

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**022424Orig1s000**

**STATISTICAL REVIEW(S)**



U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Translational Science  
Office of Biostatistics

## Statistical Review and Evaluation

### CLINICAL STUDIES

**NDA / Serial Number:** NDA 022-424 / 0000

**Drug Name:** Hydrocodone and Guaifenesin Oral Solution

**Proposed Indication(s):** [REDACTED] (b) (4)

**Applicant:** Tiber Laboratories

**Date(s):** Received: 11-29-2010  
PDUFA Due Date: 09-29-2011

**Review Priority:** Standard

**Biometrics Division:** Division of Biometrics II/Office of Biostatistics

**Statistical Reviewer:** Robert Abugov, Ph.D

**Concurring Reviewers:** Joan Buenconsejo, Ph.D.

**Statistics Supervisor:** Thomas Permutt, Ph.D (Division Director)

**Medical Division:** Division of Pulmonary and Allergy Products

**Clinical Team:** Xu Wang, Medical Reviewer  
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**Keywords:** NDA review, Clinical Studies

## Biometrics Review

### 1. Current Submission

This submission by Tiber Laboratories proposes a combination of Hycodan hydrocodone (NDA 005-213) and guaifenesin (OTC monograph) [REDACTED] (b) (4)

[REDACTED] The applicant proposes approval of this 505(b)(2) submission, which depends upon a bioequivalence study (S09-0009) and a single dose food effect study (S09-0010).

Studies S09-0009 and S09-0010 were also submitted in NDA 022-279 to support approval for an oral solution of hydrocodone, pseudoephedrine, and guaifenesin. In the Clinical Pharmacology review for NDA 022-279, Dr. Arun Agrawal noted that the guaifenesin component of the proposed drug product was not bioequivalent to the reference drug, [REDACTED] (b) (4)

[REDACTED] The issue was consequently referred to the Division of Scientific Investigations, with an inspection report by Dr. Xikui Chen on 21 January 2011 which described deficiencies including falsification of data, failure to follow protocols, and failure to follow standard operating procedures. Dr. Chen therefore concluded that the applicant's studies S09-0009 and S09-0010 should not be accepted to support NDA 022-279.

Appropriate regulatory actions for the present submission based on conclusions from NDA 022-279 are being explored.

### 2. Biometrics Evaluation

Because the current submission includes no trials assessing clinical efficacy, Biometrics has no comments.

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/s/  
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ROBERT ABUGOV  
02/01/2011

JOAN K BUENCONSEJO  
02/02/2011  
I concur with Dr. Abugov's review.