Pyridine; CASRN 110-86-1

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 Pyridine

File First On-Line 09/30/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/30/1987
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 — Pyridine
CASRN — 110-86-1
Last Revised — 09/30/1987

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

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
Increased Liver Weight **90-Day Rat Oral Gavage Study** **U.S. EPA, 1986**	NOAEL: 1.0 mg/kg/day LOAEL: 10 mg/kg/day	1000	1	1E-3 mg/kg/day

*Conversion Factors -- none

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

U.S. EPA. 1986. Pyridine. 90-Day subchronic oral toxicity in rats. Sponsored by Office of Solid Waste, Washington, DC.

In the U.S. EPA (1986) study Sprague-Dawley rats (10/dose/sex) were gavaged daily with 0, 0.25, 1.0, 10, 25, and 50 mg/kg/day pyridine for 90 days. Data generated included body and organ weights, food consumption, hematologic and clinical chemistry parameters, ophthalmologic evaluations and histopathologic examinations of target organs. Results of this study indicated a significant dose-related increase in the female liver-to-body weight ratios in the 10, 25 and 50 mg/kg/day dose groups. The males of the low-dose group showed a significant decrease in the relative liver weights; however, the males in other dose groups did not show any significant differences; thus, the effect seen in males exposed to 1 mg/kg/day pyridine is probably an artifact.

In order to examine the neurotoxicity of pyridine, 10 rats/group were perfused at the time of sacrifice; histopathologic examinations of brain, liver, and other target organs were conducted. The histopathologic examinations did not reveal any morphologic alterations in the brains of exposed and unexposed animals. However, histopathologic evaluations of target organs showed a 70% incidence of nonneoplastic hepatic lesions in males of the high-dose group (50

mg/kg/day) compared with 10% incidence in the vehicle control group. The 0.25 and 1.0 mg/kg/day dosed male rats also showed a 10% incidence of these lesions; however, no such lesions were observed in the 10 or 25 mg/kg/day dose groups. In the females, the frequency of incidence of these lesions was 30% in the 50 mg/kg/day group and 10% in the vehicle control group. Based on the data presented above, 1 mg/kg/day was identified as a NOAEL and 10 mg/kg/day as a LOAEL for hepatic hypertrophy in female rats.

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

UF — The UF of 1000 includes 10 for interspecies and 10 for intra- species variability in the toxicity of this chemical in lieu of specific data. An additional factor of 10 was applied to extrapolate from a subchronic to chronic effect level.

MF — None

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

The previous RfD of 0.002 mg/kg/day (7/8/85) for pyridine was based on a subchronic inhalation study in rats that was reported in the Encyclopedia of Occupational Safety and Health (1983). Because of lack of details of the study and a free-standing LOAEL, the confidence in the study was low. NTP (1979) also examined toxicity in mice and rats administered different doses of pyridine by gavage over a 90-day period. This study provided a NOAEL of 25 mg/kg/day in both mice and rats; however, mice exposed to 50 mg/kg/day showed clinical signs of CNS-related toxicity which were reported at much lower doses in the Encyclopedia of Occupational Safety and Health (1983). Because of these uncertainties concerning possible CNS-related toxicity, the Office of Solid Waste sponsored the subchronic rat oral gavage study (U.S. EPA, 1986).

The study reported in the Encyclopedia of Occupational Safety and Health (1983) contains data taken from a rat inhalation study in which the exposure chamber contained 10 to 50 ppm pyridine vapor over 7 hours/day, 5 days/week for a 6-month period. The lower dose, 10 ppm pyridine (2.15 mg/kg/day) had no effect on growth rate and mortality, but an increase in the relative liver weights was observed. Further details of the study were unavailable from the database. The 10 ppm exposure level was considered a LOAEL.

An NTP (1979) study examined toxicity in rats and mice administered different doses of pyridine by gavage over a 90-day period. Endpoints monitored included body weight changes, food consumption, mortality, clinical observations, and histopathology of target organs. The data indicated a NOAEL for rats at 25 mg/kg/day and a LOAEL (liver histopathology) at 50 mg/kg/day. In the case of mice, clinical signs were observed at 50 mg/kg/day, which may be considered a LOAEL. Consequently, the highest NOAEL above which adverse effects were not

reported for either species would be 25 mg/kg/day in rats. Mortality was observed at doses of 100 and 200 mg/kg/day in rats and at 400 mg/kg/day in mice. By applying an uncertainty factor of 1000, the NOAEL of 25 mg/kg/day in rats yields an RfD of 0.03 mg/kg/day, which is higher than the currently derived value (0.001 mg/kg/day). Continuing concerns are the reported neurotoxic symptoms associated with short-term low-level occupational exposure (Encyclopedia of Occupational Safety and Health, 1983) and the clinical signs reported in the NTP study.

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Medium
RfD — Medium

The subchronic oral study provided adequate toxicologic endpoints; therefore, a medium confidence is assigned. The database contains adequate subchronic studies to support the NOAEL of the critical study, but other chronic toxicity and reproductive studies are lacking; thus, confidence in the database can be considered medium to low. Confidence in the RfD can also be considered medium to low.

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 — 06/24/1985, 07/08/1985, 05/14/1986, 08/13/1987

Verification Date — 08/13/1987

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 Pyridine 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 — Pyridine
CASRN — 110-86-1

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Pyridine
CASRN — 110-86-1

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 — Pyridine
CASRN — 110-86-1

VI.A. Oral RfD References

Encyclopedia of Occupational Safety and Health. Vol.II, 3rd ed. 1983. International Labor Office, Geneva, Switzerland. p. 1810-1811.

NTP (National Toxicology Program). 1979. Quality assessment report subchronic study of pyridine in Fischer 344 rats and B6C3R1 mice. Report prepared by Gulf South Research Institute.

U.S. EPA. 1986. Pyridine. 90-day subchronic oral toxicity in rats. Sponsored by the Office of Solid Waste, Washington, DC.

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Pyridine
CASRN — 110-86-1

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

VIII. Synonyms

Substance Name — Pyridine
CASRN — 110-86-1
Last Revised — 09/30/1987

- 110-86-1
- AZABENZENE
- AZINE
- NCI-C55301
- PIRIDINA
- PIRYDYNA
- PYRIDIN
- Pyridine
- RCRA WASTE NUMBER U196
- TRITISAN