



December 3, 2002

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and in accordance with 21 CFR 10.30 requesting that the Commissioner of the Food and Drug Administration make a determination that the drug product, Digoxin Elixir, 0.25 mg/5 mL, is suitable for consideration in an abbreviated new drug application (ANDA).

A. Actions Requested

The petitioner requests that the Commissioner of the Food and Drug Administration make a determination that the drug product, Digoxin Elixir, 0.25 mg/5 mL, is suitable for submission as an ANDA. The reference listed drug product (RLD) upon which this petition is based is Lanoxin[®] (Digoxin) Tablets, 0.25 mg (GlaxoSmithKline) [1]. The petitioner is thus seeking a change in dosage form — from a tablet to an elixir — from that of the RLD. The proposed product will be available in the same strength, 0.25 mg/5 mL, as the RLD.

Background

On November 24, 2000, the Food and Drug Administration published a proposed rule (65 FR 70538) that would revoke the regulation that established conditions for marketing digoxin products for oral use (§310.500 [21 CFR 310.500]). Regulation 310.500 originally announced FDA's determination that digoxin products for oral use are new drugs within the meaning of 201(p) of the Act [21 U.S.C. 321(p)], and set forth conditions for marketing the products.

Until recently, FDA has regulated all digoxin products for oral use under the labeling requirements set forth in §310.500, with digoxin tablets also subject to the certification procedure set forth in §310.500. On September 30, 1997, FDA approved an NDA for digoxin tablets (Lanoxin[®], Glaxo Wellcome). As a result, manufacturers of digoxin tablets are now eligible to obtain ANDAs, and the Agency reaffirmed its determination that *all* oral digoxin products are new drugs, and lifted the stay of the requirements for submitting ANDAs.

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Because the products, which are new drugs, can be regulated under the approval process for new drug applications (NDAs) and abbreviated new drug applications (ANDAs) as set forth in section 505 of the Act, the FDA has determined that manufacturers will be required to obtain approved applications, including manufacturers of digoxin elixir. The November 24, 2000 proposed rule (65 FR 70538) is attached to this letter as **Exhibit A**.

Roxane Laboratories provided comments to the Agency regarding this proposed rule on February 16, 2001, attached here as **Exhibit B**. The final rule was published in the Federal Register (Vol 67, No. 123) on June 26, 2002, attached to this letter as **Exhibit C**.

ANDA Citizen Petition #01P-0449/CP1 was submitted by Roxane Laboratories to the Agency in October, 2001, requesting that the Commissioner make a determination that the drug product, Digoxin Elixir 0.25 mg/5 mL, is suitable for consideration in an abbreviated new drug application. The Agency, in December 2001, indicated that this petition would not be approved since it was subject to the Pediatric Rule at that time and asked that it be withdrawn. Accordingly, Roxane Laboratories withdrew the petition. However, based on the ruling of the United States District Court for the District of Columbia, Association of American Physicians and Surgeons, Inc., et al., v. United States Food and Drug Administration, et al., Defendants, Roxane does not believe that the Pediatric Rule is a basis for denial of this petition.

B. Statement of Grounds

B.1 Change in Dosage Form

The RLD is a tablet form of digoxin. The proposed drug product is a currently marketed elixir dosage form of digoxin that FDA has permitted to be marketed for years in accord with 21 CFR 310.500 without the requirement for a marketing application. It contains the same active ingredient as the RLD. Although the dosage form differs from that of the RLD, the absolute bioavailability of digoxin from the tablet (60% → 80%) and elixir (70% → 85%) are comparable and the recommended doses are the same based on the approved labeling of the RLD [2]. Recommended doses of digoxin are individualized for each patient. The difference in strength and dosage form merely means that the total dose of the elixir will be based on a specified volume of drug product rather than a fixed dose as provided by the tablet dosage form.

In support of the change in dosage form requested by this petition, the petitioner would like to point out that the agency has previously approved numerous ANDA suitability petitions allowing for a change in dosage form from a tablet to an oral solution. There are no proposed changes in labeling with the exception of the obvious changes for formulation and supplier since the FDA approved labeling includes reference-use of an elixir dosage form. Proposed Draft labeling for the elixir is included in Attachment 1. A copy of the approved labeling of the RLD is included in Attachment 2.



The dosing recommendations of the proposed product will be consistent with that of the RLD (Attachment 2). The proposed oral solution (elixir) dosage form will benefit those elderly or infirmed patients who because of preference or their disease state may not be able to swallow tablets.

C. Conclusion

Roxane Laboratories has been marketing Digoxin Elixir USP pursuant to the provisions of 21 CFR 310.500 since 1988 and seeks to maintain the availability of digoxin elixir to the marketplace. To that end, the petitioner requests the Commissioner to find that a change in dosage form from a tablet to an elixir dosage form of digoxin raises no questions of safety or effectiveness and that the elixir is suitable for submission as an ANDA.

The undersigned requests that the Commissioner grant this petition and authorize submission of an ANDA for a liquid form of Digoxin (elixir) 0.25 mg/5 mL.

D. Environmental Impact

According to 21 CFR 25.31(a), this petition qualifies for a categorical exemption from the requirement to submit an environmental assessment.

E. Economic Impact

According to 21 CFR 10.30(b), petitioner will, upon request by the Commissioner, submit economic impact information.

F. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, 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 are unfavorable to the petition.

Correspondence concerning this petition should be directed to my attention. I can be reached by telephone at (614) 272-4785 and by telefax at (614) 276-2470.

Respectfully submitted,

Elizabeth A. Ernst
Associate Director, Regulatory Affairs
DRA-Multisource Products for Roxane Laboratories

Cc: G. Davis, OGD



G. References¹

1. Electronic Orange Book (www.fda.gov/cder/ob).
2. Lanoxin[®] (digoxin) Tablets, USP. Product Information. GlaxoSmithKline (www.glaxowellcome.com).

H. Exhibits/Attachments:

Exhibit A: Federal Register: The November 24, 2000 proposed rule (65 FR 70538)

Exhibit B: Comments from Roxane Laboratories regarding the proposed rule (see Exhibit A) on February 16, 2001.

Exhibit C: Federal Register: The June 26, 2002 final rule (Vol 67, No. 123-42992-42997).

Attachment 1: Proposed Draft labeling for Digoxin Elixir.

Attachment 2: Copy of the labeling of the RLD (Lanoxin[®] Tablets 0.25 mg).

Attachment 3: References.

¹ Copies of references are included in Attachment 3.