820K88008

August, 1987

BENTAZON

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.

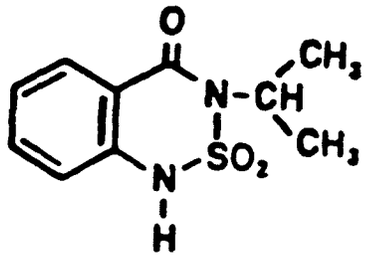
Health Advisories serve as informal technical guidance to assist Federal, State and local officials responsible for protecting public health when emergency spills or contamination situations occur. They are not to be construed as legally enforceable Federal standards. The HAs are subject to change as 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. 25057-89-0

Structural Formula



3-(1-Methylethyl)-1H-2,1,3-benzothiadiazin-4(3H)-one,2,2-dioxide

Synonyms

- Basagran; Bendioxide; Bentazone (Worthing, 1983).

Uses

- Selective postemergent herbicide used to control broadleaf weeds in soybeans, rice, corn, peanuts, dry beans, dry peas, snap beans for seed, green lima beans and mint (Meister, 1986).

Properties (Worthing, 1983)

Chemical Formula	$C_{10}H_{12}N_2O_3S$
Molecular Weight	240.3
Physical State	Colorless crystalline powder
Boiling Point	--
Melting Point	137 to 139°C
Density	--
Vapor Pressure	--
Water Solubility	500 mg/L
Log Octanol/Water Partition Coefficient	--
Taste Threshold	--
Odor Threshold	--
Conversion Factor	--

Occurrence

- Bentazon was not found in sampling performed at two water supply stations in the STORET database (STORET, 1987). No information on the occurrence of bentazon was found in the available literature.

Environmental Fate

- Bentazon, at 1 ppm, was stable to hydrolysis for up to 122 days in unbuffered water (initial pH 5, 7, and 9) at 22°C (Drescher, 1972c).

The bentazon degradate, 2-amino-N-isopropyl benzamide (AIBA) at 1 ppm, was stable to hydrolysis in unbuffered, distilled water at pH 5, 7, and 9, during 28 days' incubation in the dark at 22°C (Drescher, 1973b).

- ^{14}C-Bentazon at 2 to 10 ppm, degraded with a half-life of less than 2 to 14 weeks in a sandy clay loam, loam, and three loamy sand soils (Drescher and Otto, 1973a; Drescher and Otto, 1973b). The soils were incubated at 14 to 72% of field capacity and 23°C. The bentazon degradation rate was not affected by soil moisture content but was decreased by lowering the temperatures to 8 to 10°C. At pH 6.4, the degradation rate in a loamy sand soil was 2.5 times longer than at pH 4.6 and 5.5. The bentazon degradate, AIBA, was identified at less than 0.1 ppm. AIBA degraded in loamy sand soil with a half-life of 1 to 10 days (43% of field capacity). ^{14}C-Bentazon at 1.7 ppm did not degrade appreciably in a loamy sand soil during 8 weeks of incubation; AIBA was detected at a maximum concentration of 0.008 ppm.

- Bentazon did not adsorb to Drummer silty clay loam, adjusted to pH 5 and 7, and 11 other soils tested at pH 5 (Abernathy and Wax, 1973). In the same study, using soil TLC, (^{14}C)bentazon was very mobile in 12 soils, ranging in texture from sand to silty clay loam, with an R_f value of 1.0.

- Bentazon was very mobile in a variety of soils, ranging in texture from loamy sand to silty clay loam and muck, based on soil column tests (Drescher and Otto, 1972; Abernathy and Wax, 1973; Drescher, 1973a; Drescher, 1972a). Approximately 73 to 103% of the bentazon applied to the columns was recovered in the leachate.

- AIBA (100 ug applied to loamy sand soil) was very mobile (Drescher, 1972b). After leaching a 12-inch soil column with 500 ml (10 inches) of distilled water, 86.3% of the applied material was found in the leachate.

- Bentazon has the potential to contaminate surface waters as a result of its mobility in runoff water and application to rice fields (Devine, 1972; Wuerzer, 1972).

- In the field, bentazon at 0.75 to 10 lb ai/A dissipated with a half-life of less than or equal to 1 month in the upper 6 inches of soil, ranging in texture from sand to clay (Daniels et al., 1976; Devine and Hanes, 1973; Stoner and Hanes, 1974b; Stoner and Hanes, 1974a; BASF Wyandotte Corporation, 1974; Devine and Tietjens, 1973; Devine et al., 1973). In the majority of soils (6 of 9), bentazon had a half-life of less than 7 days. AIBA was detected at less than or equal to 0.09 ppm. Collectively, the available data indicated that geographic region (NC, TX, MS, AL, MN, or ID) and crops treated (peanuts, soybeans, corn or fallow soil) had little or no effect on the dissipation rate of bentazon in soil.

