

## Aldicarb sulfone; CASRN 1646-88-4

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

### STATUS OF DATA FOR Aldicarb sulfone

**File First On-Line 09/26/1988**

Category (section)	Assessment Available?	Last Revised
<b>Oral RfD (I.A.)</b>	yes	11/01/1993
<b>Inhalation RfC (I.B.)</b>	not evaluated	
<b>Carcinogenicity Assessment (II.)</b>	not evaluated	

## I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

### I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Aldicarb sulfone  
CASRN — 1646-88-4  
Primary Synonym — Aldoxycarb  
Last Revised — 11/01/1993

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of

substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

### I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
<b>Brain ChE inhibition in females</b>	NOAEL: 5 ppm (0.11 mg/kg-day)	100	1	1E-3 mg/kg-day
<b>1-Year Dog Feeding Study</b>	LOAEL: 25 ppm (0.58 mg/kg/day)			
<b>Union Carbide Agricultural Products Co., 1987</b>				

\*Conversion Factors and Assumptions — Actual dose calculated by weekly food intake

### I.A.2. Principal and Supporting Studies (Oral RfD)

Union Carbide Agricultural Products Company. 1987. MRID No. 40259901. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Groups of beagle dogs (6/sex/dose) were administered aldicarb sulfone in the diet for 1 year at levels of 0, 5, 25, or 100 ppm (0, 0.11, 0.58 or 2.21 mg/kg-day). Since aldicarb sulfone was found to be unstable in the diet at room temperature, fresh diets were prepared weekly and frozen immediately following mixing. Plasma and red blood cell cholinesterase activities were determined for each animal three times prior to treatment (weeks -3, -2, and -1) and during weeks 5, 13, 26, and 52. Brain cholinesterase was determined at termination only.

No treatment-related clinical signs were noted at any dose level in this study. Brain cholinesterase activity at study termination showed statistically significant inhibition in high-dose males (24% inhibition of control value) and mid- and high-dose females (19-23% inhibition of control). At the lowest dose tested, no significant effects were noted in either sex. Statistically significant inhibition of plasma cholinesterase was observed in males at all doses tested (20-80%

inhibition of control value) and at the mid- and high-doses in females (40-72% inhibition of control value) at all test intervals. Red blood cell cholinesterase was also significantly inhibited in high-dose males and females (25-36% inhibition of concurrent control value) and in mid-dose females (up to 22%). However, at the low dose, the effect was marginal on plasma ChE in males (mean value is 25%), and insignificant in females; no significant effect on red blood cells ChE was noted at this dose in either sex.

Based on brain cholinesterase, the LOAEL for systemic toxicity is 25 ppm (0.58 mg/kg-day). The NOAEL for systemic toxicity is 5 ppm (0.11 mg/kg-day).

### **I.A.3. Uncertainty and Modifying Factors (Oral RfD)**

UF — An uncertainty factor of 100 was used to account for the inter- and intraspecies differences (10 each). An additional uncertainty factor to account for the lack of a chronic rat study was not considered necessary, since the available subchronic data in both the dog and rat indicated that the dog is a more sensitive species. Although the lack of a chronic rat study is still considered a data gap, it is not of considerable concern given the available information on both aldicarb sulfone and its parent compound, aldicarb.

MF — None

### **I.A.4. Additional Studies/Comments (Oral RfD)**

1) 1-Year Feeding - dog: Principal study -- see previous description; core grade supplementary (Union Carbide Agricultural Prod. Co., 1987).

2) 3-Generation Reproduction - rat: Core grade minimum (Union Carbide Corp., 1977).

Harlan-Wistar rats (10 males and 20 females/group) were administered aldoxycarb in the diet at dose levels of 0, 0.6, 9.6, 2.4 and 9.6 mg/kg-day for 3 generations (1 litter per generation). Male rats fed 9.6 mg/kg-day exhibited reduced body weights. Cholinesterase depression was noted at 9.6 mg/kg-day. Reduced pup survival and marginal effects on lactation were noted at 9.6 mg/kg-day. Based on reduced body weight in males, the NOEL and LEL for systemic toxicity are 2.4 and 9.6 mg/kg-day, respectively. Based on reduced pup survival, the NOEL and LEL for reproductive toxicity are 2.4 and 9.6 mg/kg-day, respectively.

