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July 1, 2020

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

Citizen Petition

The undersigned ("Petitioner") submits this 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 to request that the Food and Drug Administration ("FDA") designated Reference Listed Drugs ("RLDs") for Vancomycin HCl for Oral Solution, 250 mg (base)/5 mL and 500 mg (base)/6 mL. FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book") does not currently identify any RLD for Vancomycin HCl for Oral Solution, 250 mg (base)/5 mL and 500 mg (base)/ 6 mL, whether approved under a New Drug Application ("NDA") or Abbreviated NDA ("ANDA"). For this reason, Petitioner requests that FDA take action to maintain a pathway for ANDA submissions. Specifically, Petitioner requests that FDA designate both VANCOCIN (vancomycin HCl for Oral Solution), 250 mg (base)/5 mL and 500 mg (base)/6 mL, approved under ANDA 061667 as RLDs, and amend the Orange Book to reflect RLD status. The 500 mg (base)/6 mL and 250 mg (base)/5 mL strengths approved under ANDA 061667 were approved on July 24, 1972 (500 mg (base)/ 6 mL) and July 13, 1983 (250 mg (base)/5 mL), prior to the September 1984 enactment of the Hatch-Waxman Amendments, and may serve as RLDs for the drug products for the reasons discussed below.

I. ACTION REQUESTED

Petitioner requests that FDA designate both Vancomycin HCl for Oral Solution, 250 mg (base)/5 mL and 500 mg (base)/6 mL, approved under ANDA 061667 as RLDs[1] for purposes of FDA evaluation of ANDAs for Vancomycin HCl for Oral Solution, 250 mg (base)/5 mL and 500 mg (base)/6 mL. Petitioner further requests that, based on the prior status of ANDA 061667 as an RLD—and effectively as an NDA—FDA expedite a response to this petition so that an ANDA can be submitted to FDA.

II. STATEMENT OF GROUNDS

FDC Act § 505(j) allows the marketing of generic versions of previously approved drug products. 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—either as "RLD" in the electronic Orange Book, or with a "+" in the paper version of the publication—as the drug product on which an ANDA applicant should rely in seeking approval of an application. The product designated by FDA as the "Reference Standard" in the Orange Book—either as "RS" in the electronic Orange Book, or with a "!" in the paper version of the publication—must be used to conduct the in vivo bioequivalence testing required for

[1] Petitioner acknowledges that FDA does not typically assign RLD status to an ANDA. In this case, however, ANDA 061667, approved prior to the Hatch-Waxman Amendments, previously served as a RLD for ANDA submission and approval purposes.

FDA approval.[2] "If FDA has designated a listed drug as an RLD, but the potential applicant intends to refer to a different listed drug that is a pharmaceutical equivalent to the drug designated as an RLD, the potential applicant may submit a citizen petition under 21 CFR 10.25(a) and 10.30 to request that FDA designate that different listed drug as an additional RLD."[3]

As discussed in detail below, there is a sound basis for selecting both strengths under ANDA 061667 as RLDs.

The Orange Book ("Prescription Drug Product List" and "Discontinued Drug Product List" sections) does not currently identify Product No. 001 (500 mg (base)/6 mL) or Product No. 002 (250 mg (base)/5 mL) approved under ANDA 061667—or any Vancomycin HCl for Oral Solution, 250 mg (base)/5 mL or 500 mg (base)/6 mL, drug product—as a RLD or RS.

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[2] In 2017, FDA began to differentiate between RLD and RS Orange Book listings. See FDA, *Draft Guidance for Industry, Referencing Approved Drug Products in ANDA Submissions*, at 6-7 (Jan. 2017) ("Prior to 2017, the column in the electronic Orange Book labeled 'RLD', and the symbol in the printed version described as identifying the RLD, at times indicated the drug product FDA selected as the reference standard and at other times indicated the RLD, contributing to the confusion about which drug is the RLD and which drug is the reference standard. Starting in 2017, FDA intends to modify the Orange Book to clarify which listed drugs are RLDs and which are reference standards, and to indicate which products in the Discontinued Section may be referred to as an RLD.").

