LOG OF MEETING

SUBJECT: Musk Xylol

DATE: March 21, 1996

TIME: 10:00 a.m. to 12:30 p.m.

PLACE: Commissioner's Conference Room, U.S. Food and Drug Administration (FDA), 200 "C" St., S.W., Washington, DC

ENTRY SOURCE: Michael A. Babich, EHHE MAB

COMMISSION REPRESENTATIVE: Michael A. Babich, ESHE

FOOD and DRUG ADMINISTRATION REPRESENTATIVES: David Hattau, Karen Ekelman, Bob Bronaugh, Ronald W. Moch, Prem N. Dua, Harris H. Wisneski, Donald C. Havery, John Bailey, and Ron Lorentzen.

NON-FEDERAL REPRESENTATIVES: Emil A. Pfitzer, Research Institute for Fragrance Materials, and Lois Lehman-McKeeman, Procter and Gamble.

Summary:

This meeting was requested by the Research Institute for Fragrance Materials (RIFM). Dr. Pfitzer, RIFM, presented an overview of musk xylol (MX) and other nitro musk fragrances. They are used in cosmetics, toiletries, and household detergents. Substitutes are not readily available. RIFM plans to conduct a use inventory of its member companies in the spring. MX is carcinogenic in male and female mice. Musk ambrette, which is no longer used, is a male reproductive toxicant. Nitro musks have been found in the environment and in human breast milk. Dr. Lehman-McKeeman, Procter and Gamble, presented results of mechanistic studies on MX. MX resembles phenobarbital in some of its effects on the mouse liver. The role of mechanistic information in hazard identification and risk assessment was discussed. Dr. Pfitzer provided some written materials, which will be distributed by FDA. A meeting agenda and list of attendees are attached.

attachments:

Presentation on Nitromusk Fragrances:

Mechanistic Studies on Mouse Liver Tumors with Musk Xylene

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Introduction and Background (10 minutes)

- comparative structures of nitromusks
- history of musk ambrette
- comparative toxicity of nitromusks
- occurrence in environmental media
- milk transfer study in rats
- risk assessment considerations
- carcinogenicity in $B6C3F_1$ mice
- studies supporting nongenotoxicity

Mechanistic Studies with Nitromusks (35 minutes)

- enzyme induction with musk xylene
- mechanism-based inactivation of P450
- potential for amine metabolites
- significance of mouse liver tumors

Discussion (15 minutes)

- scientific basis for the significance of secondary mechanisms relevant to cancer in rodents
- potential needs for further research

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