III. PHARMACOKINETICS

Absorption

- Male and female rats (200 to 250 g) given 0.8 mg ^{14}C-bentazon in 1 mL of 50% ethanol by stomach tube excreted 91% of the administered dose in the urine within 24 hours. This suggests that bentazon is almost completely absorbed when ingested (Chasseaud et al., 1972).

Distribution

- Whole-body autoradiography of rats indicated high levels of radioactivity in the stomach, liver, heart and kidneys after 1 hour of dosing with ^{14}C-bentazon. Radioactivity was not observed in the brain or spinal cord (Chasseaud et al., 1972).

Metabolism

- Bentazon is poorly metabolized. Two unidentified metabolites were detected (Chasseaud et al., 1972).

Excretion

- Rats given radiolabeled bentazon excreted 91% of the administered dose in the urine as parent compound. Feces contained 0.9% of the administered dose (Chasseaud et al., 1972).

IV. HEALTH EFFECTS

Humans

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

Animals

Short-term Exposure

- The oral LD_{50} of bentazon in the rat was reported to be 2,063 mg/kg (Meister, 1986).

- LD_{50} values for bentazon in the rat, dog, cat and rabbit are reported to be 1,100, 900, 500 and 750 mg/kg, respectively (RTECS, 1985).

- Acute, subchronic and chronic oncogenicity studies on bentazon have been invalidated because of data gaps and deficiencies. However, the RfD Workgroup (U.S. EPA 1986a) calculated a Reference Dose (RfD) for bentazon from a 13-week study in dogs. This study is described in detail in Section V. Quantification of Toxicological Effects. Note that the calculated RfD value has a low confidence level.

Dermal/Ocular Effects

- No valid information on the dermal/ocular effects of bentazon was found in the available literature.

Long-term Exposure

- As indicated under Short-term Exposure, long-term studies, including reproductive effects and carcinogenicity studies, have been invalidated.

Reproductive Effects

- No valid information on the reproductive effects of bentazon was found in the available literature.

Developmental Effects

- No valid information on the developmental effects of bentazon was found in the available literature.

Mutagenicity

- No valid information on the mutagenic effects of bentazon was found in the available literature.

Carcinogenicity

- No valid information on the carcinogenic effects of bentazon was found in the available literature.

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 found in the available literature that were suitable for determination of One-day HA values. It is, therefore, recommended that the Longer-term HA value for a 10-kg child (0.25 mg/L, calculated below) be used at this time as a conservative estimate of the One-day HA.

Ten-day Health Advisory

No data were found in the available literature that were suitable for determination of Ten-day HA values. It is, therefore, recommended that the Longer-term HA value for a 10-kg child (0.25 mg/L, calculated below) be used at this time as a conservative estimate of the Ten-day HA.

Longer-term Health Advisory

A 13-week study in beagle dogs has been selected for the calculation of a Longer-term HA (Leuschner et al., 1970). Beagle dogs (three dogs/sex/dose) were gven 0 (control), 100, 300, 1,000 and 3,000 ppm (0, 2.5, 7.5, 25 and 75 mg/kg/day; Lehman, 1959) of bentazon for 13 weeks. At a dose level of 3,000 ppm, overt signs of toxicity, including weight loss and ill health, were observed; 1/3 males and 2/3 females died. At 3,000 ppm, all males showed signs of prostatitis. Similar signs were observed in one male each at the 300- and 1,000-ppm levels. This study suggests a NOAEL of 100 ppm (2.5 mg/kg/day).

Utilizing this NOAEL, a Longer-term HA for a 10-kg child is calculated as follows:

$$\text{Longer-term HA} = \frac{(2.5 \text{ mg/kg/day})\ (10 \text{ kg})}{(100)\ (1 \text{ L/day})} = 0.25 \text{ mg/L } (250 \text{ ug/L})$$

where:

2.5 mg/kg/day = NOAEL, based on absence of prostatic effects in dogs.

10 kg = assumed body weight of a child.

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.

The Longer-term HA for the 70-kg adult is calculated as follows:

$$\text{Longer-term HA} = \frac{(2.5 \text{ mg/kg/day})\ (70 \text{ kg})}{(100)\ (2 \text{ L/day})} = 0.875 \text{ mg/L } (875 \text{ ug/L})$$

where:

2.5 mg/kg/day = NOAEL, based on absence of prostatic effects in dogs.

