DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-129

Sciele Pharma, Inc.
ATTENTION: Debra Hayes, RAC
Five Concourse Parkway
Suite 1800
Atlanta, GA 30328

Dear Ms. Hayes:

Please refer to your new drug application (NDA) dated June 15, 2007, received June 15, 2007, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for TRADENAME (benzyl alcohol) Lotion 5%.

We acknowledge receipt of your submissions dated July 19, August 31, September 17, September 21, September 28, October 12, and December 28, 2007; January 25, February 5, March 4, March 19, April 14, May 23, and June 5, 2008.

We also acknowledge receipt of your submission dated July 10, 2008. This submission was not reviewed for this action. You may incorporate this submission by specific reference as part of your response to the deficiencies cited in this letter.

We completed our review of this application, as amended, and it is approvable. Before the application may be approved, however, it will be necessary for you to address the following:

> The in-vivo pharmacokinetic study SU-01-2007 resulted in a number of plasma concentrations of benzyl alcohol. While the median value of all 32 positive samples was ~2.7ug/mL, the upper quartile of them were above 48 ug/mL. Because the plasma concentrations of benzyl alcohol observed are sporadic, it is difficult to adequately interpret the observed high concentrations of benzyl alcohol. Since these plasma concentrations of benzyl alcohol are used to support the systemic safety of the drug product, it is important that you provide further clarification (e.g. are they true representative concentrations) as to why these plasma concentrations were observed and their potential safety impact, including but not limited to, a discussion vis a vis the reported association of plasma levels of benzyl alcohol and infant gasping syndrome.

Also, it will be necessary for you to submit draft labeling. The draft texts for the package insert and the patient package insert should be revised according to the enclosed labeling. The draft texts for the immediate container and carton labels should be revised as follows.

1. Delete the proposed tradename, **(b) (4)**

2. Change the dosage form statement from (b) (4) "Lotion."

3. Delete the (b) (4) designation after the dosage form statement.

4. Relocate the wording (b) (4) from the side panel of the carton label to the principal display panel and increase the size of the wording to make it more prominent on the label. Consider rewording this statement to (b) (4) in order to make the warning more specific.

5. Add "Warning: Keep out of reach of children" on both the immediate container and carton labels to help prevent accidental oral ingestion of the product. Also, consider adding the warning, "Harmful if swallowed" to both the immediate container and carton labels.

6. The instructions for use in the Dosage and Administration, as presented on the side panel of the carton label, are incomplete. Revise the statement, (b) (4) to "See package insert, including the patient information section, for complete information."

7. Delete Product Description, including the indication statement. Reword the section as follow: Contents Description: TRADENAME is supplied as a white topical lotion containing benzyl alcohol, 5%. Inactive ingredients in this formulation are water, mineral oil, sorbitan monooleate, polysorbate 80, carbomer 934P and trolamine.

8. Decrease the size of the distributor's name logo.

9. Increase the size of the statement of strength "8 oz. (227 g)," slightly, in order to increase its visibility on the label.

10. Add Lot #, Expiration Date, and barcode on the immediate container label.

In addition, your container/closure proposal, consisting of an orifice reducing plug (b) (4) and current cap, should be implemented.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

During a recent inspection of the manufacturing facility for this application, our field investigator conveyed deficiencies to the facility's representative. Satisfactory resolution to these deficiencies is required before this application may be approved.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all non-clinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.

2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

   - Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.
   - Present tabulations of the new safety data combined with the original NDA data.
   - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
   - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

3. Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.

4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.

5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.

6. Provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries.

Provide English translations of current approved foreign labeling not previously submitted.

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
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Maria Walsh, Project Management Officer, at (301) 796-1017.

Sincerely,

{See appended electronic signature page}

Daniel Shames, M.D.
Deputy Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

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

/s/

Daniel A. Shames
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