIFICATION

Petitioner certifies that, to the best knowledge and belief of Petitioner, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which is unfavorable to the petition.

Sincerely,



Kurt R. Karst