3) Developmental toxicity - rat: Core grade minimum (Union Carbide Corp., 1977).

Female Wistar rats were administered aldoxycarb at dose levels of 0, 0.6, 2.4 and 9.6 mg/kg-day at one of the following time intervals of gestation: 1- 20 days, 6-15 days, or 7-9 days following

evidence of mating. The percentage of pregnant control dams was 77% as compared with 82, 83, and 88% for the groups treated at 0-20, 6-15 and 7-9 days post-mating, respectively. Resorption sites per female were slightly increased in the 9.6 mg/kg-day treated females in the 6-15 day treatment period. No increase in resorption was seen at the same dosage level in females treated from days 1-20. Anomalies in treated pups were virtually non-existent as in controls. At 9.6 mg/kg-day diarrhea due to possible ChE inhibition was observed. Based on the occurrence of diarrhea, the NOEL and LEL for maternal toxicity are 2.4 and 9.6 mg/kg-day, respectively. The NOEL for developmental effects is greater than or equal to 9.6 mg/kg-day, the highest dose tested.

#### Other Data Reviewed:

1) 3-Month Feeding - dog: Core grade minimum (supplementary for cholinesterase) (Union Carbide Corp., 1968a).

Beagle dogs were fed diets containing 0, 0.2, 0.6, 1.8 and 5.4 mg/kg-day aldicarb sulfone for 3 months. Mean body weights were only slightly reduced in the animals but some showed a loss of weight from the start of dosing at 5.4 mg/kg-day. Cholinesterase activity was significantly reduced at 5.4 mg/kg-day in both sexes at 1.5 weeks. RBC ChE activity on the average was not significantly different from the control group after 3 months of treatment. Brain tissue ChE mean values were reduced in both sexes at doses above 0.2 mg/kg-day. However, due to removal of the animals up to 24 hours prior to analysis, the ChE data is only applicable to reversal ChE inhibition and does not give an accurate indication of ChE depression immediately following dosing. Therefore, based on weight loss the NOEL and LEL for systemic toxicity are 1.8 and 5.4 mg/kg-day, respectively. The NOEL and LEL for Brain ChE inhibition are 0.2 and 0.6 mg/kg-day, respectively. The NOEL for RBC ChE inhibition is equal to or greater than 5.4 mg/kg-day, the highest dose tested.

2) 3 and 6-Month Feeding - rat: Core grade minimum (Union Carbide Corp., 1968b).

Harlan-Wistar rats (15/sex/dose) were fed diets containing 0, 0.2, 0.6, 1.8, 5.4 or 16.2 mg/kg-day aldicarb sulfone for a maximum period of 6 months. Five animals/sex were sacrificed at 3 months and the remaining animals were sacrificed at 6 months. Gross and histopathological examination were performed. Cholinesterase activity was determined for plasma, RBC, and brain by acetic acid liberation and titration. 3-Month Results: Body weight gains were only slightly (not statistically) reduced at the 16.2 mg/kg-day dose level in both sexes. Liver and kidney weights were not significantly different from controls for either sex. Plasma ChE was reduced in males at 1.8 mg/kg-day by 36% and at 5.4 mg/kg-day in females by 62%. RBC ChE levels were depressed 31% in both males and females at 1.8 mg/kg-day and 52%, in both males and females at 5.4 mg/kg-day. Brain ChE was reduced 15% in males and 27% in females at 5.4 mg/kg-day.

6-Month Results: Body weights were significantly reduced at 16.2 mg/kg-day in males. At 1.8 mg/kg-day plasma ChE was reduced by 24% in females but not in males. RBC ChE in males and females was reduced by 28 and 26%, respectively. Brain ChE was lower by 26% in males at 5.4 mg/kg-day and 15% at 1.8 mg/kg-day, while females exhibited a reduction of 16% ( $p < 0.05$ ) at 1.8 mg/kg-day. A 16% reduction in brain ChE was also noted in females at 0.2 mg/kg-day.

3) 2-Month Feeding - rat: Core grade minimum (Union Carbide Corp., 1975).

