



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

IND 50,076

Summers Laboratories  
Attention: Jules Mitchel, M.B.A., Ph.D., President, Target Health, Inc.  
261 Madison Avenue, 24<sup>th</sup> Floor  
New York, NY 10016

Dear Dr. Mitchel:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lice Asphyxiator.

We also refer to the meeting between representatives of your firm and the FDA on September 9, 2004. The purpose of the meeting was to address the adequacy of the proposed CMC, toxicology and clinical plans for the treatment of head lice.

The official minutes of that meeting are enclosed. You are responsible for notifying us of any significant differences in understanding regarding the meeting outcomes.

Sincerely,

*{See appended electronic signature page}*

Jonathan Wilkin, M.D.  
Division Director  
Division of Dermatologic and Dental Drug  
Products  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research

Enclosure

**MEMORANDUM OF MEETING MINUTES**



**Meeting Date:** September 9, 2004                      **Time:** 10:30 A.M.  
**Location:** N225                                              **Meeting ID:** 13433  
**Topic:** IND 50,076, Lice Asphyxiator for <sup>(b)</sup><sub>(4)</sub> the treatment of head lice  
**Subject:** End-of-Phase 2 meeting  
**Sponsor:** Summers Laboratories  
**Meeting Chair:** Jonathan Wilkin, M.D./Division Director, DDDDP, HFD-540  
**Meeting Recorder:** Melinda Harris, M.S./Regulatory Project Manager, DDDDP, HFD-540

**FDA Attendees:**

Jonathan Wilkin, M.D./Division Director, DDDDP, HFD-540  
Jonca Bull, M.D./Director ODE V, HFD-105  
Terri Rumble, R.N., B.S.N/Associate Director of Regulatory Affairs, ODE V, HFD-105  
Ramesh Sood, Ph.D./Team Leader, Chemistry, ONDC/DNDCIII, HFD-830  
Allan Fenselau, Ph.D./Chemistry Reviewer, DNDCIII, HFD-830  
Barbara Hill, Ph.D./Pharmacology Reviewer, DDDDP, HFD-540  
Raman Baweja, Ph.D., R.ph./Team Leader, Pharmacokinetics, DPEIII, HFD-880  
Lei Zhang, Ph.D./Pharmacokinetics Reviewer, DPEIII, HFD-880  
Markham Luke, M.D., Ph.D./Team Leader, Clinical, Dermatology, DDDDP, HFD-540  
Jill Lindstrom, M.D./Clinical Reviewer, DDDDP, HFD-540  
Mohamed Al-Osh, Ph.D./Team Leader, Biostatistics, DBIII, HFD-725  
Shiowjen Lee, Ph.D./Biostatistician, DBIII, HFD-725  
Mat Soukup, Ph.D./Biostatistician, DBIII, HFD-725  
Melinda Harris, M.S./Regulatory Project Manager, DDDDP, HFD-540

**Sponsor Attendees:**

**Summers Laboratories**

Mike Precopio/President  
John Colyar, M.B.A./Vice President  
(b) (4)  
Terri Meinking/President, Global Health Associates of Miami  
Ralph D' Agostino, Jr., M.D./Associate Professor/Statistician, Wake Forest University/Target Health, Inc.  
Amy Lau, M.P.H./Director of Biostatistics and Data Management, Target Health, Inc.  
(b) (4)

Jules Mitchel, Ph.D./Regulatory Affairs, Target Health, Inc.

**Purpose:**

To provide general guidance on the content and format of the Investigational New Drug Application under 21CFR 312. The pre-meeting briefing document (submitted August 5, 2004) provides background and questions (p 8) for discussion. The sponsor requests input from the Agency on the proposed CMC, toxicology, and clinical plans.

**Chemistry, Manufacturing and Controls:**

**Sponsor's Question 1:**

The CMC section outlines with some detail of the manufacturing processes, stability program, container closer systems and analytical methods for the drug substance and drug product. Does FDA agree that the provided information is sufficient for Phase 3 clinical testing and commercialization? If necessary, the sponsor will meet with FDA to discuss CMC issues prior to submission of the NDA.

**Agency's Response:**

The information provided on the manufacturing processes, stability program, container closer systems, and analytical methods for the drug substance and drug product is NOT sufficient for an NDA submission and hence, commercialization of the proposed product. Phase 3 clinical testing may proceed, but a possibility exists that additional studies will need to be performed in the event that

[REDACTED] (b) (4)

Assuming successful completion of the proposed Phase 3 studies, the following items should be addressed during preparation of an NDA.

