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AMMONIUM SULFAMATE

DRAFT

Health Advisory
Office of Drinking Water
U.S. Environmental Protection Agency

I. INTRODUCTION

The Health Advisory (HA) Program, sponsored by the Office of Drinking Water (ODW), provides information on the health effects, analytical methodology and treatment technology that would be useful in dealing with the contamination of drinking water. Health Advisories describe nonregulatory concentrations of drinking water contaminants at which adverse health effects would not be anticipated to occur over specific exposure durations. Health Advisories contain a margin of safety to protect sensitive members of the population.

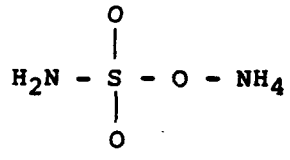
Health Advisories serve as informal technical guidance to assist Federal, State and local officials responsible for protecting public health when emergency spills or contamination situations occur. They are not to be construed as legally enforceable Federal standards. The HAs are subject to change as new information becomes available.

Health Advisories are developed for one-day, ten-day, longer-term (approximately 7 years, or 10% of an individual's lifetime) and lifetime exposures based on data describing noncarcinogenic end points of toxicity. Health Advisories do not quantitatively incorporate any potential carcinogenic risk from such exposure. For those substances that are known or probable human carcinogens, according to the Agency classification scheme (Group A or B), Lifetime HAs are not recommended. The chemical concentration values for Group A or B carcinogens are correlated with carcinogenic risk estimates by employing a cancer potency (unit risk) value together with assumptions for lifetime exposure and the consumption of drinking water. The cancer unit risk is usually derived from the linear multistage model with 95% upper confidence limits. This provides a low-dose estimate of cancer risk to humans that is considered unlikely to pose a carcinogenic risk in excess of the stated values. Excess cancer risk estimates may also be calculated using the One-hit, Weibull, Logit or Probit models. There is no current understanding of the biological mechanisms involved in cancer to suggest that any one of these models is able to predict risk more accurately than another. Because each model is based on differing assumptions, the estimates that are derived can differ by several orders of magnitude.

II. GENERAL INFORMATION AND PROPERTIES

CAS No. 7773-06-0

Structural Formula



ammonium sulfamate

Synonyms

- Amicide; Amidosulfate; Ammonium amidosulfate; Ammonium amidosulfonate; Ammonium amidotrioxosulfate; AMS; Fyran 206k; Ikurin.

Uses

- Herbicide used to control woody plant species. May be used for poison ivy control in apple and pear orchards (Meister, 1983).

Properties (Meister, 1983)

Molecular Weight	114.14
Physical State (25°C)	Colorless crystals
Boiling Point	--
Melting Point	131 to 132°C
Density (20°C)	>1
Vapor Pressure	Not available
Water Solubility	Highly soluble
Log Octanol Water/Partition Coefficient	--
Taste Threshold	--
Odor Threshold	--
Conversion Factor	--

Occurrence

- No information was found in the available literature on the occurrence of ammonium sulfamate.

Environmental Fate

- Konnai et al. (1974) showed that ammonium sulfamate was very mobile in soil.

III. PHARMACOKINETICS

Absorption

- No information was found in the available literature on the absorption of ammonium sulfamate.

Distribution

- No information was found in the available literature on the distribution of ammonium sulfamate.

Metabolism

- The metabolism of ammonium sulfamate in the urine of dogs was reported by Bergen and Wiley (1938); however, details of the study were not clearly defined for assessment.

Excretion

- Bergen and Wiley (1938) reported 80 to 84% excretion of sulfamic acid in the urine of two dogs following oral administration of ammonium sulfamate in capsules for 5 days.

IV. HEALTH EFFECTS

Humans

- No information was found in the available literature on the health effects of ammonium sulfamate in humans.

Animals

Short-term Exposure

- No information was found in the available literature on the effects of short-term exposure to ammonium sulfamate in animals.

