



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

IND 50,076

Summers Laboratories  
Attention: Glen Park, Pharm.D.  
Senior director, Clinical & Regulatory Affairs, Target Health Inc.  
261 Madison Avenue, 24<sup>th</sup> Floor  
New York, NY 10016

Dear Dr. Park:

We refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for 5% Lice Asphyxiator.

We also refer to your September 16, 2005, request, serial number 018, for a special clinical protocol assessment, received September 19, 2005. The protocol is entitled "A Multi-center, Randomized, Vehicle Controlled, Double Blind Clinical Trial to Evaluate the Efficacy and Safety of Summers Non-Pesticide Lice Asphyxiator (5% L.A.) for the Treatment of Head Lice."

We have completed our review of your submission and, based on the information submitted, have the following responses to your questions.

**Clinical**

1. The sponsor is again requested to complete their non-clinical studies prior to the initiation of Phase 3, as was discussed in the teleconference of May 18, 2005, so that the Phase 3 study may be conducted in such a way that it would be consistent with the anticipated labeling for pregnant and lactating women. In the absence of nonclinical reprotox studies, pregnant and lactating patients and caretakers would need to be excluded from the study. This may result in restrictive labeling because pediculosis occurs in children and it is likely that caretakers of reproductive age may be exposed to the drug.
2. Merely demonstrating statistically significant superiority over vehicle may not be sufficient to garner approval for this product. The sponsor needs to demonstrate a clinically meaningful effect. Please describe the difference that you would consider to be clinically meaningful. Since your study is powered to detect a 30 percent difference we could assume that this would be clinically meaningful.
3. The primary timepoint for evaluation, 14 days after the last treatment, is acceptable.

4. The primary endpoint, treatment success defined as the absence of live lice, is acceptable.
5. All safety assessments and any evaluations to determine whether dosing occurs must be performed by a licensed prescriber.
6. At the first and second evaluation visits please weigh rather than visually estimate, to the nearest ¼ bottle, any remaining product to assess compliance.
7. The time window (within 72 hours of treatment) for safety evaluation is too large. The sponsor should propose a single time point (e.g. 1 hour or 24 hours after treatment) for safety evaluation, a time at which side effects are most likely to be observed.
8. The Division prefers that the ITT population be defined as all patients randomized and dispensed study drug irregardless of whether they have received a dose of the drug.
9. Please submit Form 1572 prior to study initiation. Additionally please provide the name and credentials of the licensed prescribers who will be responsible for study drug administration.
10. Please specify in which languages, in addition to English, the consent form will be available.

### **Biostatistics**

1. The primary efficacy analysis indicates that the goal of the study is to show that the proportion of subjects achieving treatment success in the Summers 5% L.A. arm is significantly higher than the proportion in the vehicle arm. It should be noted that statistical superiority of Summers 5% L.A. over vehicle by itself is not sufficient for approval. The Phase 3 trial is powered to detect treatment effect of 30% (with expected response rate of 40% for the vehicle and 70% for L.A.). The goal of the study should be establishing superiority over the vehicle with efficacy margin of at least 30% (see clinical comments).
2. The protocol in Section 14.4.3 under 'Additional Analysis' lacks specificity of the utility of the proposed logistics regression and testing for center-by- treatment interaction. For significant center-by-treatment interaction the protocol should propose an approach to carrying out a sensitivity analysis in this case to ensure efficacy results are not driven by extreme centers, such as carrying out the analysis after excluding extreme center(s).
3. Efficacy evaluation of the secondary endpoint (cumulative proportions of subjects determined to be treatment failure) at multiple visits raise the need for multiplicity adjustment. To reduce the impact of multiplicity adjustment, secondary endpoints should be limited to clinically relevant endpoints and their number should be very small.
4. The Division re-iterates the previous comment conveyed to the sponsor on May 19, 2005 that the protocol should provide details about randomization including block size. The treatment allocation list should be generated prior to study enrollment.

5. For safety analysis the lack of statistical significance when testing does not imply 'similarity' as the study is not powered for safety parameters.

If you wish to discuss our responses, you may request a meeting. Such a meeting will be categorized as a Type A meeting (refer to our "*Guidance for Industry; Formal Meetings With Sponsors and Applicants for PDUFA Products*"). Copies of the guidance are available through the Center for Drug Evaluation and Research from the Drug Information Branch, Division of Communications Management (HFD-210), 5600 Fishers Lane, Rockville, MD 20857, (301) 827-4573, or from the internet at <http://www.fda.gov/cder/guidance/index.htm>. This meeting would be limited to discussion of this protocol. If a revised protocol for special protocol assessment is submitted, it will constitute a new request under this program.

If you have any questions, call Melinda Harris-Bauerlien, M.S., Project Manger, at 301-796-2110.

Sincerely,

*{See appended electronic signature page}*

Stanka Kukich, M.D.  
Acting Director  
Division of Dermatology & Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Stanka Kukich

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Target Health, Inc. for Summers Laboratories, Inc.  
Attention: Glen Park, Pharm.D., Regulatory Affairs  
261 Madison Avenue, 24<sup>th</sup> Floor  
New York, NY 10016

Dear Dr. Park:

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 August 8, 2005. The purpose of the meeting was to discuss the sponsor's Phase 3 protocols.

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 III  
Center for Drug Evaluation and Research

Enclosure