DEPARTMENT OF HEALTH & HUMAN SERVICES

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

NOV 07 2014

Amanda Dixon
Director of Regulatory Affairs and Quality
Nomax, Inc.
9735 Green Park Industrial Drive
St. Louis, MO 63123

Re: Docket No. FDA-2013-P-0504

Dear Ms. Dixon:

This letter responds to your citizen petition received on May 2, 2013 (Petition), requesting that the Food and Drug Administration (FDA or Agency) amend the *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book) to designate Potassium Citrate (new drug application (NDA) 019647) as a reference listed drug (RLD) product. For the reasons explained further below, we are denying the Petition because FDA need not take further action for abbreviated new drug applicants to reference Potassium Citrate (NDA 019647).

Potassium Citrate, 10 milliequivalents/packet (mEq/packet) and 20 mEq/packet, held by Nova-K LLC, was approved under NDA 019647 on October 13, 1988. Potassium Citrate (NDA 019647) is indicated for the management of renal tubular acidosis with calcium stones, hypocitraturic calcium oxalate nephrolithiasis of any etiology, and uric acid lithiasis with or without calcium stones. The 20 mEq/packet was designated as the RLD in the Orange Book. Subsequently, the sponsor discontinued marketing Potassium Citrate, 10 mEq/packet and 20 mEq/packet, and FDA moved the products to the "Discontinued Drug Product List" section of the Orange Book.

The Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Amendments) created section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)), which established the ANDA approval process. To obtain approval, an ANDA applicant is not required to submit clinical studies to demonstrate the safety and effectiveness of the drug product; instead, an ANDA relies on FDA's previous finding that the RLD[1] is safe and effective. To rely on a previous

[1] A *listed drug* is a new drug product that has an effective approval under section 505(c) of the FD&C Act for safety and effectiveness, or under section 505(j), that has not been withdrawn or suspended under section 505(e)(1) through (5) or (j)(5) of the FD&C Act, and that has not been withdrawn from sale for what FDA determines are reasons of safety or effectiveness. Listed drugs are identified as drugs with an effective approval in FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" (The Orange Book). See 21 CFR 314.3. A *reference listed drug* is the listed drug identified by FDA as the drug product upon which an applicant relies in seeking approval of its abbreviated application. *Id.*

finding of safety and effectiveness, an ANDA applicant must demonstrate, among other things, that its drug product is bioequivalent to the RLD (section 505(j)(2)(A)(iv) of the FD&C Act).[2] In addition, an ANDA must contain, with certain exceptions, information to show that the proposed generic drug product has the same active ingredient(s), indications for use, route of administration, dosage form, strength, and labeling as the RLD (section 505(j)(2)(A) and section 502(j)(4) of the FD&C Act). FDA must approve the ANDA unless, among other things, the information submitted in the ANDA is insufficient to meet the requirements delineated in section 505(j)(2)(A) and section 505(j)(4) of the FD&C Act.

FDA regulations in § 314.161 (21 CFR 314.161) provide that a person may petition FDA for a determination, or FDA may determine on its own initiative, whether a listed drug that has been voluntarily withdrawn from sale was withdrawn for safety or effectiveness reasons. This determination may be made at any time after the drug has been voluntarily withdrawn from sale.[3]

As noted previously, Potassium Citrate, 10 mEq/packet and 20 mEq/packet, (NDA 019647) is currently listed in the "Discontinued Drug Product List" section of the Orange Book. On April 18, 2013, you submitted a second citizen petition (Docket No. FDA-2013-P-0503) requesting that FDA determine whether Potassium Citrate (NDA 019647) was voluntarily withdrawn from sale for safety or effectiveness reasons (Relisting Petition). FDA considered your Relisting Petition, reviewed Agency records, and determined that the product was not withdrawn for reasons of safety or effectiveness. In a *Federal Register* notice dated October 23, 2013 (78 FR 63228), and in accordance with § 314.161(c), FDA published its determination that Potassium Citrate, 10 mEq/packet and 20 mEq/packet, was not discontinued for reasons of safety or effectiveness.[4] This *Federal Register* notice also announced that ANDAs that refer to Potassium Citrate, 10 mEq/packet and 20 mEq/packet, may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs.[5]

In summary, the 20 mEq/packet strength of Potassium Citrate (NDA 019647) was previously designated as an RLD, and FDA has made a relisting determination for Potassium Citrate (NDA 019647) finding that the products were not removed for reasons of safety or effectiveness. No additional designation is needed for ANDA applicants to reference these drug products in their applications.

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[2] Under the FD&C Act, "[a] drug shall be considered to be bioequivalent to a listed drug if . . . the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses." See section 505(j)(8)(B)(i); see also implementing regulations at 21 CFR part 320.

[3] 21 CFR 314.161(a).

[4] On October 24, 2013, FDA sent Nomax, Inc., a letter providing a copy of the *Federal Register* notice for the Relisting Petition.

[5] 78 FR 63228 at 63229.

For these reasons, your Petition is denied.

Sincerely,

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