Kurt R. Karst
Hyman, Phelps & McNamara P.C.
700 Thirteenth Street, N.W., Suite 1200
Washington, D.C. 20005-5929

July 31, 2020

Re: Docket No. FDA-2019-P-3903

Dear Mr. Karst:

This letter responds to your citizen petition received on August 16, 2019 (Petition) requesting that the Food and Drug Administration (FDA or Agency) designate lidocaine hydrochloride (HCl) oral solution, 2%, approved under abbreviated new drug application (ANDA) 040014, held by Hi-Tech Pharmacal Co. Inc., as a reference standard in the *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).[1]

We have carefully considered the Petition. For the reasons described below, your Petition is granted, and FDA will select lidocaine HCl oral solution 2%, held by Hi-Tech Pharmacal Co. Inc., as a new reference standard.

I. BACKGROUND

Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) allows the submission of an ANDA to market a generic version of a previously approved drug product. To obtain approval, the ANDA applicant must show, among other things, that the generic drug product (1) has the same active ingredient(s), dosage form, route of administration, strength, conditions of use, and, with certain exceptions, labeling as the listed drug; and (2) is bioequivalent to the listed drug.

A *listed drug* is a new drug product (1) that has been approved under section 505(c) of the FD&C Act for safety and effectiveness or under section 505(j) of the FD&C Act; (2) whose approval has not been withdrawn or suspended under section 505(e)(1) through (e)(5) or (j)(6) of the FD&C Act; and (3) has not been withdrawn from sale for what FDA has determined are reasons of safety or effectiveness.[2] Listed drug status is evidenced by the drug product's identification in the current edition of FDA's Orange Book as an approved drug.[3] A *reference*

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

[2] § 314.3(b) (21 CFR 314.3(b)).

[3] Id.

listed drug (RLD) is the listed drug identified by FDA as the drug product on which an applicant relies in seeking approval of its ANDA.[4] Generally, an RLD is a drug product approved in a new drug application (NDA) under section 505(c) of the FD&C Act.

A *reference standard* is the drug product selected by FDA that an applicant seeking approval of an ANDA must use in conducting an in vivo bioequivalence study required for approval.[5] FDA generally selects a single reference standard that ANDA applicants must use in any in vivo bioequivalence testing required for approval. A single reference standard ensures the greatest level of consistency between a generic drug and its RLD and among generic drugs. Generally, the RLD will be the drug product selected by the Agency as the reference standard for conducting in vivo bioequivalence testing.[6] In certain circumstances, however, the Agency may select a generic drug product as the reference standard for bioequivalence testing. For instance, if the RLD has been discontinued from marketing, FDA may select a therapeutically equivalent[7] generic drug product as the reference standard.[8]

II. DISCUSSION

In the Petition, you request that FDA designate lidocaine HCl oral solution 2%, approved under ANDA 040014 held by Hi-Tech Pharmacal Co. Inc., as a reference standard (Petition at 1). You state that "[t]he current RS, approved under Abbreviated New Drug Application ("ANDA") 040708, is commercially unavailable" (Petition at 1). You further state that:

> Lidocaine Hydrochloride Oral Solution, 2%, held by Hi-Tech Pharmaceuticals (ANDA 040014), appears to lead the U.S. market in terms of the number of units sold (as per IMS data), and should therefore be more readily accessible and more appropriate for RS designation.[9]

We have reviewed the information submitted in the docket, regulatory filings for the current reference standard, ANDA 040708, and third-party commercial data regarding lidocaine HCl oral solution 2%. Based on the information available to us, FDA concludes that ANDA 040708 held by Lannett Company, Inc., is no longer available in the market. Therefore, we agree that you have stated grounds for selecting a new reference standard.[10]

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[4] Id.

[5] See id.

[6] § 314.94(a)(3) (21 CFR 314.94(a)(3)).

[7] "Therapeutic equivalents are approved drug products that are pharmaceutical equivalents for which bioequivalence has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling" (§ 314.3(b)).

[8] *Abbreviated New Drug Applications and 505(b)(2) Applications*, 81 FR 69580, 69619 (Oct. 6, 2016).

[9] Petition at 1.

[10] See "Abbreviated New Drug Applications and 505(b)(2) Applications" 81 FR 69580 at 69619 (October 6, 2016).

In this instance, we have determined that it is appropriate to select lidocaine HCl oral solution 2%, approved under ANDA 040014 held by Hi-Tech Pharmacal Co. Inc., as the new reference standard. It is therapeutically equivalent to the RLD, and it is the current market leader as determined by FDA on the basis of commercial data.

III. CONCLUSION

For the reasons described in this response, the Petition is granted, and FDA will select lidocaine HCl oral solution 2%, approved under ANDA 040014 held by Hi-Tech Pharmacal Co. Inc., as a new reference standard.

Sincerely,

Douglas C. Throckmorton -S

Digitally signed by Douglas C. Throckmorton -S
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Date: 2020.07.31 11:25:00-04'00'

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