

## MEMORANDUM OF TELECON

**Date:** December 23, 2008

**Time:** 9:30 a.m.

**Application:** NDA 22-129, Tradename (benzyl alcohol) 5% lotion

**Meeting Chair:** Jill Lindstrom, M.D., Clinical Team Leader

**Meeting Recorder:** Nichelle Rashid, Regulatory Project Manager

### FDA Participants:

Jill Lindstrom, M.D., Clinical Team Leader, DDDP  
Gordana Diglisic M.D., Clinical Reviewer, DDDP  
Shulin Ding, Ph.D., Pharmaceutical Assessment Lead, ONDQA  
Tarun Mehta, Ph.D., Chemistry Reviewer, ONDQA  
Margo Owens, Project Management Team Leader, DDDP  
Nichelle Rashid, Regulatory Project Manager, DDDP  
Jeannie David, Regulatory Project Manager, ONDQA

### Applicant:

#### Sciele Pharma, Inc.

Debra Hayes, Regulatory Affairs Manager, Sciele  
Allison Lowry, Sr. Regulatory Manager, Sciele  
Larry Dillaha, MD, EVP and Chief Medical Officer, Sciele  
Mike Precopio, President, Summers Laboratories  
John Colyar, VP Manufacturing and Development

### Background:

Sciele Pharma, Inc. submitted a complete response to the Approvable Letter issued on October 17, 2008 for NDA 22-129, Tradename (benzyl alcohol) 5% lotion. In an email dated December 15, 2008, the applicant requested a telecon to discuss a change in drug substance container/closure system. The change was triggered by a 483 observation made by the (b) (4) in the first cycle review during the GMP inspection on the drug substance manufacturer, (b) (4). The applicant proposed to discuss in the telecon the submission of a CMC amendment for the change, and the content of the amendment.

The following points were discussed:

- The applicant stated that the change is with the (b) (4)
- The Agency asked how much drug substance stability data had been generated using the (b) (4). The applicant replied that (b) (4) had forwarded the 3 month of 25°C data from one drug substance lot. The applicant further stated that the stability study was a one year study, and had no accelerated temperature arms.
- The applicant stated their intent to include the 3 month 25°C data in the incoming CMC amendment to support the (b) (4), and agreed to put on stability three drug product batches made of the drug substance stored in the (b) (4)
- The applicant also agreed to conduct full release testing on drug substance before releasing for compounding of the drug product.
- The Agency informed the applicant that the retest date of the drug substance lots would be re-assessed.
- The Agency requested the applicant to make sure that the drug substance DMF would be submitted in a timely manner to allow adequate review time. The applicant estimated that the DMF could be amended by (b) (4) by end of December.
- FDA requested the applicant to amend the NDA in the following CMC sections for this change: container-closure system (S.6) , stability (S.7), and post-approval stability protocols (S. 7.7 and P.7.2).
- The Agency requested that the applicant submit their amendment to the NDA by no later than mid-January. The applicant agreed.

The discussion ended amicably.

#### ADDENDUM

The applicant submitted an amendment with the agreed upon changes on December 29, 2008.

The applicant conveyed that (b) (4) filed the update to DMF (b) (4), benzyl alcohol, NF on January 2, 2009.

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/s/

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Nichelle Rashid  
2/27/2009 01:55:33 PM  
CSO

Jill Lindstrom  
2/27/2009 03:21:32 PM  
MEDICAL OFFICER

## MEMORANDUM OF TELECON

**Date:** August 8, 2008  
**Time:** 2:30 – 3:30 p.m.  
**Application:** NDA 22-129 TRADENAME (benzyl alcohol) Lotion 5%  
**Meeting Chair:** Jill Lindstrom, M.D.  
**Meeting Recorder:** Dawn Williams, R.N.

### FDA Participants:

#### Office of Drug Evaluation III

Maria Walsh, M.S., Project Management Officer

#### Division of Dermatology and Dental Products

Jill Lindstrom M.D., Medical Team Leader

Gordana Diglisic, M.D., Medical Officer

Dawn Williams, R.N., Regulatory Project Manager

#### Office of Clinical Pharmacology

#### Division of Clinical Pharmacology III

Lydia Velazquez Ph.D., Clinical Pharmacology Team Leader

Abimbola Adebawale Ph.D., Clinical Pharmacology Reviewer

### Sciele Participants:

#### Regulatory Affairs

Stephanie Cook, M.S., RAC, Vice President

Larry Dillaha, M.D., Chief Medical Officer/Executive Vice President

Glenn Park, Pharm.D./Target Health, Inc.

