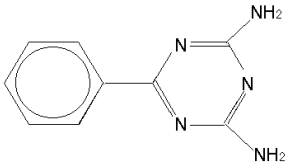
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	91-76-9
Chemical Name	2,4-diamino-6-phenyl-1,3,5-triazine
Structural Formula	

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

There is no available information on toxicokinetics and metabolism of this substance. The oral LD_{50} of rats was 933 mg/kg for males and 1231 mg/kg for females [OECD TG 401]. The major toxicity was edema in the forestomach. The LC_{50} value in the acute inhalation toxicity was 2.932 mg/L (4 hr, rat) [OECD TG 403]. This substance was not irritating to the skin in rabbits [OECD TG 404] and mildly irritating to the eyes in rabbits. There is no information on skin sensitization.

In the OECD combined repeat dose and reproductive/developmental toxicity screening test by gavage [OECD TG 422], this substance was given at 0, 4, 20 and 100 mg/kg/day to rats for at least 39 days. One male and one female rat died and the body weight gain was decreased in the 100 mg/kg group. Hematological and blood chemical examination showed decreases in the erythrocyte counts and hematocrit values with increased reticulocyte counts, and increases of GOT, GPT and total bilirubin with centrilobular hypertrophy of hepatocyte in the 100 mg/kg group. The severity of these changes, however, were toxicologically not significant or adaptive changes, except for the increase in reticulocyte count whose significance was equivocal. The NOAEL in this study was considered as 20 mg/kg/day.

In the 90-day feeding study of rats at 0, 1.9, 19.0, and 173.0 mg/kg/day [OECD TG 408], the body weight gain was decreased in the high dose group. In the histopathological examination, centrilobular hepatocyte enlargement, an increased severity of extramedullary hemopoiesis in the spleen and hemosiderin pigment accumulation in the kidneys and the spleen, hypertrophy and vacuolation of adrenal zona glomerulosa cells, and degeneration of pancreatic exocrine cells together with associated inflammatory cell infiltrates were observed in the high dose group. At the mid dose, the severity of hemosiderin pigment accumulation in the spleen was also increased moderately in males. This change in the spleen was considered not to be an adverse effect because no other changes were observed at this dose level. Therefore, the NOAEL in this study was considered to be 19 mg/kg/day.

On basis of these two studies, the NOAEL for repeated dose toxicity was considered to be 20 mg/kg/day.

For genotoxicity of this substance, there were two Ames tests, three non-bacterial *in vitro* studies, and two genotoxic *in vivo* studies reported. This substance was not mutagenic in bacteria [OECD TG 471 & 472]. It induced

chromosomal aberration in CHL/IU cells with and without an exogenous metabolic activation system even under the soluble concentrations. It also gave a positive response in the human lymphocyte test [OECD TG 473] and the mouse lymphoma TK assay [OECD TG 476] but only under the insoluble dose levels. The cytogenetic effect observed in *in vitro* assays however, could not be reproduced in the micronucleus tests *in vivo* [OECD TG 474]. Based on the weight of evidence, it could be concluded that this substance was not genotoxic *in vivo*.

For carcinogenicity, two dietary studies using male rats and male/female mice for 18 months showed no tumorigenic activity of this substance. However, these studies were considered to be insufficient for assessment of the carcinogenicity because of insufficient testing protocol compared to current test guidelines.

In the OECD combined repeat dose and reproductive/developmental (one generation) toxicity screening test [OECD TG 422], this substance was given for 49 days from 14 days before mating in males and from 14 days before mating to day 3 of lactation in females. At 100 mg/kg, one female died in gestation and another female was not impregnated. Birth index was decreased with increase in stillborns at 100 mg/kg. All pups of two dams at 20 mg/kg and seven dams at 100 mg/kg died due to the lack of nursing activity, and the viability index on day 4 after birth was consequently decreased in these groups. The body weights of pups were also decreased at birth and at day 4 of lactation in the 100 mg/kg group. The decrease of litter size observed at 100 mg/kg seems to be the chemical-induced effect although it is not statistically significant. No malformations or variations were observed in the pups.

From these results, the parental NOAEL of reproductive toxicity was considered to be 100 mg/kg/day for males, and 4 mg/kg/day for females, based on the lack of nursing activity, and the NOAEL of developmental toxicity was considered to be 20 mg/kg/day, based on the decrease of birth index and body weight of pups.

Environment

This substance (2,4-diamino-6-phenyl-1,3,5-triazine) is slightly soluble in water (320 mg/L at 25°C). The vapour pressure of this substance is estimated as very low (1.6×10^{-5}Pa at 25°C). This substance would be released into the aquatic environment from waste water, and distributed almost entirely in the water compartment from the calculation using the fugacity model [Mackey level III]. Although this substance is stable in water biotically and abiotically, this substance has a low potential of bioaccumulation based on BCF = 6.4, estimated from log Pow = 1.38.

In acute toxicity to aquatic species, the toxicity to algae [OECD TG 201] was 53.7 mg/L for EC50 (72 hr, *Selenastrum capricornutum*, biomass) and the toxicity to daphnids [OECD TG 202] was 52.0 mg/L for EC50 (48 hr, *Daphnia magna*, immobility). The toxicity to fish [other method] was 99 mg/L for LC_{50} (48 hr, *Leuciscus idus* (L.)).

In chronic toxicity to aquatic species, the toxicity to daphnids [OECD TG 211] was 1.91 mg/L for NOEC (21 day, *Daphnia magna*, reproduction). The toxicity to algae [OECD TG 201] was 24.4 mg/L for NOEC (72 hr, *Selenastrum capricornutum*, biomass).

PNEC = 0.0191 mg/L for the aquatic organisms was calculated from the 21 day – NOEC (1.91 mg/L) for *Daphnia magna* using an assessment factor of 100, because two chronic data (*Daphnia magna* and alga) were available.

Exposure

Production volume of this substance (2,4-diamino-6-phenyl-1,3,5-triazine or benzoguanamine) is estimated 3,000 t/y in Japan and 5,000 t/y world-wide in 2000. The producing countries are Japan, Germany and the People's Republic of China. This substance can be produced in closed systems. The main use is as an intermediate in benzoguanamine-formaldehyde resins whose applications are coatings, paints, thermosetting resins and others. In the case of coatings, the resins are used as outside and/or inside coatings of cans for storing foods and beverages.

The fugacity model suggests that if released from air or soil, the majority of this substance would distribute into the water and soil. It would not distribute into the air and soil from water. From the uses and properties of this substance, estimated exposures are considered in the following three scenarios. The effects are as follows:

(1) Occupational exposure scenario: inhalation of dust without breathing protection in the factory;
Dust level was 0.25 mg/m^3 by measurement at the packing workplace;
EHEinh = 0.027 mg/kg/day and EHEder = 1.7 mg/kg/day (estimate).

In Japan, this substance has been manufactured since 1964, and no persons handling or contacting this substance have experienced any adverse symptoms regarding skin or respiratory organs.

(2) Environmental exposure scenario: emission to aquatic compartment from waste water;
PEClocal water = 0.0176 mg/L (calculation).

(3) Consumer use exposure scenario: intake through migration from can coating of benzoguanamine-formaldehyde resins for storing foods and beverages;
EHE for consumer use was calculated as 0.076 mg/kg/day at the worst scenario based on the migration tests.

NATURE OF FURTHER WORK RECOMMENDED

No recommendation.