70 kg = assumed body weight of an adult.

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, 1986b), then caution should be exercised in assessing the risks associated with lifetime exposure to this chemical.

Lifetime studies were not available to calculate a Lifetime HA. However, with the addition of another safety factor of 10 for studies of less-than-lifetime duration, the Lifetime HA may be calculated from the 13-week feeding study in dogs (Leuschner et al., 1970).

Using the NOAEL of 2.5 mg/kg/day, the Lifetime HA for bentazon is calculated as follows:

Step 1: Determination of a the Reference Dose (RfD)

$$RfD = \frac{(2.5 \text{ mg/kg/day})}{(1{,}000)} = 0.0025 \text{ mg/kg/day}$$

where:

2.5 mg/kg/day = NOAEL, based on the absence of prostatic effects in dogs.

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

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

$$DWEL = \frac{(0.0025 \text{ mg/kg/day})\ (70 \text{ kg})}{(2 \text{ L/day})} = 0.0875 \text{ mg/L } (87.5 \text{ ug/L})$$

where:

0.0025 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 = (0.0875 mg/L) (20%) = 0.0175 mg/L (17.5 ug/L)

where:

0.0875 mg/L = DWEL.

20% = assumed relative source contribution from water.

Evaluation of Carcinogenic Potential

- No valid data are available to make a determination of the carcinogenic potential of bentazon.
- Applying the criteria described in EPA's guidelines for assessment of carcinogenic risk (U.S. EPA, 1986b), bentazon may be classified in Group D: not Classified. This category is for agents with inadequate animal evidence of carcinogenicity.

VI. OTHER CRITERIA, GUIDANCE AND STANDARDS

- In response to a bentazon-tolerance review petition, EPA's Office of Pesticide Programs has concluded that "a tolerance cannot be supported at this time."

VII. ANALYTICAL METHODS

- Analysis of bentazon is by a gas chromatographic (GC) method applicable to the determination of bentazon in water samples (U.S. EPA, 1985). In this method, an aliquot of sample is acidified and extracted with ethyl acetate. The extract is dried, concentrated to 1 to 2 mL, and methylated with diazomethane. The methylated extracts are analyzed by gas chromatography with flame photometric detection. The method detection limit for bentazon has not been determined.

VIII. TREATMENT TECHNOLOGIES

- There is no information available regarding treatment technologies used to remove bentazon from contaminated water.

IX. REFERENCES

Abernathy, J. R. and L. M. Wax. 1973. Bentazon mobility and adsorption in twelve Illinois soils. Weed Science. 21(3):224-226.

BASF Wyandotte Corporation. 1974. Analytical residue reports (soil and water): bentazon. Unpublished study.

Chasseaud, L.F., D.R. Hawkins, B.D. Cameron, B.J. Fry and V.H. Saggers. 1972. The metabolic fate of bentazon. Xenobiotica. 2(3):269-276.

Daniels, J., J. Gricher and T. Boswell. 1976. Determination of bentazon (BAS 351-H) residues in sand soil samples from Yoakum, Texas: Report No. IRDC-3; BWC Project No. I-2-G-73. Unpublished study prepared by International Research and Development Corporation, submitted by BASF Wyandotte Corporation, Wyandotte, MI.

Devine, J. M. 1972. Determination of BAS 351-H (3-isopropyl-1H-2,1,3-benzothiadiazin-4(3H)-one-2,2-dioxide) residues in soil and runoff water. Report No. 133.

Devine, J. M. and R. E. Hanes. 1973. Determination of residues of BAS 351-H(3-isopropyl-1H-2,1,3-benzothiadiazin-4(3H)-one-2,2-dioxide) and its benzamide metabolite, AIBA (2-amino-N-isopropyl benzamide), in Sharkey silty clay soil from Greenville, Mississippi: Field Experiment No. 72-99. Unpublished study prepared by State University of New York--Oswego, Lake Ontario Environmental Laboratory and United States Testing Company, Inc., submitted by BASF Wyandotte Corporation, Parsippany, NJ.

Devine, J. M. and F. Tietjens. 1973. Determination of BAS 351-H (3-isopropyl-1H-2,1,3-benzothiadiazin-4(3H)-one-2,2-dioxide) residues in Commerce silt loam soil from Greenville, Mississippi: Field Experiment No. 72-76. Unpublished study prepared by State Univeristy of New York--Oswego, Lake Ontario Environmental Laboratory and United States Testing Company, Inc., submitted by BASF Wyandotte Corporation, Parsippany, NJ.

