Systhane; CASRN 88671-89-0

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 Systhane

File First On-Line 09/26/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/26/1988
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 — Systhane
CASRN — 88671-89-0
Primary Synonym — Rally
Last Revised — 09/26/1988

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.

NOTE: The Oral RfD for systhane may change in the near future pending the outcome of a further review now being conducted by the RfD/RfC Work Group.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Testicular atrophy **2-Year Chronic Rat Feeding Study** **Rohm and Haas, 1986a**	NOEL: 50 ppm (2.49 mg/kg/day) LEL: 200 ppm (9.84 mg/kg/day	100	1	2.5E-2 mg/kg/day

* Conversion Factors: Actual dose tested

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

Rohm and Haas Company. 1986a. MRID No. 00165247. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Groups of 110 rats of each sex were fed RH-3866 in the diet at three dose levels for a period of 24 months. The following dose levels were used: 0, 25, 100, and 400 ppm for 2 weeks; 0, 35, 140, and 560 ppm for 2 weeks and 0, 50, 200, and 800 ppm for the remainder of the exposure period. The overall mean daily consumption was 0, 2.49, 9.84, and 39.21 mg/kg/day for males and 0, 3.23, 12.86, and 52.34 mg/kg/day for females. Slight increases in hepatic mixed function oxidase activity (MFO) were observed in high dose males at 3 and 6 months and in the mid- and high-dose females at 3 months. There was a marginal effect of the exposure to the chemical on the mean liver weights in females. A significant increase in the incidence of unilateral and bilateral testicular atrophy was observed in the mid- and high-dose males. The seminiferous tubules were frequently devoid of spermatid formation and germinal epithelial cells. In several cases, only Sertoli cells remained. The NOEL in this study is, therefore, considered to be 2.49 mg/kg/day (50 ppm) and the LEL is 9.48 mg/kg/day (200 ppm) for testicular atrophy.

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.

MF — None

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

Data Considered for Establishing the RfD:

1) 2-Year Feeding (oncogenic) - rat: Principal study - see previous description;

2) 1-Year Feeding - dog: NOEL=100 ppm (3.09 mg/kg/day for males and 3.83 mg/kg/day for females); LEL=400 ppm (14.28 mg/kg/day for males and 15.68 for females) (hepatocellular hypertrophy); core grade minimum (Rohm and Haas Co., 1986b)

3) 2-Generation Reproduction - rat: Systemic NOEL=2.32 mg/kg/day; Systemic LEL=9.28 mg/kg/day (increase in liver weight, hepatocellular hypertrophy); Reproductive NOEL=9.28 mg/kg/day; Reproductive LEL=46.4 mg/kg/day (testicular atrophy, increase in stillborns, decrease in body weight gain of offspring during lactation); core grade guideline (Rohm and Haas Co., 1985)

4) Teratology - rat: Embryotoxicity NOEL=29 mg/kg/day; Embryotoxicity LEL=87 mg/kg/day (decrease in viable fetuses, increase in early resorptions); Fetotoxicity NOEL=87 mg/kg/day; Fetotoxicity LEL=290.1 mg/kg/day (increase in incidence of developmental variations); Maternal toxicity NOEL=290.1 mg/kg/day; Maternal toxicity LEL=435.1 mg/kg/day (clinical signs of toxicity, decrease in body weight gain); core grade minimum (Rohm and Haas Co., 1984a)

5) Teratology - rabbit: Maternal toxicity NOEL=20 mg/kg/day; Maternal toxicity LEL=60 mg/kg/day (reduced body weight gain); Fetotoxicity NOEL=60 mg/kg/day; Fetotoxicity LEL=200 mg/kg/day (increased number of resorptions/litter, number of litters with greater than 2 resorptions, and number of litters totally resorbed; reduced viability index and reduced litter size); Not teratogenic up to 200 mg/kg/day (HDT); core grade minimum (Rohm and Haas Co., 1984b)

Other Data Reviewed:

1) 24-Month Chronic Feeding (oncogenic) - mice: Systemic NOEL=20 ppm (3 mg/kg/day); Systemic LEL=100 ppm (15 mg/kg/day) (increase in liver mixed function oxidase); Centrilobular hepatocytic hypertrophy, Kupffer cell pigmentation, periportal vacuolation and altered foci were seen at 500 ppm (75 mg/kg/day); core grade guideline for chronic feeding; (Rohm and Haas Co., 1986c)

2) 90-Day Feeding - dog: NOEL=0.3 mg/kg/day; LEL=5.9 mg/kg/day (liver centrilobular or midzonal hepatocellular hypertrophy); core grade minimum (Rohm and Haas Co., 1984c)

3) 90-Day Feeding - rat: NOEL=49.1 mg/kg/day; LEL=147.2 mg/kg/day (increase in liver weight, hepatocellular necrosis and hypertrophy, increase in kidney weight, pigmented convoluted tubules of kidney, vacuolated adrenal cortex); core grade minimum (Rohm and Haas Co., 1984d)

Data Gap(s): None

I.A.5. Confidence in the Oral RfD

Study — High
Database — High
RfD — High

The critical study is of good quality and is given a high confidence rating. Additional studies are supportive and of good quality; therefore, the database is given a high confidence rating. High 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 — Pesticide Registration Files

Agency Work Group Review —- 02/25/1988, 12/09/1994

Verification Date — 02/25/1988

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 Systhane conducted in September 2002 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 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 — Systhane
CASRN — 88671-89-0
Primary Synonym — Rally

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Systhane
CASRN — 88671-89-0
Primary Synonym — Rally

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]

VI. Bibliography

Substance Name — Systhane
CASRN — 88671-89-0
Primary Synonym — Rally

VI.A. Oral RfD References

Rohm and Haas Company. 1984a. EPA Accession No. 072901. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

Rohm and Haas Company. 1984b. EPA Accession No. 266098. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

Rohm and Haas Company. 1984c. EPA Accession No. 072899 - 072900. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

Rohm and Haas Company. 1984d. EPA Accession No. 072897 - 072898. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

Rohm and Haas Company. 1985. EPA Accession No. 073522. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

Rohm and Haas Company. 1986a. MRID No. 00165247. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

Rohm and Haas Company. 1986b. EPA Accession No. 266088. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

Rohm and Haas Company. 1986c. EPA Accession No. 266090. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Systhane
CASRN — 88671-89-0
Primary Synonym — Rally

Date	Section	Description
09/26/1988	I.A.	Oral RfD summary on-line
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Systhane
CASRN — 88671-89-0
Primary Synonym — Rally
Last Revised — 09/26/1988

- 88671-89-0
- alpha-BUTYL-alpha-(4-CHLOROPHENYL)-1H-1,2,4-TRIAZOLE-1-PROPANENITRILE
- 2-p-CHLOROPHENYL-2-(1H-1,2,4-TRIAZOL-1-YLMETHYL)HEXANENITRILE
- MYCLOBUTANIL
- Rally
- RH 3866
- Systhane
- 1H-1,2,4-TRIAZOLE-1-PROPANENITRILE, alpha-BUTYL-alpha-(4-CHLOROPHENYL)-