DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

FDA Docket No. FDA-1975-N-0012

GENERAL ADVICE

Lewis & Harrison
Attention: Eliot Harrison
Consultant to Lonza, Inc and Henkel Consumer Goods, Inc
122 C Street, NW, Suite 505
Washington, DC 20001

Dear Mr. Harrison:

We refer to your July 10, 2015 submission containing a revised human pharmacokinetics protocol for benzethonium chloride. This protocol (TM&R-0250-14-TXC) is entitled: *A Maximal Use Study to Measure the Systemic Absorption of Benzethonium Chloride after Using the Antimicrobial Soap on Intact and Abraded Skin in Healthy Volunteers.*

You submitted this protocol on behalf of Lonza, Inc., and Henkel Consumer Goods, Inc. The protocol was originally submitted on December 13, 2014 and has been updated based on feedback at the May 6, 2015 public meeting between Lonza, Inc. and the FDA.

We have reviewed the referenced material and have the following comments based on your revised protocol:

1. The duration of the protocol is not sufficient. As designed, the protocol includes dosing for only three days. Given the average healthcare worker works approximately 8 hours per day five days a week, extend the dosing period to at least five days. This recommendation reflects the upper end of expected use in keeping with the MUsT paradigm.
2. While acknowledging that "efforts" will be made to enroll subjects above the age of 65, we recommend that the protocol identify a dedicated cohort (numerically) of subjects within this age group for enrollment purposes.
3. For inclusion in the monograph, GRASE must be established for a single ingredient that can be formulated in many different ways and presentations. Therefore, in order to support GRASE status of an ingredient, we recommend testing of at least 4 different formulations in the MUsT. Regarding choosing the representative material for testing, we recommend testing formulations anticipated to enhance absorption. In vitro testing using a human cadaver skin permeation system (e.g., static or flow-through cells)[1] may be useful in choosing and providing justification of which formulations to test.

[1] Bronaugh R and Stewart F, 1985, Methods for In Vitro Percutaneous Absorption Studies IV: The Flow-Through Diffusion Cell, J. Pharm. Sci, 74(1), 64-67.

4. Provide additional details regarding the selection of the antimicrobial hand soaps to be used in this study. Specify whether each formulation is a currently marketed formulation or one specially formulated for this study, the rationale for selecting the formulations, and the composition of the formulations (quantity and function of the active and inactive ingredients).

If you have any questions, call Celia Peacock, Senior Regulatory Project Manager at (301) 796-4154.

Sincerely,

Theresa M Michele, MD

Theresa Michele, MD
Director
Division of Nonprescription Drug Products
Office of Drug Evaluation IV
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