UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

008642

OCT - 8 1991

MEMORANDUM:

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Review of a data package and label for Silver Copper Zeolite.

TOX. CHEM. NO.: 129057 HED PROJECT NO.: 1-0266

FROM: SanYvette Williams, D.V.M. 9/27/91
Review Section IV, Tox. Branch II (H7509C)

TO: Valdis Goncarous/John Lee, PM 17
Registration Division

THRU: Elizabeth Doyle, Ph.D. E A Doyle 9/27/91
Section IV, Tox. Branch II (H7509C)

and

Marcia van Gemert, Ph.D., Chief 9/27/91
Toxicology Branch II
Health Effects Division (H7509C)

Registrant: Kanebo Zeolite, USA, Inc.

Action Requested:

Toxicology was requested to review their data package. They also wished the label to be reviewed and an outline of any additional data requirements for Silver Copper Zeolite.

A. Toxicology Branch II has completed the review of all toxicology studies submitted by the Registrant on Silver Copper Zeolite. The conclusions of study findings are as follows:

1. Developmental Toxicity (#83-3)
Accession No: 416385-02

Maternal toxicity was evidenced at 2000 mg/kg by reduced body weight gain. Daily observations also indicated that silver copper zeolite was having an effect on the high dose animals. Developmental toxicity was observed at 2000 mg/kg as skeletal variations.

This study does not satisfy guideline requirements (#83-3) for a developmental

toxicity study. It can be upgraded with the submission of historical control data.

Maternal NOEL = 700 mg/kg
Maternal LOEL = 2000 mg/kg based on reduced body weight gain.
Developmental Toxicity NOEL = 700 mg/kg
Developmental Toxicity LOEL = 2000 mg/kg based on abnormal fetuses from a dam that exhibited signs of maternal toxicity.

Classification: Supplementary

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2. In vivo mammalian cytogenetics assay in Sprague-Dawley rats (84-2)
Accession No.: 416158-10

The administration of Silver Copper Zeolite by oral gavage did not induce a significant increase in chromosomal aberration in the male and female rats at the 6-, 18- and 24-hour exposure periods. It was, therefore, considered to be non-clastogenic in Sprague-Dawley rats at the dose levels tested (500, 1500 and 5000 mg/kg).

This study satisfies requirements according to guidelines (84-2) for an in vivo mutagenicity study.

Classification: Acceptable

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3. Salmonella/mammalian activation gene mutation assay (84-2)
Accession No: 416158-08

After a preliminary assay and three subsequent assays to determine whether Silver Copper Zeolite was able to induce mutations in Salmonella typhimurium in the presence and absence of a metabolic activation system, it was determined that this substance was not mutagenic to TA98, TA100, TA1535 and TA1537 strains of Salmonella typhimurium at the concentrations tested (0.005 to 0.15 mg/plate without activation; 0.005 to 1.5 mg/plate with activation.

This study satisfies requirements according to guidelines for a mutagenicity study (84-2).

Classification: acceptable.

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4. Mammalian cells in culture cytogenetics assay in Chinese hamster ovary) cells (#84-2)
Accession No.: 416158-09

Silver Copper Zeolite was tested for its ability to induce chromosomal damage in vitro using Chinese hamster ovary (CHO) cells using both activated and

nonactivated assays. Although there was no increase in the percentage of aberrant cells in the non-activated assays, there was a significant increase in the 10-hour activated assays. At the 75, 100 and 125 ug/ml concentrations, during the 10-hour activated assay, there was a statistically significant increase in the percentage of aberrant cells.

This study satisfies requirements according to guidelines for a mutagenicity study (84-2).

Classification: acceptable.

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5. Eye Irritation in Rabbits (#81-4)
Accession No: 416385-01

Based on the no rinse group mean irritation scores, Silver Copper Zeolite is considered to be a moderate (Mean irritation scores > 6.0 at 24 hours, but maximum mean irritation score ≤ 30.0 and any corneal or iridial changes having been totally reversed by day 14) ocular irritant in the rabbit (Tox. Category III).

III

This study satisfies the data requirements for according to guidelines (#81-4).

Classification: Guideline.

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6. Acute oral toxicity in rats (#81-1)
Accession No.: 416158-02

IV

Based on results of this study, the LD50 for Silver Copper Zeolite seems to be greater than 5 g/kg in male and female rats. It is considered to be very low in toxicity (Tox. Category IV).

