DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204307

NDA APPROVAL

Cypress Pharmaceutical, Inc.
2944 W. 143rd Terrace
Leawood, Kansas 66224

Attention: Janet K. DeLeon, R.A.C.
Director of Product Development

Dear Ms. DeLeon:

Please refer to your New Drug Application (NDA) dated April 24, 2012, received April 24, 2012, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Vituz, (hydrocodone bitartrate and chlorpheniramine maleate) Oral Solution 5mg/4mg per 5mL.

We acknowledge receipt of your amendments dated July 26, August 02, October 15, and 29, and December 03, 2012, January 08, and 15, and February 13, 14, and 19, 2013.

This new drug application provides for the use of Vituz (hydrocodone bitartrate and chlorpheniramine maleate) oral solution for relief of cough and symptoms associated with upper respiratory allergies or a common cold.

We have 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 editorial revisions indicated in the enclosed labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE-CONTAINER LABELS

Submit final printed carton and immediate-container labels that are identical to the carton and immediate-container labels submitted on February 14, 2013, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 204307**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

EXPIRATION DATING PERIOD

The proposed expiry of twenty-four (24) months for the products packaged as oral solution in HDPE container when stored at controlled room temperature (20 to 25°C or 68 to 77°F) is granted.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 5 years because there is evidence strongly suggesting that the drug product would be unsafe in this pediatric group. Your combination product, Vituz, contains hydrocodone which, because of the risk of fatal respiratory depression, is not recommended for use as an antitussive in children less than 6 years of age.

We are deferring submission of your pediatric study for ages 6 to 17 years for this application because this product is ready for approval for use in adults and the pediatric study have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. The required studies are listed below.

2017-1 Conduct a study to assess the pharmacokinetics of each Vituz drug component (hydrocodone and chlorpheniramine) in approximately 25-35 children ages 6-17 years with symptoms of the common cold. The study can be conducted with a

formulation containing hydrocodone, chlorpheniramine, and pseudoephedrine. The results of this study will be used to determine the appropriate dose of the combination product to evaluate in a safety study in children ages 6-17 years.

Final Protocol Submission:	March 8, 2013
Trial Completion:	December 31, 2013
Final Report Submission:	June 30, 2014

2017-2 Conduct a study to assess the safety of Vituz (hydrocodone and chlorpheniramine) in approximately 400-450 children ages 6-17 years with symptoms of the common cold. The study can be conducted with a formulation containing hydrocodone, chlorpheniramine, and pseudoephedrine. The dose used in this study will be based upon the pharmacokinetic study in children ages 6-17 years.

Final Protocol Submission:	September 30, 2014
Trial Completion:	December 31, 2015
Final Report Submission:	September 30, 2016

Submit the protocol(s) to your IND 102177, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more

information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Leila P. Hann, Regulatory Project Manager, at (301) 796-3367.

Sincerely,

{See appended electronic signature page}

Lydia I. Gilbert-McClain, M.D., F.C.C.P.
Deputy Director
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling

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

/s/

LYDIA I GILBERT MCCLAIN
02/20/2013