[3] FDA, *Draft Guidance for Industry, Referencing Approved Drug Products in ANDA Submissions*, at 5 (Jan. 2017). FDA also notes the following in the draft guidance:

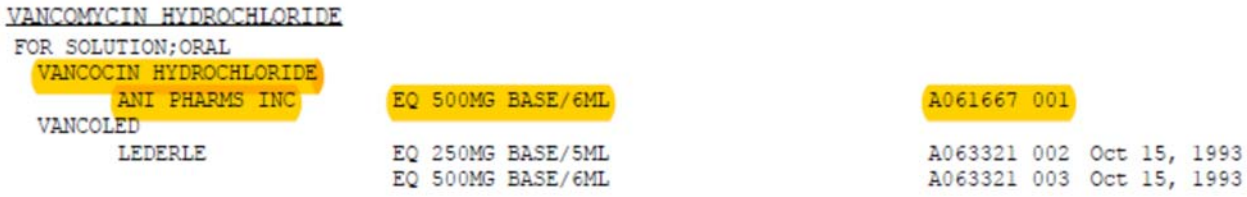
> The principles in this draft guidance focus on the appropriate identification of products referred to in ANDAs for generic drugs that are intended to duplicate listed drugs approved after enactment of the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub.L. 98-417), commonly referred to as the Hatch-Waxman Amendments. If an applicant is seeking approval of an ANDA that is intended to duplicate a listed drug approved prior to enactment of the Hatch-Waxman Amendments, the applicant may consult the Agency if it has questions regarding appropriate identification of products.

Id., at 4, n. 19 (Jan. 2017).

Prescription Drug Product List[4]

VANCOMYCIN HYDROCHLORIDE			
FOR SOLUTION;ORAL			
FIRVANQ KIT			
+!	RXMTM THERAPS LLC	EQ 25MG BASE/ML	N208910 001 Jan 26, 2018
+!		EQ 50MG BASE/ML	N208910 002 Jan 26, 2018
VANCOCIN HYDROCHLORIDE			
	ANI PHARMS INC	EQ 250MG BASE/5ML	A061667 002 Jul 13, 198

Discontinued Drug Product List[5]



VANCOMYCIN HYDROCHLORIDE			
FOR SOLUTION;ORAL			
VANCOCIN HYDROCHLORIDE			
	ANI PHARMS INC	EQ 500MG BASE/6ML	A061667 001
VANCOLED			
	LEDERLE	EQ 250MG BASE/5ML	A063321 002 Oct 15, 1993
		EQ 500MG BASE/6ML	A063321 003 Oct 15, 1993

Vancomycin HCl for Oral Solution, 500 mg (base)/6 mL, was approved under ANDA 061667 on July 24, 1972, and Vancomycin HCl for Oral Solution, 250 mg (base)/5 mL, was approved under ANDA 061667 on July 13, 1983. At that time, prior to the September 1984 enactment of the Hatch-Waxman Amendments and the creation of the contemporary ANDA, antibiotics were approved pursuant to FDC Act 507. In

[4] Orange Book, Prescription Drug Product List, at 3-440 (Mar. 20, 2020 Ed.).

[5] Orange Book, Discontinued Drug Product List, at 6-422 (Mar. 20, 2020 Ed.).

addition, FDC Act § 507 required FDA to publish regulations (i.e., antibiotic monographs) that set forth standards of identity, strength, quality, and purity for each marketed antibiotic drug.[6]

FDA explained the complex history of ANDA 061667 in the context of approving a supplement to the application in June 2019:

> The regulatory history of this application is convoluted and complex as it was originally filed in 1971 pursuant to the Form-6 procedures per [FDC Act § 507] i.e. under the abbreviated antibiotic application (AADA) pathway. Under the FDA Modernization Act of November 1997 ("FDAMA"), section 507 was repealed, and certain antibiotic applications were considered approved under 505(j); therefore, although ANDA 061667 was the first application approved for Vancomycin HCl for Oral Solution and considered the innovator product, it was ***not*** designated as an NDA, rather an ANDA.[7]

Although approved under an ANDA, FDA has nevertheless previously identified ANDA 061667 in the Orange Book as a RLD. Thus, for example, the 1998 Orange Book[8] shows the following:

