DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-494

Reliant Pharmaceuticals, Inc.
Attention: Robert Mandetta
Director, Regulatory Affairs
110 Allen Road
Liberty Corner, NJ 07938

Dear Mr. Mandetta:

Please refer to your new drug application (NDA) dated April 10, 2002, received April 10, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Axid® (nizatidine) Oral Solution, 15mg/ml. We determined this application to be approvable in our letter dated February 10, 2003.

We acknowledge receipt of your submissions dated October 10, 17, 24; November 24, 25; and December 03, 2003; and February 18; March 11, 12, 30; and April 06, 08, 12, 13, 14, 16, 19, 29; and May 06, 17, and 24, 2004.

The November 24, 2004 submission, received November 25, 2004, constituted a complete response to our February 10, 2003, Approvable letter

This new drug application provides for the use of Axid® (nizatidine) Oral Solution, 15mg/ml for the following indications:

In Adults:

1. For up to 8 weeks for the treatment of active duodenal ulcer. In most patients, the ulcer will heal within 4 weeks.
2. For maintenance therapy for duodenal ulcer patients at a reduced dosage of 150 mg h.s. after healing of an active duodenal ulcer. The consequences of continuous therapy with nizatidine for longer than 1 year are not known.
3. For up to 12 weeks for the treatment of endoscopically diagnosed esophagitis, including erosive and ulcerative esophagitis, and associated heartburn due to GERD.
4. For up to 8 weeks for the treatment of active benign gastric ulcer. Before initiating therapy, care should be taken to exclude the possibility of malignant gastric ulceration.

In Pediatric Patients 12 years of age and older:

1. For up to 12 weeks for the treatment of endoscopically diagnosed esophagitis, including erosive and ulcerative esophagitis, and associated heartburn due to GERD.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor revisions indicated in the enclosed labeling.

In addition, we would like for you to change the term "children" to "pediatric patients" in your 05/24/04 label prior to your first printing.

We remind you of your Chemistry, Manufacturing, and Controls postmarketing study commitments listed in your submission dated April 14 and 29, 2004. These commitments are listed below.

1. To provide information on degradation controls as requested in the Chemistry, Manufacturing, and Controls (CMC) Deficiency Letter, dated March 11, 2004. Specifically, to submit summaries and copies of all relevant chemical literature of paraben and drug substance degradants in similar dosage forms.

   Final Report Submission:……..…August 24, 2004

2. Study Protocol Entitled "Isolation and Identification, Through Structural Characterization Techniques, the Degradant Products of Nizatidine and Paraben Excipients in the Drug Product"

   Protocol Submission date .....3rd Quarter 2004
   Study start date ……....1st Quarter 2005
   Final report submission date ……4th Quarter 2005

3. Study Protocol Entitled "Investigation of Complexation Reactions of Nizatidine with Excipients in the Drug Product"

   Protocol submission date …….3rd Quarter 2004
   Study start date ……..1st Quarter 2005
   Final report submission date …….4th Quarter 2005

   Based upon the findings and results of the above investigations, the existing analytical test method and specifications will be reviewed and reassessed. Additional proposed tests and specifications may be generated based on the scientific understanding of the collected data/information to be submitted as a supplement to the NDA. Beforehand, a request may be placed to the Division to have an opportunity for an open dialog with the chemistry reviewers in order to reach a consensus on setting specifications that meet FDA's expectations.

Submit your Chemistry, Manufacturing, And Controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently

labeled **"Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please submit final printed labeling (FPL) identical to the enclosed labeling (text for the package insert, immediate container labels, and carton labels). These revisions are terms of the NDA approval. Marketing the product before making the revisions, exactly as stated, in the product's labeling may render the product misbranded and an unapproved new drug.

You may submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-494". Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product to the NDA when it is available.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have fulfilled the pediatric study requirement for this application.

We remind you that you must comply with the reporting requirements for an approved NDA (21 CFR 314 .80 and 314.81).

If you have any questions, call Paul E. Levine, Jr., R.Ph., J.D., Regulatory Health Project Manager, at (301) 443-8347.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D., M.S.
Director
Division of Gastrointestinal and

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

/s/

Joyce Korvick
5/25/04 03:17:46 PM
for Dr. Robert Justice