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RESEARCH**

*APPLICATION NUMBER:*

**21-648**

**APPROVABLE LETTER**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service  
Food and Drug Administration  
Rockville, MD 20857

NDA 21-648

Roxane Laboratories, Inc.  
Attention: Ms. Elizabeth Ernst  
1809 Wilson Rd.  
Columbus, Ohio 43228

Dear Ms. Ernst:

Please refer to your new drug application (NDA) dated April 10, 2003, received April 25, 2003 (user fee receipt date), submitted under section 505(b)/pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Digoxin 0.05 mg/mL Elixir USP.

We acknowledge receipt of your submissions dated April 9, June 12, July 9 and 11, September 4, October 2, and December 3, 2003, and January 16, February 2, 4, 11, 12, and 18, 2004.

We have completed our review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary to develop final printed labeling (FPL) for the drug. We have not enclosed marked-up draft labeling because there are several labeling issues to be resolved, and we may suggest further changes. We have discussed many of these labeling issues in the February 20, 2004 teleconference with you, which include:

- appropriate language to describe pediatric use, including dosing instructions,
- appropriate information on drug-drug interactions, and
- appropriate language regarding \_\_\_\_\_

The CMC deficiencies enumerated below also require resolution.

1. Drug Product and Drug Substance Issues

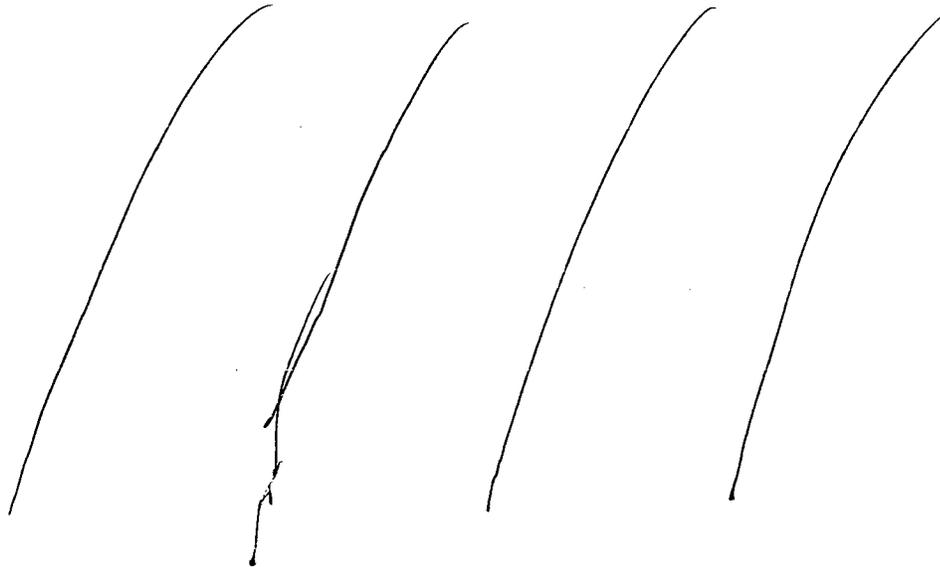
- Provide either a timeline for lowering the threshold for \_\_\_\_\_ in the drug substance to acceptable limits (e.g., \_\_\_\_\_, or an adequate justification for the current level \_\_\_\_\_ or a product intended for use in children.
- Revise the acceptance criteria for the drug product impurities as shown below.

Degradant	Release Limits (%)	Stability Limits (%)
/	/	/
/	/	/
/	/	/
/	/	/
Total	/	/

- Provide additional information regarding \_\_\_\_\_ in the drug product. Depending on the results, further tightening of the \_\_\_\_\_ limit for this impurity may be needed:
  - Structure.
  - Origin (i.e., process impurity or degradant).
  - Levels in drug substance.

- d. Provide a revised specification table for the drug product, incorporating all the changes listed above.

2. Chemistry Labeling Issues



If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

If you have any questions, please contact:

Mr. Edward Fromm  
Regulatory Health Project Manager  
(301) 594-5332

Sincerely,

*{See appended electronic signature page}*

Douglas C. Throckmorton, M.D.  
Director  
Division of Cardio-Renal Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

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/s/

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Doug Throckmorton  
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