

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-374**

**CORRESPONDENCE**

# Fax



**Division of Anti-Inflammatory, Analgesic,  
Ophthalmic Drug Products**  
Center for Drug Evaluation and Research, HFD-550  
Parklawn Building  
5600 Fishers Lane, Rockville, MD 20857

**To: David Smith**

**From: Barbara Gould**

**Fax: 973 660-7187**

**Fax: 301-827-2531**

**Phone: 973 660-6806**

**Phone: 301-827-2019**

**Pages: 1 (including cover)**

**Date: 10-Sep-01**

**Re: NDA 21-374**

**Urgent**    **For Review**    **Please Comment**    **Please Reply**    **Please Recycle**

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● **Comments:**

Please provide the following safety update from the AAPC and DAWN databases since 1999 for NDA 21-374.

Please call if you have any questions or concerns.

BJ

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/s/

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Barbara Gould  
9/10/01 07:23:00 AM  
CSO

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**Phone:** 973 660-6806

**Phone:** 301-827-2019

**Pages:** 1 (including cover)

**Date:** 25-Sep-01

**Re:** NDA 21-374 Pharm/Tox Info Request

**Urgent**     **For Review**     **Please Comment**     **Please Reply**     **Please Recycle**

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● **Comments:**

In the fax dated June 28, 2000, Whitehall-Robins Healthcare was requested to provide the results of the chemical analysis of the dosing solutions for mutagenicity studies. The Sponsor provided tables with the doses for each experiment. However, the Sponsor needs to clarify the following issues:

- Please, specify whether the values in the dose tables are theoretical values or actual levels measured analytically.
- Please, clarify based on which active ingredient the \_\_\_\_\_ was obtained. If it was based on the pseudoephedrine concentration (as specified or \_\_\_\_\_, supplement N-006, GC, p. 4-1-5), then the numbers given in the table do not agree with the respective percentage.
- The protocol for the Ames test states that the ibuprofen/pseudoephedrine/ \_\_\_\_\_ was received by the performing laboratory (Bacterial Reverse Mutation Assay, page 8). It is then assumed that this stock was used to prepare the different dilutions with final concentrations of \_\_\_\_\_  $\mu\text{g}/\text{plate}$ . The table, therefore, is not adequate because ibuprofen/pseudoephedrine containing \_\_\_\_\_ may have not been used in the assay. Please, specify the actual dose of \_\_\_\_\_ ( $\mu\text{g}/\text{plate}$ ) used and how they were obtained.

Please call if you have any questions or concerns.

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/s/

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Barbara Gould  
9/25/01 09:41:10 AM  
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