

Amdro; CASRN 67485-29-4

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 Amdro

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 — Amdro

CASRN — 67485-29-4

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 organ weights	NOEL: 0.33 mg/kg/day	1000	1	3E-4 mg/kg/day
26-Week Dog Feeding Study	LEL: 1.0 mg/kg/day			
American Cyanamid, 1980				

* Conversion Factors: none

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

American Cyanamid Company. 1980. MRID No. 00035529. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Amdro (AC 217,300) was administered to 4 dogs/sex/dose for 26 weeks. The dose levels were 0 (control), 0.33, 1.0, and 3.0 mg/kg/day after the dogs had been fed. The only compound-related effects were increased liver weights and increased liver/body weight and brain/body weight ratios. Pathology, clinical chemistry, and hematology were unremarkable. The effects were noted at the 1.0 and 3.0 mg/kg/day levels, but not at the 0.33 mg/kg/day level.

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 since the critical study was only 26 weeks, instead of at least 1 year; additionally, the effects in dogs are shown to become more intense with time, as evidenced by comparison with the 13-week study.

MF — None

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

Data Considered for Establishing the RfD:

- 1) 26-Week Feeding - dog: Principal study - see previous description; core grade minimum
- 2) 2-Year Feeding - rat: NOEL=50 ppm (2.5 mg/kg/day); LEL=100 ppm (5 mg/kg/day) (decreased testicular weight, testicular atrophy, decreased LDH values, organ weight changes, decreased food consumption and weight gain); core grade minimum (American Cyanamid, 1982a)
- 3) 3-Generation Reproduction - rat: Maternal NOEL=50 ppm (2.5 mg/kg/day); Maternal LEL=100 ppm (5 mg/kg/day) (decreased food consumption, body weight gain); Reproductive NOEL=50 ppm; Reproductive LEL=100 ppm (male infertility); core grade minimum (American Cyanamid, 1982b)
- 4) Teratology - rat: Maternal NOEL=3 mg/kg/day; Maternal LEL=10 mg/kg/day (decreased mean body weight gain and discoloration of body fat); Fetal toxic NOEL=10 mg/kg/day; Fetal toxic LEL=30 mg/kg/day (decreased fetal weight); Teratogenic NOEL=30 mg/kg/day; LEL=none; core grade minimum (American Cyanamid, 1979a)
- 5) Teratology - rabbit: Maternal NOEL=none; Maternal LEL=5 mg/kg/day (decreased body weight gain); Fetotoxic NOEL=5 mg/kg/day; Fetotoxic LEL= 10 mg/kg/day (reduced fetal weight gain); Teratogenic NOEL=20 mg/kg/day; LEL=none; core grade minimum (American Cyanamid, 1982c)

Other Data Reviewed:

- 1) 18-Month Feeding (oncogenic) - mouse: Systemic NOEL=25 ppm (2.75 mg/kg/day); Systemic LEL=50 ppm (3.75 mg/kg/day) (increased testicular lesions, decreased body weight gain, increased renal amyloidosis); core grade minimum (American Cyanamid, 1982d)
- 2) 90-Day Feeding - dog: NOEL=3 mg/kg/day; LEL=6 mg/kg/day (testicular atrophy and decreased body weight and food consumption); core grade minimum (American Cyanamid, 1979b)
- 3) 90-Day Feeding - rat: NOEL=50 ppm (2.5 mg/kg/day); LEL=100 ppm (5 mg/kg/day) (testicular atrophy and decreased body weight); core grade minimum (American Cyanamid, 1979c)

Data Gap(s): None

I.A.5. Confidence in the Oral RfD

Study — Medium

Database — High

RfD — High

The chosen study provides sufficient data to rate a medium confidence. The database provides sufficient data to rate a high confidence, although some of the studies are of good but not outstanding quality. The total evaluation provides for high confidence in the derived RfD.

I.A.6. EPA Documentation and Review of the Oral RfD

Pesticide Registration Files

Agency Work Group Review — 03/11/1986, 05/20/1987

Verification Date — 05/20/1987

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 amdro conducted in August 2003 identified one or more significant new studies. IRIS users may request the references for those studies from 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 — Amdro

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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Amdro
CASRN — 67485-29-4

Not available at this time.

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Amdro
CASRN — 67485-29-4

VI.A. Oral RfD References

American Cyanamid Company. 1979a. MRID No. 00032638, 00061790. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1979b. MRID No. 00032634, 00061794. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1979c. MRID No. 00032641, 00061793. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1980. MRID No. 00035529. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1982a. MRID No. 00035527, 00061768, 00101565, 00126106. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1982b. MRID No. 00035525, 00101575. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1982c. MRID No. 00101558. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

American Cyanamid Company. 1982d. MRID No. 00035526, 00061767, 00101563, 00109466. 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 — Amdro
CASRN — 67485-29-4

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

VIII. Synonyms

Amdro
CASRN — 67485-29-4
Last Revised — 09/30/1987

- 67485-29-4
- AC 217300
- Amdro

- CL 217300
- 2(1H)-PYRIMIDINONE, TETRAHYDRO-5,5-DIMETHYL-, (3-(4-TRIFLUOROMETHYL)PHENYL-1-(2-(4-TRIFLUOROMETHYL)PHENYL)ETHENYL)-2-PROPENYLIDENE)HYDRAZONE