DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-438/S-005

Reliant Pharmaceuticals, LLC
Attention: Ms. Paulette F. Kosmoski
110 Allen Road
Liberty Corner, NJ 07938

Dear Ms. Kosmoski:

Please refer to your supplemental new drug application dated March 11, 2004 submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for InnoPran XL (propranolol hydrochloride) 80 and 120 mg Extended Release Capsules.

We acknowledge receipt of your submissions dated June 17 and July 19, 2004.

Your submission dated July 19, 2004 constituted a complete response to our June 7, 2004 action letter.

This supplemental new drug application provides for the following changes to the labeling:

1. The first paragraph of the **PHARMACOKINETICS AND DRUG METABOLISM/*Drug Interactions/Cardiovascular Drugs/Antiarrhythmics*** section has been changed from:

   The AUC of propafenone is increased by more that 200% by co-administration of propranolol.

   To:

   The concomitant administration of propranolol and propafenone increased propranolol average steady-state plasma concentrations (213%), AUC (113%), C_{max} (83%), T_{max} (55%), and $T_{½}$ (30%), and significantly decreased plasma levels of 4-hydroxy-propranolol. Co-administration of propranolol and propafenone did not produce any significant change in propafenone pharmacokinetics. While the therapeutic range for propranolol is wide, a reduction in dosage may be necessary during concomitant administration with propafenone.

2. The description of the capsule appearance markings in the **HOW SUPPLIED** section has been changed from "RD201" to "InnoPran XL".

3. The company name has been changed in the **HOW SUPPLIED** section from "Reliant Pharmaceuticals, LLC" to "Reliant Pharmaceuticals".

In addition, the following changes were noted which were to be made at the time of the next printing as described in our letters dated March 12, 2003 and April 11, 2003:

1. In the **DESCRIPTION** section, the second sentence of the first paragraph has been changed from:

   The capsules contain sustained-release beads available as 80 mg and 120 mg capsules.

   To:

   InnoPran XL is available as 80 mg and 120 mg capsules which contain sustained-release beads.

2. In the **PHARMACOKINETICS AND DRUG METABOLISM/Special Populations/Race** section and the **PHARMACODYNAMICS AND CLINICAL EFFECTS/Hypertension**, "Caucasians" has been changed to "Whites" in all places where it occurred.

3. In the **PRECAUTIONS/Carcinogenesis, Mutagenesis, Impairment of Fertility** section and **PRECAUTIONS/Pregnancy: Pregnancy Category C** section, "propranolol" has been changed to "propranolol HCl" wherever it occurred.

We have completed our review of this supplemental new drug application, as amended. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) dated July 19, 2004.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call:

Ms. Melissa Robb
Regulatory Health Project Manager
(301) 594-5313.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Acting Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Norman Stockbridge

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