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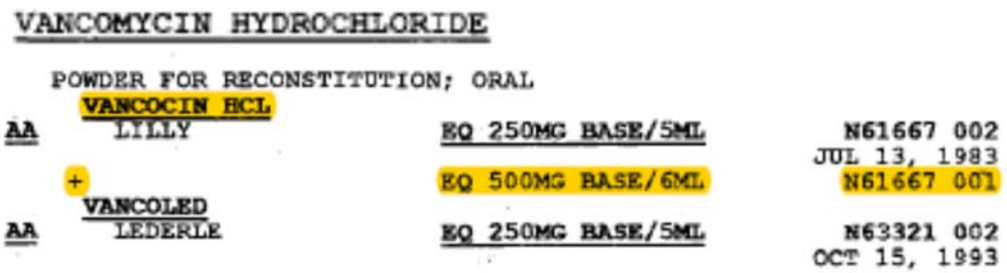
6 In September 1972, just two months after approving Vancomycin HCl for Oral Solution, 500 mg (base)/6 mL, under ANDA 061667, FDA amended the antibiotic monograph for vancomycin HCl to include a monograph for "Vancomycin hydrochloride for oral solution." See FDA, Vancomycin Hydrochloride and Vancomycin Hydrochloride for Oral Solution, 37 Fed. Reg. 20,325 (Sept. 29, 1972), available at https://www.govinfo.gov/content/pkg/FR-1972-09-29/pdf/FR-1972-09-29.pdf. The approval of Vancomycin HCl for Oral Solution, 500 mg (base)/6 mL, under ANDA 061667 appears to have been based, in part, on another vancomycin HCl approval: an NDA for Vancomycin HCl Injection. See National Academy of Sciences-National Research Council Drug Efficacy Study, Log No. 1828 (Vancocin HCI Vancomycin Hydrochloride Ampules USP) (original approval Oct. 23, 1958); see also Vancomycin HCl Injection, NDA 060180.

7 FDA, ANDA 061667/S-26, Division of Bioequivalence Review, at 3, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/061667Orig1s026.pdf (emphasis in original).

8 Orange Book, Prescription Drug Product List, at 3-322 (18th Ed. 1998).



VANCOMYCIN HYDROCHLORIDE

POWDER FOR RECONSTITUTION; ORAL

	VANCOCIN HCL		
AA	LILLY	EQ 250MG BASE/5ML	N61667 002 JUL 13, 1983
+		EQ 500MG BASE/6ML	N61667 001
	VANCOLED		
AA	LEDERLE	EQ 250MG BASE/5ML	N63321 002 OCT 15, 1993

Without the re-listing of ANDA 061667 as a RLD (and any accompanying RS listing), a generic drug manufacturer is unable to submit a contemporary ANDA referencing an RLD, thus shielding Vancomycin HCl for Oral Solution, 250 mg (base)/5 mL and 500 mg (base)/6 mL, under ANDA 061667—effectively a brand-name drug—from generic competition. Moreover, FDA's failure to identify ANDA 061667 in the Orange Book as a RLD would result in the Agency treating two similarly situated parties in a dissimilar manner, which is a clear violation of the Administrative Procedure Act,[9] particularly with respect to FDA-regulated products.[10] After all, FDA recently recognized in approving a supplement to ANDA 031667 that the application itself was the "basis of submission"—that is, the RLD—for purposes of submission and approval of the supplement.[11] Thus, if ANDA 061667 can serve as the RLD for ANDA supplement purposes, then it should serve as an RLD for any ANDA applicant.

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9 See, e.g., Huntington Hosp. v. Thompson, 319 F.3d 74, 75-76 (2d Cir. 2002) citing Independent Petroleum Ass'n of America v. Babbitt, 320 U.S. App. D.C. 107, 92 F.3d 1248, 1260 (D.C. Cir. 1996) ("The treatment of cases A and B, where the two cases are functionally indistinguishable, must be consistent. That is the very meaning of the arbitrary and capricious standard."); see also, Plunkett v. Castro, 67 F. Supp. 3d 1, 21-22 (D.D.C. 2014) citing Etelson v. Office of Pers. Mgmt., 684 F.2d 918, 926, 221 U.S. App. D.C. 396 (D.C. Cir. 1982) ("Government is at its most arbitrary when it treats similarly situated people differently.").

10 See Bracco Diagnostics, Inc. v. Shalala, 963 F. Supp. 20, 28 (D.D.C. 1997) (FDA may not "permit two sets of similar products to run down two separate tracks, one more treacherous than the other, for no apparent reason.").

11 See FDA, ANDA 061667/S-26, Division of Bioequivalence Review, at 3, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/061667Orig1s026.pdf ("It is important to note that the current ANDA ***is*** the innovator product, which is also listed as the basis of submission for the current PAS") (emphasis in original).

Accordingly, the undersigned requests that FDA designate in the Orange Book Vancomycin HCl for Oral Solution, 250 mg (base)/5 mL and 500 mg (base)/6 mL, approved under ANDA 061667 as RLDs.

III. ENVIRONMENTAL IMPACT

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

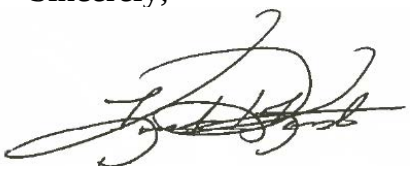
IV. ECONOMIC IMPACT

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

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