

Flutolanil; CASRN 66332-96-5

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 Flutolanil

File First On-Line 05/01/1989

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	05/01/1989
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 — Flutolanil
CASRN — 66332-96-5
Primary Synonym — Moncut
Last Revised — 05/01/1989

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
Decreased body weight and body weight gains in both doses; Increased liver weights at high dose	NOEL: None LEL: 63.7 mg/kg/day	1000	1	6E-2 mg/kg/day
3-Generation Reproduction and Teratology Study in Rats				
NOR-AM Chemical Co., 1982a				

*Conversion Factors: Actual dose tested

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

NOR-AM Chemical Company. 1982a. MRID No. 40342923. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Rats (Wistar-Imamichi), 25/sex/dose level, were administered flutolanil in the diet at dose levels of 0, 1000, and 10,000 ppm for 3 generations. In the low- dose group, the actual dose received by the animals across generations varied from 63.7 to 96.7 and 86.3 to 90.1 mg/kg/day for males and females, respectively. The high-dose group males and females received 661.8 to 1002.0 and 880.8 to 982.5 mg/kg/day, respectively. There were no treatment related clinical toxicity signs, mortality, differences in food consumption or efficiency and water consumption. No treatment-related effects were noted on mating performance, duration of pregnancy and litter size. There were increases in absolute and relative liver weights in the high-dose males and females in all

generations. Reproductive toxicity was observed at both dose levels in the form of reduced pup body weights and body weight gains during the lactation period and subsequent reduced adult body weights in both males and females. The reproductive segment is considered as supplementary data because of multiple study deficiencies. However, in the teratology segment, increased fetal mortality (post implantation loss) was noted in the high-dose group. There also was reduced fetal body weights in both dose groups. Viseral examination revealed a possible treatment related enlargement of the renal pelvis (statistically significant in the high-dose group).

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 was used to account for the lack of an established NOEL in the reproduction/teratology study.

MF — None

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

Data Considered for Establishing the RfD

- 1) Reproduction and Teratology - rat: Principal study - see previous description
- 2) 2-Year Feeding - dog: Systemic NOEL=50 mg/kg/day; Systemic LEL=250 mg/kg/day (emesis, salivation, soft stools, lower body weight gains and decreased food consumption); core grade minimum (NOR-AM Chemical Co., 1982b)
- 3) 2-Year Feeding (oncogenic): Systemic NOEL=2000 ppm (100 mg/kg/day); Systemic LEL=10,000 ppm (500 mg/kg/day) [reduced body weight and body weight gains in males (during the first 13 weeks of the study); decreased absolute liver, liver-to-body, and liver-to-brain weights in males and females]; No treatment related oncogenic effects were noted at any dose level; core grade minimum (NOR-AM Chemical Co., 1982c)
- 4) Teratology - rabbit: Maternal toxicity NOEL=40 mg/kg/day; Maternal toxicity LEL=200 mg/kg/day (increase in resorptions); Developmental toxicity NOEL=40 mg/kg/day; Developmental toxicity LEL=200 mg/kg/day (increase in resorptions); core grade minimum (NOR-AM Chemical Co., 1987)

Other Data Reviewed:

1) 90-Day Feeding - dog: Systemic NOEL=80 mg/kg/day; Systemic LEL=400 mg/kg/day (enlarged livers and increased severity of glycogen deposition in males and females); core grade guideline (NOR-AM Chemical Co., 1986a)

2) 90-Day Feeding - rat: Systemic NOEL=500 ppm (25 mg/kg/day); Systemic LEL=4000 ppm (200 mg/kg/day) (increased absolute and relative liver weights in males and females); core grade guideline (NOR-AM Chemical Co., 1986b)

Data Gap(s): Rat Reproduction Study; Rat Teratology Study

I.A.5. Confidence in the Oral RfD

Study — Low
Database — Medium
RfD — Medium

The critical study is of poor quality; therefore, it is given a low confidence rating. Because of the lack of an acceptable reproduction study, the data base is given a medium confidence rating. Medium 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 — 01/18/1989, 02/16/1989

Verification Date — 02/16/1989

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 Flutolanil 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 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 — Flutolanil

CASRN — 66332-96-5

Primary Synonym — Moncut

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Flutolanil

CASRN — 66332-96-5

Primary Synonym — Moncut

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 — Flutolanil

CASRN — 66332-96-5

Primary Synonym — Moncut

VI.A. Oral RfD References

NOR-AM Chemical Company. 1982a. MRID No. 40342923. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

NOR-AM Chemical Company. 1982b. MRID No. 40342922. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

NOR-AM Chemical Company. 1982c. MRID No. 40342921. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

NOR-AM Chemical Company. 1987. MRID No. 40342924. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

NOR-AM Chemical Company. 1986a. MRID No. 40342920. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

NOR-AM Chemical Company. 1986b. MRID No. 40342919. 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 — Flutolanil

CASRN — 66332-96-5

Primary Synonym — Moncut

Date	Section	Description
05/01/1989	I.A.	Oral RfD summary on-line

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

VIII. Synonyms

Substance Name — Flutolanil

CASRN — 66332-96-5

Primary Synonym — Moncut

Last Revised — 05/01/1989

- 66332-96-5
- Benzamide, N-(3-(1-methylethoxy)phenyl)-2-(trifluoromethyl)- (9CI)
- Flutolanil
- Moncut