Devine, J. M., C. Carter, L. W. Hendrick et al. 1973. Determination of residues of BAS 351-H (3-isopropyl-1H-2,1,3-benzothiadiazin-4(3H)-one-2,2-dioxide) and its benzamide metabolite, AIBA (2-amino-N-isoopropyl benzamide), in Webster Glencoe silty clay loam soil from Prior Lake, Minnesota: Field Experiment No. III-B-6-72. Unpublished study prepared by State University of New York--Oswego, Lake Ontario Environmental Laboratory and others, submitted by BASF Wyandotte Corporation, Parsippany, NJ.

Drescher, N. 1972a. A comparison between the leaching of bentazon and 2,4-D through a soil in a model experiment: Laboratory Report No. 679.

Drescher, N. 1972b. Leaching of 2-amino-N-isopropyl benzamide (AIBA) from the soil. Laboratory Report No. 682.

Drescher, N. 1972c. The effect of pH on the rate of hydrolysis of bentazon (BAS 351-H) in water: Laboratory Report No. 1107. Translation; unpublished study prepared by Badische Anilin- and Soda-Fabrik, AG, submitted by BASF Wyandotte Corporation, Parsippany, NJ.

Drescher, N. 1973a. Leaching of bentazon in a muck soil. Laboratory Report No. 1138.

Drescher, N. 1973b. The influence of pH on the hydrolysis of the bentazon metabolite AIBA (2-amino-N-isopropyl benzamide) in water. Laboratory Report No. 1136.

Drescher, N. and S. Otto. 1972. Penetration and leaching of bentazon in soil: Laboratory Report No. 1099. Translation; unpublished study prepared by BASF, AG, submitted by BASF Wyandotte Corporation, Parsippany, NJ.

Drescher, N. and S. Otto. 1973a. Degradation of bentazon (BAS 351-H) in soil. Report No. 1140.

Drescher, N., and S. Otto. 1973b. Degradation of bentazon (BAS 351-H) in soil. Report No. 1149.

Lehman, A.J. 1959. Appraisal of the safety of chemicals in foods, drugs and cosmetics. Assoc. Food Drug Off. U.S.

Leuschner, F., A. Leuschner, W. Schwerdtfeger and H. Otto. 1970. 13-Week toxicity study of 3-isopropyl-1H-2,1,3-benzothiadiazin-4(3H)-one-2,2-dioxide to beagles when administered with the food. Unpublished report prepared by Laboratory of Pharmacology and Toxicology, W. Germany. September 28.

Meister, R., ed. 1986. Farm chemicals handbook. Willoughby, OH: Meister Publishing Co.

RTECS. 1985. Registry of Toxic Effects of Chemical Substances. National Institute for Occupational Safety and Health. National Library of Medicine Online File.

Stoner, J.H., and R.E. Hanes. 1974a. Determination of residues of bentazon and AIBA (2-amino-N-isopropyl benzamide) in Commerce silt loam soil from Greenville, MS: Field Experiment No. 73-41. Unpublished study prepared in cooperation with Stoner Laboratories, Inc., and United States Testing Company, Inc., submitted by BASF Wyandotte Corporation, Parsippany, NJ.

Stoner, J. H., and R. E. Hanes. 1974b. Determination of residues of bentazon (BAS 351-H) and AIBA in Commerce silt loam soil from Greenville, MS: Field Experiment No. 73-43. Unpublished study prepared in cooperation with Stoner Laboratories, Inc. and United States Testing Company, Inc., submitted by BASF Wyandotte Corporation, Parsippany, NJ.

STORET. 1987.

U.S. EPA. 1985. U.S. Environmental Protection Agency. U.S. EPA Method 107 - Revision A, Bentazon. Fed. Reg. 50:40701. October 4, 1985.

U.S. EPA. 1986a. U.S. Environmental Protection Agency. RfD Work Group. Worksheet dated April 7.

U.S. EPA. 1986b. U.S. Environmental Protection Agency. Guidelines for carcinogen risk assessment. Fed. Reg. 51(185):33992-34003. September 24.

Worthing, C.R., ed. 1983. The pesticide manual. Great Britain: The Lavenham Press, Ltd., p. 39.

Wuerzer, B. 1972. Bentazon model box runoff study: Runoff Report 73-6. Unpublished study prepared in cooperation with United States Testing Company, submitted by BASF Wyandotte Corporation, Parsippany, NJ.