This study satisfies the requirements according to guidelines for an acute oral toxicity (#81-1).

CLASSIFICATION: Core - Minimum

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7. Acute dermal toxicity in rabbit (#81-2)
Accession No.: 416158-03

IV

Based on results of this study, the acute dermal LD50 toxicity for Silver Copper Zeolite is considered to be greater than 5 g/kg (Tox. Category IV).

This study satisfies requirements for an acute dermal toxicity study according to guidelines (81-2).

Classification: Guideline.

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8. Primary Dermal Irritation in Rabbit (#81-5)
Accession No: 416158-05

IV

Based on results of this study, Silver Copper Zeolite, when applied to the skin for four hours, is regarded as a slight skin irritant (P.I.I. = 0.08).

This study satisfies guideline requirements for a primary dermal irritation study (81-5).

CLASSIFICATION: Core - Guideline

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9. 13-Week Sub-Chronic Dermal Toxicity Study on Silver-Copper Zeolite in the Rat (#82-3)
Accession No.: 416158-07

After dermal exposure to Silver Copper Zeolite at concentrations of 100, 300 or 1000 mg/kg for a period of 90 days, test animals were found to exhibit no signs of toxicity. Under conditions of this study, Silver Copper Zeolite is not toxic by dermal exposure at doses as high as 1000 mg/kg (limit dose). The NOEL is greater than 1000 mg/kg.

This study satisfies requirements according to guidelines for a 13-Week Subchronic Dermal Toxicity study (82-3).

Classification: guideline.

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10. Acute Inhalation Study in Rats (#81-3)
Accession No.: 416158-04

The results of this study indicate that the acute inhalation LC50 for Sprague Dawley rats exposed to the highest attainable concentration of Silver Copper Zeolite by whole body exposure is greater than 2.59 mg/liter. [Tox. Category III]

This study satisfies guideline requirements for an acute inhalation study according to Guideline #81-3.

Classification: guideline.

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11. Guinea Pig sensitization (#81-6)
Accession No: 416158-06

Based on results of this study, a 60% suspension (in 0.5% Carboxymethyl

cellulose) of Silver Copper Zeolite would be regarded as a non-sensitizer on guinea pigs according to the Buehler method of testing.

This study satisfies guideline requirements for a guinea pig sensitization study (81-6).

CLASSIFICATION: Core - Guideline

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12. Leaching (#163-1)
Accession No.: 416158-18

The concentrations of silver and copper in the leachates generated in this study are below U.S. EPA drinking water guideline (50 ug/L) for silver and the ambient water quality criterion (1000 ug/L) for copper.

This study does not conform to guidelines for a leaching study (#163-1). Leaching should also be performed at neutral and basic pH's in order to mimic effects of body fluid, toiletries or laundry products.

CLASSIFICATION: Core - supplementary.

B. The concentrations of copper and silver from leaching were below U.S. EPA drinking water guidelines for silver and the ambient water quality criterion for copper. Assuming: a) an average man consumes 2 liters of water per day and that the accepted amount of each in drinking water is 100 ug/day (silver) and 2000 ug/day (copper) and b) the average weight of a pair of men's underwear impregnated with silver copper zeolite is approximately 0.3 kg/pair. It can be concluded that the potential amounts of exposure to silver and copper would be 48 ug/day and 630 ug/day. This does not take into account other impregnated clothing worn that would cause these levels to increase. It also does not give much margin of safety especially if inputs occur from other sources such as drinking water or jewelry. Due to variations in physiological conditions, pH's at the neutral and basic levels need to evaluated.

C. In regard to the use, the Agency has these concerns or stipulations:

APPLICATION

Plastic film - not if it is for food use.
polyethylene, polyvinyl chloride, polyacetate, polyester, polypropylene (no water pipes)

Paper - no food contacts

Synthetic fiber - none in intimate clothing without evaluation of pH at 8 or more. In addition, documentation showing that silver is not absorbed dermally, otherwise a dermal penetration study might be requested.
polyester, nylon, polypropylene, acrylic and rayon

Textile finishing and manufacturing - documentation showing that silver is not absorbed dermally, otherwise a dermal penetration study might be requested.