Silver Acetate

[§83-3] Developmental Toxicity/Rat

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DATA EVALUATION RECORD

STUDY TYPE: Prenatal Developmental Toxicity/Rat; OPPTS 870.3700 [§83-3]

DP BARCODE: DP316623
PC CODE: 072506

DECISION No.: 353040
REGISTRATION No.: Section 3

TEST MATERIAL (PURITY): Silver Acetate (purity unknown)

SYNONYMS: N/A

CITATION: NTP study, (2002). Development Toxicity Evaluation for Silver Acetate (CAS No. 563-63-3) Administered by Gavage to Sprague-Dawley (CD^R) Rats on Gestation Days 6-19. NTP Study: TER 20001, NTIS# PB2002-109208. Sept. 3, 2002. MRID 464533-06. Published.

SPONSOR: Eastman Kodak Co., Health Science and Environment, Rochester, NY 14652
SUMMITTER: Ag-Chem Consulting LLC, 1208 Quinque Lane, Clifton, VA 20124

EXECUTIVE SUMMARY: A Prenatal Developmental Study (MRID 464533-06) was conducted using female Sprague-Dawley derived (CD^R) rats, dosed by gavage, with silver acetate (Purity not given) in 1% aqueous methylcellulose (10, 30 or 100 mg/kg/day) or vehicle on gd 6 through 19.The dose levels used were based on a screening study.

One animals was removed from the high dose group due to a dosing accident , and another animal (confirmed pregnant) in the high dose group was euthanized on gd 12 due to morbidity. All remaining females survived until scheduled sacrifice on gd 20. Pregnancy was confirmed in 21 - 25 females per group (i.e. 87.5 - 100.0% per group) after necropsy on gd 20.

Treatment-related clinical signs were few. piloerection was noted.

Maternal body weight was comparable among groups. as was maternal body weight change. A significant ($p<0.05$) decreasing linear trend was noted for maternal body weight on gd 12. but there was no statistically significant differences between the control group and any silver acetate treated group. Maternal body weight change corrected for gravid uterine weight gravid uterine weight and absolute and relative maternal liver weigh were each unaffected by treatment with silver acetate.

Maternal absolute feed consumption did not exhibit any dose-related trends, but was significantly decrease sat the mid dose of silver acetate, but not at the low and high dose, on gd 12 to 15, 15 to 18, 6 to 20 and 0 to 20. Relative maternal feed consumption (mg/kg/day) sill did no exhibit any dose-related trends and was significantly decreased at the mid dose compared to the control group only on gd 12 to 15, and 0 to 20. Similarly, but to a lesser extent, absolute maternal water consumption was decreased at the mid dose on gd 12 to 15 and 15 to 18. Relative maternal water consumption (g/kg/day) exhibited no significant differences from the control group for any silver acetate-treated group.

There were no differences among groups for the number of ovarian corpora lutea/dam, number of implantation sites/liter, or percent of pre-implantation loss/ litter. Post-implantation loss (resorptions, late fetal deaths or non-live implants/litter, live litter size and percent/ male fetuses/litter did not differ among groups. An increasing trend was observed for the percent litters with late fetal deaths. Average body weight per litter (sexes combined) and average male fetal body weight per litter exhibited a significant decreasing trend , but no significant pair wise differences. between the silver acetate-treated groups and the control group. No statistical significant effects were noted for average female fetal body weight.

No toxicologically relevant differences were observed in the incidences of fetal malformations or variations. The percent female fetuses with malformations per litter exhibited a significant dose effect, but no significant trend or pairwise differences between the control and silver acetate treated group.

In summary, the maternal **NOAEL** for this study was considered to be >100 mg/kg/day (HDT) of silver acetate (64.6 mg silver/kg/day) based on the absence of any statistical significant developmental toxicity. A **LOAEL** was not determined. The **NOAEL** for developmental toxicity for this study was >100 mg/kg/day silver acetate (64.6 mg/kg/day silver (HDT), based on the absence of any statistical significant developmental toxicity. A **LOAEL** was not determined.

Conclusions: The conclusions of the NTP abstract were modified by the reviewer to conform to the accepted Agency's guidelines. Specifically, the maternal **NOAEL** was increased to >100 mg/kg/day (HDT) of silver acetate for both the maternal and developmental phases. **LOAEL's** were not determined. Some elements required by the Agency's guidelines seem to be missing, and the interpretation is difficult using only the abstract.

The prenatal developmental study in the rat can be used for supplemental information and clearly indicates that there are no maternal or developmental effects at a dose level substantially higher (13,000X) than the RfD dose for silver (5 mg/kg/day) that causes arygria a discoloration of the skin or mucosal surfaces through the deposition of silver in the tissues. (Note: Silver acetate contains 64.6% silver by weight. Therefore, the lowest dose (100 mg/kg/day as silver acetate) was equivalent

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The study is classified as **Acceptable** and meets the **Guideline** for a developmental study (OPPTS 870.3700 in the rat.

COMPLIANCE: The developmental study with Silver Acetate does not meet the requirements of 40CFR Part 160 and differs in the following ways.

1. No inspections were conducted.
2. No audits were conducted on this report.