Dermal/Ocular Effects

- Five rats received a 20% aqueous solution of ammonium sulfamate (dose level not specified) on the shaved skin of the back. They were killed after 16 treatments on the 27th day of the period (Read and Hueber, 1938). Another five rats received a 50% aqueous solution of ammonium sulfamate on the shaved skin of the back. These animals were killed after 11 treatments on the 19th day of the study. It should be noted that the animals were not prevented from licking the chemical. Investigators reported that there were no gross pathological changes of importance in any of the animals. On microscopic pathological examination of the animals, the spleen of 9 of 10 animals had numerous macrophages with brown pigment. The stomach sections of seven animals, revealed a brown, granular material in the surface capillaries of the mucosa.

- Read and Hueber (1938) orally administered 1 mL of a 50% aqueous solution of ammonium sulfamate (1.7 g/kg/day) to 10 rats on alternate days. Five rats were killed on the 27th day of the study after nine treatments, and the remaining five were killed on the 42nd day of the study after 15 treatments. Investigators reported that there were no gross pathological changes of importance in any of the animals. Microscopic pathology indicated the following: in one animal, superficial capillaries of the stomach mucosa occasionally contained yellow-brown granules; in three animals, there was slight vacuolation of the cytoplasm of liver cells about the central veins, but these changes were very mild; and in the spleen, three of the sections had moderate numbers of macrophages filled with hemosiderin. A fourth spleen section showed marked erythrophagia.

Long-term Exposure

- Gupta et al. (1979) reported the results of a 90-day study involving oral administration of 0, 100, 250 or 500 mg/kg of ammonium sulfamate to rats 6 days a week. No adverse effects were observed with respect to appearance, behavior or survival of animals. No significant difference in the body weights of rats was observed except in the case of rats receiving 500 mg/kg, where body weight was significantly less than controls after the end of 60 days. No significant changes in relative organ weights were noticed in any group of rats. Hematological examination conducted at 30, 60 and 90 days revealed nonsignificant increases in the numbers of neutrophils in the female adult and male weanling rats (500 mg/kg dose level) after 90 days. In the histological examination, organs in all the groups of animals appeared normal except that the liver of one adult rat (500 mg/kg) showed slight fatty degenerative changes after 90 days.

- Rosen et al. (1965) reported the findings of a study in female rats following administration of ammonium sulfamate at dietary levels of 1.1% (10 g/kg/day) or 2.1% (20 g/kg/day) for 105 days. No effect was detected at the 1% (10 g/kg/day) level of feeding, but growth retardation and a slight cathartic effect were observed at the 2% (20 g/kg/day) dietary level. No other information was provided by the authors.

- Sherman and Stula (1966) reported the results of a 19-month feeding study in 29-day-old CHR-CD male and female rats. Ammonium sulfamate was fed at dietary concentrations of 0, 350 (350 mg/kg) or 500 (500 mg/kg) ppm without any clinical or nutritional evidence of toxicity. There were no histopathological changes that could be attributed to the feeding of the test chemical. The observed pathologic lesions were interpreted as a result of spontaneous diseases.

Reproductive Effects

- Sherman and Stula (1966) reported the results of a three-generation reproduction study in rats. Rats receiving 0, 350 (350 mg/kg) or 500 (500 mg/kg) ppm ammonium sulfamate in the diet showed no evidence of toxicity as measured by histopathological evaluation and reproduction and lactation indices.

Developmental Effects

- No information was found in the available literature on the developmental effects of ammonium sulfamate.

Mutagenicity

- No information was found in the available literature on the mutagenic effects of ammonium sulfamate.

Carcinogenicity

- No information was found in the available literature on the carcinogenic effects of ammonium sulfamate.

