Cyromazine; CASRN 66215-27-8

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 Cyromazine

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 — Cyromazine
CASRN — 66215-27-8
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
Hematologic effects **6-Month Dog Study** **Oral Exposure (diet)** **Ciba-Geigy, 1980**	NOEL: 30 ppm diet (0.75 mg/kg/day) LEL: 300 ppm diet (7.5 mg/kg/day)	100	1	7.5E-3 mg/kg/day

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

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

Ciba-Geigy Corp. 1980. MRID No. 00103193. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Cyromazine was administered to 56 beagle dogs (7/sex/group) at 0, 30, 300, and 3000 ppm for 6 months. Pronounced effects on the hematocrit and hemoglobin levels were noted at 300 and 3000 ppm. The systemic NOEL was established at 30 ppm (0.75 mg/kg/day).

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 to account for the subchronic values of the study was not considered necessary since the 90-day and 2-year rat studies show that the differences between subchronic and chronic toxicities are insignificant. Likewise, an additional UF to account for a deficient database was not considered necessary since other studies generally showed higher NOELs and thus the toxicologic endpoint in the 6-month dog study is the most sensitive indicator of the toxicity of cyromazine.

MF — None

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

Data Considered for Establishing the RfD:

1) 6-Month Feeding - dog: Principal study - see previous description; core grade minimum

2) 90-Day Feeding - rat: NOEL=30 ppm (1.5 mg/kg/day); LEL=300 ppm (15 mg/kg/day) (relative liver weight decrease for males); core grade minimum (Ciba-Geigy, 1979a)

3) 2-Year Chronic (oncogenic) - rat: Systemic NOEL=30 ppm (1.5 mg/kg/day); Systemic LEL=300 ppm (15 mg/kg/day)(decreased body weight); core grade minimum (Ciba-Geigy, 1981a)

4) Teratology - rabbit: Teratogenic NOEL=5 mg/kg/day; Teratogenic LEL=10 mg/kg/day (findings of cyclopia and diaphragmatic hernia); Maternal NOEL=10 mg/kg/day; Maternal LEL=30 mg/kg/day (body weight gain depression and food consumption reduction); core grade minimum (Ciba-Geigy, 1981b)

5) Teratology - rat: Developmental toxicity NOEL=none; LEL=l00 mg/kg/day (LDT; increased skeletal variations); Maternal NOEL=100 mg/kg/day; Maternal LEL=300 mg/kg/day (increased incidences of clinical observations; decreased body weights); core grade minimum (Ciba-Geigy, 1979b)

6) 2-Generation Reproduction - rat: Reproductive NOEL=l000 ppm (50 mg/kg/day); Reproductive LEL=3000 ppm (150 mg/kg/day) (decreased pup weights and increased pup moritality); Systemic NOEL=30 ppm (1.5 mg/kg/day); Systemic LEL=1000 ppm (50 mg/kg/day) (body weight loss); core grade minimum (Ciba- Geigy, 1981c)

Data Gap(s): None

I.A.5. Confidence in the Oral RfD

Study — High
Database — High
RfD — High

The study on which the RfD is based is of high quality and of sufficient duration for the species tested (dog). Confidence in this study is high. In addition, there are generally good toxicology studies available (chronic rat and mouse studies) with cyromazine, which overall provide high confidence in the database. High 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 — 08/5/86

Verification Date — 08/5/86

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 Cyromazine 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 — Cyromazine
CASRN — 66215-27-8

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Cyromazine
CASRN — 66215-27-8

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 — Cyromazine
CASRN — 66215-27-8

VI.A. Oral RfD References

Ciba-Geigy Corporation. 1979a. MRID No. 00135433. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1979b. MRID No. 00027488. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1980. MRID No. 00103193. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1981a. MRID No. 00103202. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1981b. MRID No. 00103196. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Ciba-Geigy Corporation. 1981c. MRID No. 00103197. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Cyromazine
CASRN — 66215-27-8

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

VIII. Synonyms

Substance Name — Cyromazine
CASRN — 66215-27-8
Last Revised — 09/30/1987

- 66215-27-8
- AI3-52713 [USDA]
- Azimethiphos
- Caswell No. 167B
- CGA 72,662
- 2-cyclopropylamino-4,6-diamino-s-triazine
- Cyromazine
- Cyromazine [ANSI]
- 2,4-Diamino-6-(cyclopropylamino)-s-triazine
- EPA Pesticide Chemical Code 121301
- Larvadex
- Propanoic acid, 2-(4-((5-(trifluoromethyl)-2-pyridinyl)oxy)phenoxy)-,butyl ester
- 1,3,5-Triazine-2,4,6-triamine, N-cyclopropyl-

- Trigard
- Vetrazin