Strychnine; CASRN 57-24-9

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 <u>IRIS assessment</u> <u>development process</u>. 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 <u>guidance documents located</u> <u>on the IRIS website</u>.

STATUS OF DATA FOR Strychnine

File First On-Line 01/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	01/31/1987
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 — Strychnine CASRN — 57-24-9 Last Revised — 01/31/1987

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

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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
Toxicity/histopathology	NOAEL: none	10,000	1	3E-4 mg/kg/day
Rat Oral Short-term to Subchronic Study	LOAEL/FEL: 2.5 mg/kg/day			
Seidl and Zbinden, 1982				

*Conversion Factors: none

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

Seidl, I. and G. Zbinden. 1982. Subchronic oral toxicity of strychnine in rats. Arch. Toxicol. 51(3): 267-271.

This is the only oral short-term or subchronic study reported, in which rats received daily doses of 0 - 10 mg/kg of strychnine by gavage for 28 days. Data recorded for the surviving animals included blood cell counts, electrocardiograms, eye examinations, urine chemistry, weight gain, tissue histology, organ weights, behavioral tests, and food and water consumption. Mortality was observed in 5/12 male rats receiving 10 mg/kg, 1/12 in each of the 5 mg and 2.5 mg/kg groups. All deaths occurred 0.5-6 hours after oral doses. While one rat that died in the 2.5-mg/kg/day group showed signs of poisoning, no symptoms were exhibited by survivors, nor did any of the survivors differ from controls histologically or in any of the parameters monitored. The systemic level of this rapidly degradable toxicant [based on pharmacokinetics data, Sgaragli and Mannaioni (1973)] was probably much higher than in normal oral intake with food and water because it was administered all at once by gavage. Thus, 2.5 mg/kg/day could be considered a short-term to subchronic LOAEL for rats.

Additional studies (Gritzelmann et al., 1978) reported that a 6-month-old human patient received strychnine doses of 0.3-1.1 mg/kg/day over an 18-month period without any adverse effects. However, the patient may have had a higher strychnine tolerance as a result of nonketotic

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hyperglycinemia. The Oil and Hazardous Materials-Technical Assistance Data Systems (1984) reported that "adults may safely drink daily 0.078-0.25 gallons of water containing 10 mg/L of strychnine" (equivalent to 2.9-9.5 mg/day). This corresponds to 0.041-0.136 mg/kg.

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

UF — An RfD of 0.0003 mg/kg/day or 0.02 mg/day for a 70-kg person is derived from the Seidl and Zbinden (1982) short-term to subchronic study by applying an uncertainty factor of 10,000. This factor accounts for extrapolation from a less-than-chronic to a chronic exposure study, extrapolation from animals to humans, and differences in sensitivity among the human population. An additional 10 is used because a LOAEL/FEL (2.5 mg/kg/day) was utilized in the estimation of the RfD instead of a NOAEL. In view of this concern and the limitations in the database, the derived RfD should be viewed as an interim estimate. Despite the limitations of the database, the additional factor of 10 should result in a sufficiently protective level.

MF — None

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

None.

I.A.5. Confidence in the Oral RfD

Study — Low Database — Low RfD — Low

Confidence in the chosen study is low because a small number of animals were tested, a NOEL was not established, and the study was extremely short. Confidence in the database is low because of the limited supporting studies. Low 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 — None

Agency Work Group Review — 08/05/1985

Verification Date — 08/05/1985

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 Strychnine 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 <u>hotline.iris@epa.gov</u> 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 — Strychnine CASRN — 57-24-9

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Strychnine CASRN — 57-24-9

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

VI. Bibliography

Substance Name — Strychnine CASRN — 57-24-9

VI.A. Oral RfD References

Gitzelmann, R., B. Steinmann and M. Cuenod. 1978. Strychnine for the treatment of nonketotic hyperglycinemia. New England J. Med. 298: 1424.

Seidl, I. and G. Zbinden. 1982. Subchronic oral toxicity of strychnine in rats. Arch. Toxicol. 51(3): 267-271.

Sgaragli, G.P. and P.F. Mannaioni. 1973. Pharmacokinetic observations on a case of massive strychnine poisoning. Clin. Toxicol. 6(4): 533-540.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Strychnine CASRN — 57-24-9

Date	Section	Description
12/03/2002	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Strychnine CASRN — 57-24-9 Last Revised — 01/31/1987

- 57-24-9
- Certox
- Dolco Mouse Cereal
- Kwik-Kil
- Mole Death
- Mouse-Nots
- Mouse-Rid
- Mouse-Tox
- Pied Piper Mouse Seed
- Ro-Dex
- Sanaseed
- Strychnidin-10-one
- Strychnin
- Strychnine
- Strychnos