V. QUANTIFICATION OF TOXICOLOGICAL EFFECTS

Health Advisories (HAs) are generally determined for one-day, ten-day, longer-term (approximately 7 years) and lifetime exposures if adequate data are available that identify a sensitive noncarcinogenic end point of toxicity. The HAs for noncarcinogenic toxicants are derived using the following formula:

$$HA = \frac{(NOAEL \text{ or } LOAEL) \times (BW)}{(UF) \times (\_\_\_ \text{ L/day})} = \_\_\_ \text{ mg/L } (\_\_\_ \text{ ug/L})$$

where:

NOAEL or LOAEL = No- or Lowest-Observed-Adverse-Effect-Level in mg/kg bw/day.

BW = assumed body weight of a child (10 kg) or an adult (70 kg).

UF = uncertainty factor (10, 100 or 1,000), in accordance with NAS/ODW guidelines.

___ L/day = assumed daily water consumption of a child (1 L/day) or an adult (2 L/day).

One-day Health Advisory

No data were located in the available literature that were suitable for deriving a One-day HA value for ammonium sulfamate. It is recommended that the Longer-term HA value for the 10-kg child (21.4 mg/L, calculated below) be used at this time as a conservative estimate of the One-day HA value.

Ten-day Health Advisory

No data on ammonium sulfamate toxicity were located in the available literature that were suitable for calculation of a Ten-day HA value. It is recommended that the Longer-term HA value for the 10-kg child (21.4 mg/L, calculated below) be used at this time as a conservative estimate of the Ten-day HA value.

Longer-term Health Advisory

The subchronic oral toxicity study in rats by Gupta et al. (1979) may be considered for the Longer-term HA. In this study, rats (female adults and male and female weanlings) received ammonium sulfamate orally at dose levels of 0, 100, 250 or 500 mg/kg/day for 90 days. Hematological and histological examinations at 30, 60 and 90 days revealed nonsignificant changes in hematological and histological measures. However, adult rats fed 500 mg/kg ammonium sulfamate showed lesser weight gain compared to other groups.

Using 250 mg/kg/day as a No-Observed-Adverse-Effect-Level (NOAEL), a Longer-term HA for the 10-kg child is calculated as follows:

$$\text{Longer-term HA} = \frac{(250 \text{ mg/kg/day})\ (10 \text{ kg})\ (6/7)}{(100)\ (1 \text{ L/day})} = 21.4 \text{ mg/L } (21{,}400 \text{ ug/L})$$

where:

250 mg/kg/day = NOAEL, based on the absence of hematological and histopathological changes in rats.

10 kg = assumed body weight of a child.

6/7 = conversion from 6 days to 7 days.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

1 L/day = assumed daily water consumption of a child.

For the 70-kg adult:

$$\text{Longer-term HA} = \frac{(250 \text{ mg/kg/day})\ (70 \text{ kg})\ (6/7)}{(100)\ (2 \text{ L/day})} = 75 \text{ mg/L } (75{,}000 \text{ ug/L})$$

where:

250 mg/kg/day = NOAEL, based on the absence of hematological and histopathological changes in rats.

70 kg = assumed body weight of an adult.

6/7 = conversion from 6 days to 7 days.

100 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study.

2 L/day = assumed daily water consumption of an adult.

Lifetime Health Advisory

The Lifetime HA represents that portion of an individual's total exposure that is attributed to drinking water and is considered protective of noncarcinogenic adverse health effects over a lifetime exposure. The Lifetime HA

is derived in a three-step process. Step 1 determines the Reference Dose (RfD), formerly called the Acceptable Daily Intake (ADI). The RfD is an estimate of a daily exposure to the human population that is likely to be without appreciable risk of deleterious effects over a lifetime, and is derived from the NOAEL (or LOAEL), identified from a chronic (or subchronic) study, divided by an uncertainty factor(s). From the RfD, a Drinking Water Equivalent Level (DWEL) can be determined (Step 2). A DWEL is a medium-specific (i.e., drinking water) lifetime exposure level, assuming 100% exposure from that medium, at which adverse, noncarcinogenic health effects would not be expected to occur. The DWEL is derived from the multiplication of the RfD by the assumed body weight of an adult and divided by the assumed daily water consumption of an adult. The Lifetime HA is determined in Step 3 by factoring in other sources of exposure, the relative source contribution (RSC). The RSC from drinking water is based on actual exposure data or, if data are not available, a value of 20% is assumed for synthetic organic chemicals and a value of 10% is assumed for inorganic chemicals. If the contaminant is classified as a Group A or B carcinogen, according to the Agency's classification scheme of carcinogenic potential (U.S. EPA, 1986), then caution should be exercised in assessing the risks associated with lifetime exposure to this chemical. exposure to this chemical.

