Harmony; CASRN 79277-27-3

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 Harmony

File First On-Line 09/26/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/26/1988
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 — Harmony
CASRN — 79277-27-3
Primary Synonym — DPX-M6316
Last Revised — 09/26/1988

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
Reduced body weight gains in males, reduced serum sodium in males and females **2-Year Rat Feeding Study** **du Pont, 1986a**	NOEL: 25 ppm (1.25 mg/kg/day) LEL: 500 ppm (25 mg/kg/day)	100	1	1.3E-2 mg/kg/day

*Conversion Factors: 1 ppm = 0.05 mg/kg/day (assumed rat food consumption)

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

E.I. du Pont de Nemours and Company. 1986a. MRID No. 00161274. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Harmony was administered at dietary levels of 0, 25, 500, and 2500 ppm (0, 1.25, 25, 125 mg/kg/day) to 62 rats/sex/group for 24 months. There was an interim sacrifice of 10 animals/sex/group at 12 months. The following parameters were evaluated: mortality, physical signs, body weights, food consumption, hematology, clinical chemistry, urinalysis, macroscopic and microscopic pathology. A slight but significant body weight reduction was seen in high dose males, body weight gains were significantly lower at the two highest doses. Serum sodium levels were sporadically lower at 500 and 2500 ppm throughout the study. Sodium levels in the rat are normally around 144 mg% and vary only slightly from animal to animal and over time. However, with administration of harmony, both the mid- (500 ppm) and high-dose (2500 ppm) groups showed a consistent decrease in serum sodium levels. Given the powerful homeostatic mechanisms that must be affected to change serum sodium levels from 144 mg%, the results appear to be a clearly compound-related.

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.

MF — None

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

Data Considered for Establishing the RfD:

1) 2-Year Feeding (oncogenic) - rat: Principal study - see previous description; core grade minimum

2) 1-Year Feeding - dog: Systemic NOEL=750 ppm (18.75 mg/kg/day); Systemic LEL=7500 ppm (187.5 mg/kg/day) (decreased body weights and body weight gains; increased liver weights in males); core grade minimum (du Pont, 1986b)

3) 2-Generation Reproduction - rat: Systemic and Reproductive NOEL=2500 ppm (125 mg/kg/day) (HDT); Systemic and Reproductive NOEL=none; no toxic effects were demonstrated at any dose; core grade minimum (du Pont, 1985a)

4) Teratology - rat: Maternal NOEL=750 mg/kg/day (HDT); Maternal LEL=none; Teratogenic NOEL=159 mg/kg/day; Teratogenic LEL=725 mg/kg/day (absence of renal papilla); Fetotoxic NOEL=159 mg/kg/day; Fetotoxic LEL=725 mg/kg/day (lower fetal body weights); core grade minimum (du Pont, 1984a)

5) Teratology - rabbit: Maternal NOEL=158 mg/kg/day; Maternal LEL=511 mg/kg/day (reduced weight gain); Developmental NOEL=511 mg/kg/day (HDT); Developmental LEL=none; core grade minimum (du Pont, 1985b)

Other Data Reviewed:

1) 18-Month Study (oncogenic) - mice: Systemic NOEL=25 ppm (3.75 mg/kg/day); Systemic LEL=750 ppm (112.5 mg/kg/day) (reduced body weight gains in males and females); core grade minimum (du Pont, 1985c)

2) 90-Day Feeding - rat: NOEL=100 ppm (5 mg/kg/day); LEL=2500 ppm (125 mg/kg/day) (decreased body weights and body weights gain in both sexes; decreased spleen, liver and heart weights in males; relative brain, kidney and testes weights were increased in males and relative brain and heart weights were increased in females); core grade minimum (du Pont, 1984b)

3) 13-Week Feeding - dog: NOEL=1500 ppm (37.5 mg/kg/day); LEL=7500 ppm (187.5 mg/kg/day) (body weight and adrenal weight suppression in males); core grade minimum (du Pont, 1984c)

Data Gap(s): None

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — High
RfD — High

The critical study is of adequate quality and is given a medium confidence rating. Additional studies are supportive and 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

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — Pesticide Registration Files

Agency Work Group Review — 03/23/1988

Verification Date — 03/23/1988

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 Harmony 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 — Harmony
CASRN — 79277-27-3
Primary Synonym — DPX-M6316

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Harmony
CASRN — 79277-27-3
Primary Synonym — DPX-M6316

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 — Harmony
CASRN — 79277-27-3
Primary Synonym — DPX-M6316

VI.A. Oral RfD References

E.I. du Pont de Nemours and Company. 1986a. MRID No. 00161274. Available from EPA. Write to FOI, EPA, Washington DC 20460.

E.I. du Pont de Nemours and Company. 1986b. Accession No. 263753. Available from EPA. Write to FOI, EPA, Washington DC 20460.

E.I. du Pont de Nemours and Company. 1985a. Accession No. 263758. Available from EPA. Write to FOI, EPA, Washington DC 20460.

E.I. du Pont de Nemours and Company. 1984a. Accession No. 073010. Available from EPA. Write to FOI, EPA, Washington DC 20460.

E.I. du Pont de Nemours and Company. 1985b. Accession No. 263758. Available from EPA. Write to FOI, EPA, Washington DC 20460.

E.I. du Pont de Nemours and Company. 1985c. Accession No. 263756. Available from EPA. Write to FOI, EPA, Washington DC 20460.

E.I. du Pont de Nemours and Company. 1984b. Accession No. 072847. Available from EPA. Write to FOI, EPA, Washington DC 20460.

E.I. du Pont de Nemours and Company. 1984c. Accession No. 072848. 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 — Harmony
CASRN — 79277-27-3
Primary Synonym — DPX-M6316

Date	Section	Description

Date	Section	Description
09/26/1988	I.A.	Oral RfD summary on-line
10/28/2003	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Harmony
CASRN — 79277-27-3
Primary Synonym — DPX-M6316
Last Revised — 09/26/1988

- 79277-27-3
- DPX-M6316
- Harmony
- (((((4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino)carbonyl)amino)sulfonyl)-2-Thiophenecarboxylic acid, methyl ester
- Thiameturon-methyl