Wistar rats were fed diets containing 2.4 and 16.2 mg/kg-day aldoxycarb for 56 days. At 16.2 mg/kg-day ChE in plasma, RBC, and brain was depressed in both sexes by 70%. No physical signs or symptoms were noted. At 2.4 mg/kg-day, only plasma ChE was depressed and then only sporadically. Based on ChE inhibition, the NOEL and LEL for systemic effects are 2.4 and 16.2 mg/kg-day, respectively.

Data Gap(s): 2-Year Rat Feeding/Carcinogenicity Study; Rabbit Developmental Toxicity Study

#### **I.A.5. Confidence in the Oral RfD**

Study — Medium

Database — Medium

RfD — Medium

The critical study is given a medium confidence rating. Although the study did identify a NOAEL and LOAEL, detailed procedures for assay and sampling of brain cholinesterase activity were not provided in the study. Since a chronic feeding study in rats and a rabbit developmental study are lacking, the database is given a medium confidence rating. Medium confidence in the RfD follows.

#### **I.A.6. EPA Documentation and Review of the Oral RfD**

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — Registration Standard, November, 1983; U.S. EPA, 1987

Agency Work Group Review — 04/20/1988, 06/20/1990, 07/26/1990, 04/24/1991, 04/25/1991, 09/22/1992

Verification Date — 09/22/1992

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for aldicarb sulfone conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) or 202-566-1676.

#### **I.A.7. EPA Contacts (Oral RfD)**

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

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#### **I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)**

Substance Name — Aldicarb sulfone

CASRN — 1646-88-4

Primary Synonym — Aldoxycarb

Not available at this time.

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## **II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — Aldicarb sulfone

CASRN — 1646-88-4

Primary Synonym — Aldoxycarb

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

**III. [reserved]**

**IV. [reserved]**

**V. [reserved]**

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## **VI. Bibliography**

Substance Name — Aldicarb sulfone

CASRN — 1646-88-4

Primary Synonym — Aldoxycarb

### **VI.A. Oral RfD References**

Union Carbide Agricultural Products Company. 1987. MRID No. 40259901. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Union Carbide Corporation. 1968a. MRID No. 00054404, 00057337, 00069645, 0090574. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Union Carbide Corporation. 1968b. MRID No. 00057337, 00069645, 0090574, 00100381. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Union Carbide Corporation. 1975. MRID No. 00044738. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Union Carbide Corporation. 1977. MRID No. 0054409, 0065890. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

U.S. EPA. 1987. Health Advisory for Aldicarb, Aldicarb Sulfoxide, and Aldicarb Sulfone. Office of Water, Washington, DC.

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### **VI.B. Inhalation RfD References**

None

## VI.C. Carcinogenicity Assessment References

None

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## VII. Revision History

Substance Name — Aldicarb sulfone

CASRN — 1646-88-4

Primary Synonym — Aldoxycarb

Date	Section	Description
09/26/1988	I.A.	Oral RfD summary on-line
07/01/1990	I.A.	Withdrawn; new RfD verified (in preparation)
09/01/1990	I.A.	Oral RfD summary replaced; RfD changed
05/01/1991	I.A.	Oral RfD withdrawn pending additional review
11/01/1993	I.A.	Oral RfD summary replaced; new RfD
10/28/2003	I.A.6.	Screening-Level Literature Review Findings message has been added.

## VIII. Synonyms

Substance Name — Aldicarb sulfone

CASRN — 1646-88-4

Primary Synonym — Aldoxycarb

Last Revised — 09/26/1988

- 1646-88-4
- Aldicarb Sulfone
- Aldoxycarb
- aldoxycarbe
- ENT 4.9
- ENT AI3-29261
- 2-mesyl-2-methylpropionaldehyde O-methylcarbamoyloxime
- 2-methyl-2-(methylsulfonyl)propanal O-((methylamino)carbonyl)oxime
- 2-methyl-2-(methylsulfonyl)propionaldehyde O-(methylcarbamoyl)oxime
- propionaldehyde, 2-methyl-2-(methylsulfonyl)-, O-(methylcarbamoyl)oxime
- standak
- UC-21865