The study by Gupta et al. (1979) has been selected to serve as the basis for determination of the Lifetime HA even though the results of this subchronic study were based on 90 days' exposure. In this study, rats (female adults and weanling males and females) received ammonium sulfamate orally in drinking water at dose levels of 0, 100, 250 or 500 mg/kg/day for 90 days. The NOAEL was identified as 250 mg/kg/day, since the highest dose level of 500 mg/kg/day was associated with decreased body weight gain in rats over a 90-day exposure period). In a chronic feeding study reported by Sherman and Stula (1966) in rats, ammonium sulfamate was fed to rats at dietary levels of 0, 350 or 500 ppm over a 19-month period. The authors stated that these dose levels did not produce any significant clinical or histological changes in rats receiving the test compound, and any changes recorded were interpreted as being lesions of spontaneous diseases.

Using a NOAEL of 250 mg/kg/day, the Lifetime HA is calculated as follows:

Step 1: Determination of the Reference Dose (RfD)

$$RfD = \frac{(250 \text{ mg/kg/day}) (6/7)}{(1,000)} = 0.214 \text{ mg/kg/day}$$

where:

250 mg/kg/day = NOAEL.

6/7 = conversion from 6 days to 7 days.

1,000 = uncertainty factor, chosen in accordance with NAS/ODW guidelines for use with a NOAEL from an animal study of less than a lifetime exposure.

Step 2: Determination of the Drinking Water Equivalent Level (DWEL)

$$DWEL = \frac{(0.214 \text{ mg/kg/day})\ (70 \text{ kg})}{(2 \text{ L/day})} = 7.5 \text{ mg/L } (7{,}500 \text{ ug/L})$$

where:

0.250 mg/kg/day = RfD.

70 kg = assumed body weight of an adult.

2 L/day = assumed daily water consumption of an adult.

Step 3: Determination of the Lifetime Health Advisory

Lifetime HA = (7.5 mg/L) (20%) = 1.5 mg/L (1,500 ug/L)

where:

7.5 mg/L = DWEL.

20% = assumed relative source contribution from water.

Evaluation of Carcinogenic Potential

- No studies were found in the available literature investigating the carcinogenic potential of ammonium sulfamate. Applying the criteria described in EPA's final guidelines for assessment of carcinogenic risk (U.S. EPA, 1986), ammonium sulfamate may be classified in Group D: not classified. This category is used for substances with inadequate animal evidence of carcinogenicity.

VI. OTHER CRITERIA, GUIDANCE AND STANDARDS

- The American Conference of Government Industrial Hygienists (ACGIH) has adopted a Threshold Limit Value-Time-Weighted Average (TLV-TWA) of 10 mg/m^3 and a TLV short-term exposure limit (STEL) of 20 mg/m^3 for inhalation exposure (ACGIH, 1984).

VII. ANALYTICAL METHODS

- There is no standardized method for determination of ammonium sulfamate in water samples. A procedure has been reported for the estimation of ammonium sulfamate in certain foods, however (U.S. FDA, 1969). This procedure involves a colorimetric determination of ammonium sulfamate based on the liberation of SO_4 and reduction it to H_2S, which is measured after treating with zinc, p-aminodimethylaniline and ferric chloride to form methylene blue.

VIII. TREATMENT TECHNOLOGIES

- No information was found in the available literature on treatment technologies capable of effectively removing ammonium sulfamate from contaminated water.

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*Confidential Business Information submitted to the Office of Pesticide Programs.