DEPARTMENT OF HEALTH & HUMAN SERVICES

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

JUL 0 3 2013

Leslie Sands
Director, Regulatory Affairs (USA)
Lupin Pharmaceuticals, Inc.
Harborplace Tower
111 South Calvert Street, 21st Floor
Baltimore, MD 21202

Re: Docket No. FDA-2013-P-0040

Dear Ms. Sands:

This letter responds to your citizen petition dated January 2, 2013 (Petition), requesting that the Food and Drug Administration (FDA or Agency) designate Calcium Acetate Capsules, 667 milligrams (mg) (equivalent (eq.) to 169 mg calcium), manufactured by Roxane Laboratories, Inc. (Roxane), under ANDA 77-728, as an additional reference listed drug (RLD) in the *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).

We have carefully considered the Petition. For the reasons described below, your Petition is denied.

I. BACKGROUND

Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) allows the marketing of generic versions of a previously approved drug product when the generic drug product is the subject of an approved abbreviated new drug application (ANDA). To obtain approval, the ANDA sponsor must show, among other things, that with respect to a listed drug, the generic drug product (1) has the same active ingredient(s), (2) has essentially identical labeling, and (3) is bioequivalent.

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approval under section 505(c) of the FD&C Act for safety and effectiveness, or under section 505(j), that has not been withdrawn or suspended under section 505(e)(1) through (5) or (j)(5) of the FD&C Act and that has not been withdrawn from sale for what FDA has determined are reasons of safety or effectiveness.[1] Listed drugs are identified as drugs with an effective approval in FDA's Orange Book.[2] A *reference listed drug* (RLD) is the listed drug identified by

[1] 21 CFR 314.3.
[2] Id.

FDA as the drug product on which an ANDA applicant relies in seeking approval of its application.[3]

Our policy on the designation of RLDs is stated in the preamble to the 1992 final rule establishing the requirements for ANDAs,[4] where in response to comments asking the Agency to explain how we determine which drugs should be RLDs, we stated:

> . . . FDA will designate all reference listed drugs. Generally, the reference listed drug will be the NDA drug product for a single source drug product. For multiple source NDA drug products or multiple source drug products without an NDA, the reference listed drug generally will be the market leader as determined by FDA on the basis of commercial data. . . . If an applicant believes that there are sound reasons for designating another drug as a reference listed drug, it should consult FDA.[5]

II. DISCUSSION

In the Petition, you request that FDA designate Roxane's Calcium Acetate Capsules, 667 mg (eq. to 169 mg calcium) (ANDA 77-728), as an additional reference listed drug (RLD) in the Orange Book. Currently, the Orange Book lists PhosLo Gelcaps (manufactured by Fresenius MEDCL under NDA 21-160) as the only RLD for Calcium Acetate Capsules, 667 mg (eq. to 169 mg calcium). The Orange Book also lists as approved generics for Calcium Acetate Capsules, 667 mg (eq. to 169 mg calcium), those manufactured by Roxane (ANDA 77-728) and Paddock LLC (Paddock) (ANDA 91-312), but these drug products are not RLDs.

The Petition states that, to the best of your knowledge, the PhosLo Gelcaps are not currently available on the market. The Petition also states that, of the Roxane and Paddock generic drug products, only the Roxane product is currently available on the market. You request that the Roxane product manufactured under ANDA 77-728 be designated as an additional RLD in the *Orange Book.*

We have determined that you have not stated sufficient grounds to establish the need to designate an additional RLD for Calcium Acetate Capsules, 667 mg (eq. to 169 mg calcium). Based on our records, PhosLo is still being marketed under its NDA as an authorized generic.[6] An ANDA applicant may use the authorized generic version of the current RLD as the reference standard in the *in vivo* bioequivalence study with proper

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[3] Id.
[4] See FDA, Final Rule: Abbreviated New Drug Application Regulations, 57 Fed. Reg. 17950 (April 28, 1992).
[5] 57 Fed. Reg. 17950 at 17958.
[6] See the list of authorized generic drugs available at: http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM183605.pdf. See 21 CFR 314.3 for a definition of an "authorized generic drug."

documentation.[7] Because the RLD is still available as an authorized generic under NDA 21-160, FDA does not agree that the Roxane drug product approved under ANDA 77-728 should be designated as an additional RLD. You have not provided any other basis for justifying designation of Roxane's product as an additional RLD.

III. CONCLUSION

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

Sincerely yours,

Robert Temple, acting for

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

[7] Any ANDA applicant should provide complete lot information on this alternate product to FDA for confirmation of its acceptability for use as the reference test article in bioequivalence studies before conducting the studies.