**DRUG SUBSTANCE**

**NOTE:** Information on the chemistry, manufacturing, and controls [CMC] for the drug substance must be submitted to support the approval of original new drug applications [see Format and Content of the Chemistry, Manufacturing and Controls Section of an Application (Issued 2/1987, Posted 3/2/1998)]. This information can be included in the NDA or submitted as a DMF with a Letter of Authorization. In addition, the manufacture of benzyl alcohol drug substance will need be carried out in compliance with current Good Manufacturing Practices [cGMP].

1. **Specification:** (b) (4) [REDACTED]

(b) (4)

2. Analytical Methods: It is recommended for safety reasons that the use of odor to characterize benzyl alcohol and (b) (4) be eliminated. The ID test would be better satisfied by a chromatography method (TLC or HPLC).

## **DRUG PRODUCT**

### 3. Composition

- a. Use the NF designations for (b) (4)
- b. (b) (4)

### 4. Manufacture

- a. The sample batch record lacks specific information that permits batch-to-batch consistency (e.g., mixing speeds, temperatures, order of component addition, etc.). Inadequate attention is paid to how the technician should handle benzyl alcohol (from the perspectives of toxicity and flammability). Terms are used with inadequate definition, e.g., (b) (4)
- b. Fill Uniformity testing is inadequate, in that more sampling is needed at the beginning, middle, and end of filling operations.

5. Specification: No Identification test has been specified. No testing for Benzyl Alcohol Related Substances (degradants) has been specified. The term "lotion" is used without a clear definition.

### 6. Analytic Methods

- a. The representative methods are poorly written. Use complete sentences. State precisely the steps to be followed by the analyst.
- b. The representative chromatograms are not intelligible.
- c. "Mass Spectral Analysis" is cited as a method for use in stability studies, but no such method has been submitted in the package.

### 7. Container Closure System

- a. No detailed information on the container closure system has been provided. [See Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics—Section IIIC.]
- b. Extractable/leachable studies on the cap liner should be in accord with USP <661> Containers: Physicochemical Tests-Plastics and 21 CFR § 175.300 Testing. Depending on the results of this testing, additional studies may need to be performed.

### 8. Stability Studies

- a. Use significant figures appropriately in reporting data.
- b. Follow the guidance presented in ICH Q1A(R2) for conducting stability studies. Specify the actual conditions for temperature and relative humidity that will be employed for

- product storage during the stability studies.
- c. Perform stress stability studies with both drug substance and drug product that use conditions such as light exposure, pH differences, and treatment with peroxide [see ICH Q1A(R2)]. [The results provide critical information on the stability of drug substance and product as well as on the stability-indicating nature of the analytical methods.]
9. **Labeling:** Provide labeling. Include an appropriate warning statement regarding exposure of eyes to the benzyl alcohol in the drug product.
10. **Additional:** Provide information on the testing and manufacturing sites for drug substance and drug product. The following table format is recommended.

Name of Manufacturer	US or Foreign [U or F]	Address-Street	Address-CityState Zipcode (or Country)	CFN (or FEI) <sup>1</sup>	Responsibility Stage <sup>2</sup> Process <sup>3</sup>	Site Ready Y or N	Contact Person	Contact Phone No. [P], Fax No. [F×N], and/or E-mail address [EA]

1. If no manufacturer identification number is available, provide a copy of the facility registration form.
2. Drug substance [DS], intermediate [I], or finished dosage [FD].
3. Manufacturer [MF], Micronizer [MhyI], Packager [P], Sterilizer [S], Release Tester [RT], Stability Tester [ST], Sterility Tester [SxT], or Other [O].

**Administrative Comment:**

The Sponsor is encouraged to request a meeting to discuss specific CMC issues, if appropriate.

**Pharmacology/Toxicology:**

**Sponsor's Question 2:**

FDA has indicated that there is a requirement for Segment II rat and rabbit studies to be submitted with the NDA. The sponsor would like to discuss the timing of this requirement.

**Agency's Response:**

No additional nonclinical toxicology studies are recommended for the lice asphyxiator drug product to support the proposed Phase 3 clinical study contained in the briefing document.

The sponsor is reminded of the following recommendation that was previously relayed concerning the development of the lice asphyxiator drug product for marketing.

- 1) The reproductive and developmental toxicology studies conducted with benzyl alcohol that are reported in the literature are not adequate to determine the teratogenic potential of benzyl alcohol. Women of childbearing potential could be exposed to the lice asphyxiator drug product while applying the drug product to the hair of affected children or to themselves. Therefore, it is recommended that embryofetal developmental studies be conducted in both a