Savey; CASRN 78587-05-0

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 Savey

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 — Savey
CASRN — 78587-05-0
Primary Synonym — DPX-Y5893
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
Hypertrophy of adrenal cortex (both sexes); hematologic effects (males) **1-Year Dog Feeding Study** **du Pont, 1984a**	NOEL: 100 ppm (2.5 mg/kg/day) LEL: 500 ppm (12.5 mg/kg/day)	100	1	2.5E-2 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)

E.I. du Pont de Nemours and Company. 1984a. MRID No. 00151359. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Savey (NA-73) was administered at dietary levels of 0, 100, 500, and 5000 ppm (0, 2.5, 12.5, and 125 mg/kg/day) to 4 beagle dogs/sex/group for 1 year. The following parameters were evaluated: mortality, physical signs, body weight, food consumption, opthalmology, hematological and clinical chemistry changes, and microscopic pathological changes. All animals survived the study. No treatment related clinical, othalmological, hematology, urinalysis or gross pathological findings were reported. Body weight gain was reduced at the high dose levels. Alkaline phosphatase was reduced in high-dose males and females. The NOEL for savey in beagle dogs was 100 ppm (2.5 mg/kg/day) based on adrenal cortex hypertrophy in both sexes at 500 and 5000 ppm (12.5 and 125 mg/kg/day). Adrenal weight was increased in both sexes of the high-dose dogs. Significant relative liver weight increase and liver hypertrophy were reported in the high-dose males.

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

2) 2-Year Feeding (oncogenic) - rat: Systemic NOEL=430 ppm (23 to 29 mg/kg/day); Systemic LEL=3000 ppm (160-200 mg/kg/day) (based upon actual consumption) (increased liver weight); core grade minimum (E.I. du Pont de Nemours and Co., 1985a)

3) 2-Generation Reproduction - rat: Maternal NOEL=400 ppm (35 mg/kg/day); Maternal LEL=2400 ppm (200 mg/kg/day) (decrease in body weight gain, food consumption, food efficiency; also increase in liver, kidney, and ovarian weights); Pup NOEL=400 ppm (35 mg/kg/day); Pup LEL=2400 ppm (200 mg/kg/day) (reduced body weight during lactation, slight delay in hair growth and/or eye opening); Reproductive NOEL=2400 (200 mg/kg/day) (HDT); Reproductive LEL=none; core grade minimum (E.I. du Pont de Nemours and Co., 1985b)

4) Teratology - rat: Maternal NOEL=240 mg/kg/day; Maternal LEL=720 mg/kg/day (reduced feed consumption and weight gain, increased ovarian weights); Fetotoxic NOEL=240 mg/kg/day; Fetotoxic LEL=720 mg/kg/day (delayed ossification, minor); Teratogenic NOEL=2160 mg/kg/day (HDT; no embryotoxicity at HDT); Teratogenic LEL=none; core grade minimum (E.I. du Pont de Nemours and Co., 1983)

5) Teratology - rabbit: Maternal and Developmental NOEL=1080 mg/kg/day (HDT); Maternal and Developmental LEL=none; core grade guideline (E.I. du Pont de Nemours and Co., 1984b)

Other Data Reviewed:

1) Chronic Feeding (oncogenic) - mice: Systemic NOEL=250 ppm (37.5 mg/kg/day); Systemic LEL=1500 ppm (225 mg/kg/day) (decreased male body weight); core grade guideline (E.I. du Pont de Nemours and Co., 1985c)

2) 90-Day Feeding - rat: NOEL=70 ppm (8.1 mg/kg/day for males, 5.4 mg/kg/day for females); LEL=500 ppm (25 mg/kg/day) (increased liver weights in both sexes; increased relative ovary and female kidney weights at 500 and 3500 ppm; decrease in plasma CHE of females at 500 and 3500 ppm; increased blood total protein and albumin levels at 500 ppm after 2-months of feeding; fatty degeneration of the zona fasciculta of the adrenal cortex of both sexes at 500 and 3500 ppm); core grade minimum (Nisson Soda Co., LDT., 1983)

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 of good quality; 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 — 02/25/1988

Verification Date — 02/25/1988

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 Savey conducted in September 2002 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 — Savey
CASRN — 78587-05-0
Primary Synonym — DPX-Y5893

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Savey
CASRN — 78587-05-0
Primary Synonym — DPX-Y5893

Not available at this time.

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — Savey
CASRN — 78587-05-0
Primary Synonym — DPX-Y5893

VI.A. Oral RfD References

E.I. du Pont de Nemours and Company. 1983. EPA Accession No. 072941. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

E.I. du Pont de Nemours and Company. 1984a. MRID No. 00151359. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

E.I. du Pont de Nemours and Company. 1984b. EPA Accession No. 073562. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

E.I. du Pont de Nemours and Company. 1985a. EPA Accession No. 073564. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

E.I. du Pont de Nemours and Company. 1985b. EPA Accession No. 073562. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

E.I. du Pont de Nemours and Company. 1985c. EPA Accession No. 073556 - 073561. Available from EPA. Write to FOI, EPA, Washington D.C. 20460.

Nisson Soda Company, Ltd. 1983. EPA Accession No. 072942. 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 — Savey
CASRN — 78587-05-0
Primary Synonym — DPX-Y5893

Date	Section	Description
09/26/1988	I.A.	Oral RfD summary on-line

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

VIII. Synonyms

Substance Name — Savey
CASRN — 78587-05-0
Primary Synonym — DPX-Y5893
Last Revised — 09/26/1988

- 78587-05-0
- 5-(4-Chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-3-thiazolidinecarboxamide, trans-
- DPX-Y5893
- Hexythiazox
- Hexythiazox [BSI:ISO]
- NA 73
- Nissorun
- Savey
- 3-Thiazolidinecarboxamide, 5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-, trans-
- trans-5-(4-Chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-3-thiazolidinecarboxamide