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Norflurazon; CASRN 27314-13-2

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 Norflurazon

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 — Norflurazon

CASRN — 27314-13-2

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

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
Liver and thyroid effects	NOEL: 150 ppm (3.75 mg/kg/day)	100	1	4E-2 mg/kg/day
6-Month Dog Feeding Study	LEL: 450 ppm (10.25 mg/kg/day)			
Sandoz-Wander, 1973				

*Conversion Factors: 1 ppm = 0.025 mg/kg/day (assumed dog food consumption)

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

Sandoz-Wander, Inc. 1973. MRID No. 00111618. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Four groups of 4 male and 4 female beagle dogs were exposed to 0, 50, 150, or 450 ppm Norflurazon in the diet for 6-months. At 450 ppm, effects were seen in the liver and the thyroid. Liver effects were increased weights, congestion, and swelling of the hepatocytes. Thyroid changes involved a slight increase in colloidal vacuoles. The NOEL for Norflurazon in this study was 150 ppm.

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. An additional UF of 10 to account for the subchronic (6-month) duration of the dog study was not considered necessary since comparing the results of the 90-day rat study and the life time rat study does not indicate that Norflurazon exerts toxic effects at lower doses when exposure is of a chronic nature as compared to subchronic exposure.

MF — None

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

Norflurazon has been found to be associated with an increased incidence of hepatomas in male mice at the highest dose in the chronic mouse study. The available reviews and risk assessments are included here.

Data Considered for Establishing the RfD

- 1) 6-Month Feeding - dog: Principal study - see discussion above; core grade minimum
- 2) 2-Year Feeding - rat: NOEL=375 ppm (18.75 mg/kg/day); LEL=1025 ppm (51.25 mg/kg/day) (inhibition of body weight gain; high BUN and reduced 2,3- diphosphoglyceric acid; increased mortality; increased liver, kidney, and ovary weights; fatty changes in adrenal; endometritis; increased chromophobe adenomas in the pituitary; medullary or cortical hypertrophy in adrenals; casts in kidneys); core grade minimum (Sandoz, Inc., 1975a)
- 3) 90-Day Feeding - rat: NOEL=500 ppm (25 mg/kg/day); LEL=2500 ppm (250 mg/kg/day) (increased liver-to-body weight ratios); no core grade (Sandoz, Inc., 1971)
- 4) 3-Generation Reproduction - rat: NOEL=375 ppm (18.75 mg/kg/day); LEL=1025 ppm (51.25 mg/kg/day) (reduced fertility, gestation, and viability); core grade minimum (Sandoz, Inc., 1975b)
- 5) Teratology - rat: NOEL (maternal, fetal, teratogenic)=400 mg/kg/day (highest dose tested); core grade minimum (Sandoz, Inc., 1972)
- 6) Teratology - rabbit: Maternal NOEL=30 mg/kg/day; Maternal LEL=60 mg/kg/day (decreased weight gain, 2/15 aborted); Fetotoxic NOEL=10 mg/kg/day; Fetotoxic LEL=30 mg/kg/day (decreased weight; incomplete ossification); core grade guideline (Sandoz, Inc., 1983)

Other Data Reviewed

- 1) 2-Year Feeding - mice: NOEL=340 ppm (50 mg/kg/day); LEL=1360 ppm (200 mg/kg/day) (increased liver/body weight ratios; hyperplasia, hypertrophy); core grade minimum (Sandoz, Inc., 1975c)

Data Gap(s): None

I.A.5. Confidence in the Oral RfD

Study — High
Database — High
RfD — High

The principal study is of good quality and is given a high confidence rating. Additional studies are of good quality and there are no data gaps; 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

Pesticide Registration Standard, July 1984

Pesticide Registration Files

Agency Work Group Review — 07/08/1986

Verification Date — 07/08/1986

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 Norflurazon conducted in November 2001 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 — Norflurazon
CASRN — 27314-13-2

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Norflurazon
CASRN — 27314-13-2

Not available at this time.

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Norflurazon
CASRN — 27314-13-2

VI.A. Oral RfD References

Sandoz, Inc. 1975a. MRID No. 00082019, 00111617. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Sandoz, Inc. 1971. MRID No. 00091055. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Sandoz, Inc. 1975b. MRID No. 00080750, 00080751. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Sandoz, Inc. 1972. MRID No. 00063621. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Sandoz, Inc. 1983. MRID No. 00131152. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Sandoz, Inc. 1975c. MRID No. 00041015, 00041016, 00041401, 00044336. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Sandoz-Wander, Inc. 1973. MRID No. 00111618. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Norflurazon
CASRN — 27314-13-2

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

VIII. Synonyms

Substance Name — Norflurazon
CASRN — 27314-13-2
Last Revised — 01/31/1987

- 27314-13-2
- 4-CHLORO-5-(METHYLAMINO)-2-(alpha,alpha,alpha-TRIFLUORO-m-TOLYL)-3(2H)-PYRIDAZINONE
- EVITAL
- MONOMETFLURAZONE
- Norflurazon
- 3(2H)-PYRIDAZINONE, 4-CHLORO-5-(METHYLAMINO)-2-(alpha,alpha,alpha-TRIFLUORO-m- TOLYL)-
- SAN 9789
- SAN 9789 H
- SOLICAM
- ZORIAL