Alar; CASRN 1596-84-5

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 Alar

File First On-Line 06/30/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	06/30/1988
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Alar
CASRN — 1596-84-5
Primary Synonym — Daminozide
Last Revised — 06/30/1988

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
No adverse effects **3-Generation Reproduction Rat Study** **Uniroyal Chemical, 1966**	NOEL: 300 ppm (15 mg/kg/day) LEL: none	100	1	1.5E-1 mg/kg/day

*Conversion Factors -- 1 ppm = 0.05 mg/kg/day (assumed rat food consumption)

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

Uniroyal Chemical. 1966. MRID No. 0009413. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Three-generation reproduction and lactation studies were conducted with rats from the 2 year feeding study and a control group. When the rats were approximately 100 days of age, 20 pairs of males and females were separated from the 300 ppm (15 mg/kg/day) dosage group. Fertility, gestation, viability, lactation, and litter body weights were similar thru two cycles of each generation. There was no evidence of adverse effects by any criteria of performance at 300 ppm (15 mg/kg/day).

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

UF — An uncertainty factor of 100 was used to account for the intra- and interspecies differences.

MF — None

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

A 2-generation reproduction study (Uniroyal Chemical Co., 1987) is currently under review.

Data Considered for Establishing the RfD:

1) 3-Generation Reproduction - rat: Principal study - see previous description; no core grade

2) 2-Year Feeding (oncogenic) - rat: Systemic NOEL=3000 ppm (150 mg/kg/day) (HDT); no core grade (Uniroyal Chemical, 1966)

3) 2-Year Feeding - dog: NOEL=3000 ppm (75 mg/kg/day) (HDT); no core grade (U.S. Rubber Co., 1966)

4) 2-Year Feeding (oncogenic) - rat: Systemic NOEL=10,000 ppm (500 mg/kg/day) (HDT); (LDT; adenocarcinomas of the endomethrium and leiomyosarcomas of the uterus in females); no core grade (NCI, 1978)

5) Teratology - rat: Developmental NOEL=390 mg/kg/day; Developmental LEL=1800 mg/kg/day (HDT; fetotoxic skeletal malformations); core grade supplementary (Uniroyal Chemical, 1978)

Other Data Reviewed:

1) 2-Year Feeding (oncogenic) - mouse: Systemic NOEL=5000 ppm (750 mg/kg/day); Systemic LEL=10,000 ppm (1500 mg/kg/day) (decreased body weight and survival in females); no core grade (NCI, 1978)

2) 90-Day Feeding - rat: NOEL=2160 mg/kg/day (HDT); no core grade (Uniroyal Chemical, 1964)

3) 2-Year Feeding (oncogenic) - rat: NOEL=10,000 ppm (500 mg/kg/day) (HDT); core grade supplementary (Uniroyal Chemical Co., 1986a)

4) 2-Year Feeding (oncogenic) - mouse: Erthrocyte count, hemoglobin level and hematocrit are somewhat lower in males of 10,000 ppm level (HDT); no core grade (Uniroyal Chemical Co., 1986b)

Data Gap(s): Rat Teratology Study; Rabbit Teratology Study

I.A.5. Confidence in the Oral RfD

Study — Low
Database — Medium
RfD — Low

The critical study is given a low confidence rating. Because of the extensive but questionable quality of the database, the submission of a new reproduction study and the pending submission of new chronic rat and mouse studies, the database is given a medium confidence rating. Therefore, confidence in the RfD can be considered low to medium.

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 — Pesticide Registration Files

Agency Work Group Review — 09/16/1987

Verification Date — 09/16/1987

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 alar conducted in August 2003 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at 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 (internet address).

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

Substance Name — Alar
CASRN — 1596-84-5
Primary Synonym — Daminozide

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Alar
CASRN — 1596-84-5
Primary Synonym — Daminozide

Not available at this time.

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — Alar
CASRN — 1596-84-5
Primary Synonym — Daminozide

VI.A. Oral RfD References

NCI (National Cancer Institute). 1978. Bioassay of Daminozide for Possible Carcinogenicity. NCI Carcinogenesis Technical Report Series No. 83. DHEW Publication No. (NIH) 78-1333.

Uniroyal Chemical. 1964. MRID No. 00009727. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Uniroyal Chemical. 1966. MRID No. 0009413. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Uniroyal Chemical Company. 1978. MRID No. 00053764. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Uniroyal Chemical Company. 1986a. MRID No. 00016266. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Uniroyal Chemical Company. 1986b. MRID No. 40093501k, 40451001. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Uniroyal Chemical Company. 1987. MRID No. 40233901. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

United States Rubber Company. 1966. MRID No. 00094113. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Alar
CASRN — 1596-84-5
Primary Synonym — Daminozide

Date	Section	Description
10/28/2003	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Alar
CASRN — 1596-84-5
Primary Synonym — Daminozide
Last Revised — 06/30/1988

- 1596-84-5
- Alar
- ALAR-85
- AMINOZIDE
- B-9
- B 995
- BERNSTEINSAEURE-2,2-DIMETHYLHYDRAZID
- B-NINE
- BUTANEDIOIC ACID MONO(2,2-DIMETHYLHYDRAZIDE)
- Daminozide
- DIMAS
- DIMETHYLAMINOSUCCINAMIC ACID
- 2,2-DIMETHYLHYDRAZID KYSELINY JANTAROVE
- DMASA
- DMSA
- KYLAR
- NCI-C03827
- N-DIMETHYL AMINO-beta-CARBAMYL PROPIONIC ACID
- N-(DIMETHYLAMINO)SUCCINAMIC ACID
- N-DIMETHYLAMINO-SUCCINAMIDSAEURE
- SADH
- SUCCINIC ACID 2,2-DIMETHYLHYDRAZIDE
- SUCCINIC ACID, MONO(2,2-DIMETHYLHYDRAZIDE)
- SUCCINIC 1,1-DIMETHYL HYDRAZIDE