

8EHQ-0203-15272



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ATOFINA Chemicals, Inc.

January 31, 2003

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Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460



8EHQ-03-15272

Attn: Section 8(e) Coordinator

Contain NO CBI

Dear Sir/Madam:

ATOFINA Chemicals, Inc. (ATOFINA) is submitting the enclosed summary from a study on prenatal developmental toxicity in rats to the Environmental Protection Agency (EPA) pursuant to Toxic Substances Control Act (TSCA) Section 8(e). The study provides information on triphenyl phosphine (CAS No. 603-35-0). This study does not involve effects in humans.

Nothing in this letter or the enclosed study summary is considered confidential business information of ATOFINA.

The test substance was administered by gavage to pregnant female Wistar rats on day 6 through day 19 of gestation at doses of 0, 10, 30 and 90 mg/kg/day. No treatment-related adverse developmental effects or birth defects were observed. At the high-dose level only, signs of significant maternal toxicity were observed with some slight, but statistically significant increases in delayed ossification in offspring. Since (i) the study director indicated that the changes observed in the high-dose offspring occur very frequently in gestation day 20 rat fetuses and do not constitute an adverse effect, (ii) the slight transient delays in ossification were scattered throughout different parts of the skeleton making no particular pattern that would be indicative of a certain organotropy, and (iii) the overall rate of skeletal variations was substantially similar between control and substance-treated groups, it is ATOFINA's opinion that the nature and extent of the effects observed do not reasonably support a conclusion of substantial risk.

Although ATOFINA does not believe that this information constitutes a substantial risk, the present submission is intended to discharge any 8(e) responsibilities that might exist with regard to the statistical analysis of these findings.

Further questions regarding this submission may be directed to me at (215) 419-5890.

Sincerely,

Debra Randall, D.A.B.T.
Product Safety Manager

Enclosures

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1. SUMMARY

1.1. METHODS

Triphenylphosphin was tested for its prenatal developmental toxicity in Wistar rats. The test substance was administered as an aqueous suspension to 25 presumably pregnant female Wistar rats/group by stomach tube at doses of 10; 30 and 90 mg/kg body weight on day 6 through day 19 post coitum (p.c.). A standard dose volume of 10 ml/kg body weight was used for each group. The control group, consisting of 25 females, was dosed with the vehicle only (0.5% Carboxymethylcellulose in doubly distilled water). Between 22 - 23 females/group had implantation sites at terminal sacrifice.

Food consumption and body weights of the animals were recorded regularly throughout the study period. The state of health of the animals was checked each day.

On day 20 post coitum, blood was taken from 12 females/group, which were subsequently sacrificed like the remaining rats and assessed by gross pathology (including weight determinations of the unopened uterus, the liver and the placentae). For each dam, corpora lutea were counted and number and distribution of implantation sites (differentiated as resorptions, live and dead fetuses) were determined. The fetuses were removed from the uterus, sexed, weighed and further investigated for any external findings. Thereafter, nearly one half of the fetuses of each litter was examined for soft tissue findings and the remaining fetuses for skeletal (incl. cartilage) findings.

1.2. RESULTS

The following substance-related findings were obtained:

Test group 3 (90 mg/kg body weight/day):

- statistically significantly reduced food consumption at initiation of dosing, i.e. on days 6 – 8 p.c. (about 21% below controls); food uptake reached or exceeded control values on the subsequent days
- statistically significantly impaired absolute body weight gain at initiation of dosing, i.e. on days 6 – 8 p.c. (about 54% below controls); weight gains reached or exceeded control values on the subsequent days
- decreased alanine aminotransferase activities
- statistically significantly increased absolute and relative liver weights (about 14% above controls)
- no substance-related adverse effects on gestational parameters or fetuses

Test groups 2 (30 mg/kg body weight/day):

- decreased alanine aminotransferase activities
- no substance-related adverse effects on gestational parameters or fetuses

Test group 1 (10 mg/kg body weight/day):

- decreased alanine aminotransferase activities
- no substance-related adverse effects on gestational parameters or fetuses

1.3. CONCLUSION

Under the conditions of this prenatal developmental toxicity study, the oral administration of Triphenylphosphin to pregnant Wistar rats from implantation to one day prior to the expected day of parturition (days 6 - 19 p.c.) elicited **substance-induced effects on the dams including signs of maternal toxicity** at 90 mg/kg body weight/day. At the low and mid dose (10 and 30 mg/kg body weight/day) the only effect on the dams was a decrease in alanine aminotransferase activity, which does not represent an adverse toxic effect.

The test substance had **no influence on gestational parameters** and induced **no adverse signs of developmental toxicity** up to and including the high dose level (90 mg/kg body weight/day); especially, **no indications of teratogenic effects** occurred which could be causally related to the test substance administration.

Based on these results, the **no observed adverse effect level (NOAEL) for maternal toxicity is 30 mg/kg body weight/day**. The **NOAEL for prenatal developmental toxicity is 90 mg/kg body weight/day**.