### Background:

NDA 22-129, TRADENAME (benzyl alcohol) Lotion 5%, was submitted on June 15, 2007 for the treatment of head lice. An approvable letter was issued on July 14, 2008 which included the following deficiency:

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 48ug/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 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.

The sponsor requested today's teleconference to discuss this deficiency further and to discuss possible ways to adequately address it.

**Discussion:**

The sponsor explained that according to the protocol, an indwelling intravenous catheter was to be placed into each subject participating in the trials. In some subjects, a catheter could not be successfully placed. The intravenous catheters were flushed at least once with a ½ cc of bacteriostatic saline solution to maintain patency. The saline flush product used was preserved with benzyl alcohol which could account for the observed plasma concentrations of benzyl alcohol.

The sponsor reported that consulting neonatologists stated that infant gasping syndrome was usually caused by a metabolic acidosis in premature neonates. According to the sponsor, the neonatologists were not aware of any cases of infant gasping syndrome associated with topical products containing benzyl alcohol.

In response to FDA's question about documentation regarding the administration of the saline flush product, the sponsor said the medical charts state that the product used for flushing the catheters was bacteriostatic saline preserved with benzyl alcohol. However, the medical charts do not provide details on the administration of the saline flushes regarding amount used and frequency. The information relayed today is based on the memory of the phlebotomy team. FDA advised the sponsor to respond to the deficiency as comprehensively as possible. The sponsor will need to decide whether there is enough information to adequately address the concerns about the observed plasma concentrations of benzyl alcohol and infant gasping syndrome or whether another study is warranted.

The sponsor asked whether an abbreviated pharmacokinetic study would be adequate to address the deficiency so as to reduce the number of intravenous punctures to the infants. The FDA advised the sponsor that a proposed protocol summary may be submitted for review.

The sponsor asked if it were acceptable to address this issue in a less formal way prior to submitting a complete response. FDA reiterated that a proposed protocol summary may be submitted for review. FDA also reminded the sponsor that the complete response must also address the manufacturing facility deficiencies.

The sponsor acknowledged the need to address the manufacturing facility deficiencies. They also verbalized understanding that they needed to adequately address the observed plasma levels of

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benzyl alcohol and infant gasping syndrome or complete another study.

The call was then concluded.

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Dawn Williams, RN, BSN

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Jill Lindstrom, M.D.

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/s/

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Dawn Williams  
4/1/2009 06:31:35 AM  
CSO

Jill Lindstrom  
4/6/2009 01:36:21 PM  
MEDICAL OFFICER

## MEMORANDUM OF TELECON

DATE: 3/3/08, 1:00 P.M.

APPLICATION NUMBER: NDA 22-129

DRUG PRODUCT: Lice Asphyxiator, 5% (b) (4)

**BETWEEN:**

Name: Mike Precopio, President, Summers Laboratories  
John Colyar, Vice President, Summers Laboratories  
Larry Dillaha, M.D. EVP and Chief Medical Officer, Sciele  
Pharmaceuticals  
Dan Tokich, Director Supplier Management, Sciele Pharmaceuticals

Representing: Summers Laboratories

**AND**

Name: Division of Dermatology and Dental Products  
Jill Lindstrom, M.D., Clinical Team Leader, Dermatology  
Gordana Diglisic, M.D., Clinical Reviewer  
Shulin Ding, Ph.D., PAL, OPS, ONDQA  
Tarun Mehta, Ph.D., CMC Reviewer, ONDQA  
Melinda Bauerlien, M.S., Regulatory Project Manager

SUBJECT: NDA 22-129

The teleconference was requested by the sponsor to discuss issues regarding the container for the product.

The sponsor stated that they have been looking at (b) (4). They have been unable to find a (b) (4). They have found an (b) (4). When the label is placed on the bottle, there is a 1 inch window where the patient can see the level of material in the bottle.

The Agency responded that at this time they cannot give feedback or agreement on the (b) (4) bottle. The sponsor should provide the following items for the new bottle:

- A comparison of dimention, thickness and resin/colorant between the 2 bottles.
- The manufacturer and DMF number for the new bottle.
- Information on the vapor permeability of the bottle.

- For the 2 pivotal trials and the open label safety, provide the mean and median values of 5% LA used as a single application by category of hair length for the safety population.
- Provide the demographics and hair characteristics of safety population for the 3 studies.

The conversation ended amicably.

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/s/

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Melinda Bauerlien  
5/1/2008 02:06:55 PM  
CSO

Jill Lindstrom  
5/1/2008 02:21:39 PM  
MEDICAL OFFICER