Furan; CASRN 110-00-9

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 Furan

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 — Furan CASRN — 110-00-9 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
Hepatic lesions	NOAEL: 2 mg/kg converted to 1.4 mg/kg/day on	1000	1	1E-3 mg/kg/day
Mouse Subchronic Oral Study	5 days/7 days basis			
NTP, 1982	LOAEL: 4 mg/kg/day (rat)			

*Conversion Factors -- 5 days/week feeding schedule

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

NTP (National Toxicology Program). 1982. Subchronic toxicity report on furan in B6C3F1 mice. Prepared by Southern Research Institute under Contract No. 1- CP-95641-01 for NTP, Bethesda, MD.

NTP (1982) performed a 13-week gavage study using mice and rats (10 animals/sex/group) treated 5 days/week with furan in corn oil at 0-60 mg/kg. In this study, data on mortality, body weight, organ weight, and clinical and histopathologic signs of toxicity were evaluated.

Clinical signs of toxicity were, for the most part, confined to male and female rats and female mice in the high-dose (60 mg/kg) group. High-dose male and female rats and high-dose (30 mg/kg) male mice had treatment-related reduced rates of body weight gain. In rats, histopathologic examination revealed a dose-related increased severity in liver lesions; lesions observed at the 4 mg/kg dose level were considered "minimal to mild." Measurement of relative organ weights revealed a dose-related increase in liver size in all treated groups of males and in all but the lowest dose (4 mg/kg) groups of female rats. In mice, relative organ weight measurements suggest that treatment-related increases in liver weight occurred in male mice at doses greater than or equal to 15 mg/kg and in females at doses greater than or equal to 30 mg/kg. Upon histopathologic examination, toxic hepatitis of dose- related severity was noted in

male mice at doses greater than or equal to 8 mg/kg and in female mice at doses greater than or equal to 15 mg/kg. Doses of 2 and 4 mg/kg/day were without toxic effect.

Examination of the NTP (1982) data indicated that the rat study failed to define a threshold for toxic hepatitis, the major lesion in the target organ for the toxicity of furan. The mouse study (NTP, 1982) indicated a threshold for toxic hepatitis, in that 2 and 4 mg/kg were doses in males at which lesions did not occur; mild lesions of toxic hepatitis occurred at 8 mg/kg. In females, lesions of toxic hepatitis were absent at 8 mg/kg and present at 15 mg/kg. Considering these data together, a dose of 2 mg/kg/day is a reasonable choice for the NOAEL. Since treatment was performed 5 days/week, the 2 mg/kg dose can be transformed to an equivalent dose of 1.4 mg/kg/day. By applying an uncertainty factor of 1000 to the mouse NOAEL of 1.4 mg/kg/day, an oral RfD (ADI) of 1 ug/kg/day or 0.1 mg/day for a 70-kg human can be recommended.

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

UF — An uncertainty factor of 1000 was applied: 10 for extrapolation from subchronic to chronic studies, 10 for interspecies extrapolation and another factor of 10 to provide added protection for sensitive individuals.

MF — None

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

Availability of rat and mouse subchronic oral toxicity data provided a medium level of confidence for the RfD. The National Toxicology Program (NTP, 1985) is currently evaluating histopathologic data of a chronic gavage bioassay of furan in rats and mice. The data from this study may change the RfD and the level of confidence.

I.A.5. Confidence in the Oral RfD

Study — Medium Database — Low RfD — Low

The principal study provided toxicologic parameters in well-designed subchronic studies in both rats and mice and, thus, rated medium. The data base lacks supporting studies and is rated low. 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 — 02/26/1986

Verification Date — 02/26/1986

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 Furan 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 <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 <u>hotline.iris@epa.gov</u> (internet address).

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

Substance Name — Furan CASRN — 110-00-9

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Furan CASRN — 110-00-9

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 — Furan CASRN — 110-00-9

VI.A. Oral RfD References

NTP (National Toxicology Program). 1982. Subchronic toxicity report on furan in B6C3F1 mice. Prepared by Southern Research Institute under Contract No. 1- ES-95651-01 for NTP, Bethesda, MD.

NTP (National Toxicology Program). 1985. Management Status Report dated 08/07/1985. Bethesda, MD.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Furan CASRN — 110-00-9

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

VIII. Synonyms

Substance Name — Furan CASRN — 110-00-9 Last Revised — 01/31/1987

- 110-00-9
- Divinylene oxide
- Furan
- Furfuran
- Oxacyclopentadiene
- Oxole
- Tetrole