United States Environmental Protection Agency

Office of Prevention, Pesticides and Toxic Substances (7501C)

Pesticide Fact Sheet

Name of Chemical: **CYMOXANIL**
Reason for Issuance: **Registration**
Date Issued: **April 21, 1998**

DESCRIPTION OF CHEMICAL

Chemical Name:	2-cyano-N-[(ethylamino)carbonyl]-2-(methoxyimino) acetamide
Common Name:	Cymoxanil
Trade Name:	Curzate 60 DF
EPA Chemical Code:	129106
Chemical Abstracts Service (CAS) Number:	57966-95-7
Year of Initial Registration:	1998
Pesticide Type:	Fungicide
U.S. Producer:	E. I. DuPont de Nemours & Company DuPont Agricultural Products Registration &Regulatory Affairs P.O. Box 80038 Wilmington, Delaware 19880-0038

USE PATTERN, FORMULATIONS, AND TARGET PEST

Cymoxanil is applied as a seed treatment to cut potato seed pieces or as a foliar application to the plants to control late blight *(Phytophthora infestans)*. The end-use product, Curate 60 DF is formulated as a 60% dry flowable formulation. Curate 60 DF is to be used only in combination (tank mixed) with other protectant fungicides such as mancozeb, chlorothalonil, triphenyltin hydroxide, or metiram. As a seed treatment, the product is applied by dipping the

seed pieces in a concentrated slurry or by mist seed treating equipment. The maximum application rate is 1.0 oz per hundred weight of cut seed pieces. As a foliar application, the product is applied by ground, air or chemigation. The maximum application rate for foliar applications is 3 ⅓ oz per acre using a minimum of 20 gals/acre for conventional ground spray, 10 gals/acre for air assisted ground spray, and 5 gals/acre for aerial spray.

Cymoxanil Technical is concentrated cymoxanil used as the active ingredient to manufacture cymoxanil end-use products.

SUMMARY OF SCIENCE FINDINGS

Acute Toxicity: The acute toxicity data show that this chemical is not acutely toxic by the oral, inhalation, and dermal routes of exposure.

Subchronic Toxicity: In a subchronic oral study in mice, the NOEL was 8.25 mg/kg/day for males and 11.3 mg/kg/day for females. In a subchronic oral toxicity in dogs, a NOEL was not established and the LOEL was 3 mg/kg/day. In a subchronic oral toxicity/neurotoxicity study in rats, the NOEL was 47.6 mg/kg/day in males and 59.9 mg/kg/day for females. In a 28 day dermal toxicity study, the NOEL was 1000 mg/kg/day (highest dose tested).

Chronic Toxicity: In a combined chronic/carcinogenicity study, the NOEL was 4.08 mg/kg/day for males and 5.36 mg/kg/day of females. In a chronic toxicity study in dogs, the NOEL was 5.7 mg/kg/day for males and 3.1 mg/kg/day for females.

Carcinogenicity: Cymoxanil showed no evidence of carcinogenic potential and was classified as a "Not Likely" carcinogen.

Developmental Toxicity: In a prenatal developmental toxicity study in rats, the maternal and developmental NOEL was 10 mg/kg/day. In a prenatal developmental toxicity study in rabbits, the maternal and developmental NOEL was ≥ 16 mg/kg/day. In another prenatal developmental toxicity study in rabbits, the maternal and developmental NOEL was 4 mg/kg/day.

Reproductive Toxicity: In a two-generation reproduction study in rats, the parental systemic NOEL was 100 ppm (6.5 mg/kg/day for males and 7.9 mg/kg/day for females) and the offspring NOEL was 100 ppm.

Neurotoxicity Toxicity: In the neurotoxicity portion of the subchronic/neurotoxicity study in rats, the NOEL for neurotoxicity was 224 mg/kg/day for males and 333 mg/kg/day for females. In the combined chronic toxicity/carcinogenicity study in rats, sciatic nerve axon/myelin degeneration was reported in females at dose levels of 30.3 and 90.1 mg/kg/day and hyperactivity and aggressiveness were reported in males at 30.3 and 90.1 mg/kg/day. In the carcinogenicity study in mice, absolute brain weight was decreased in both sexes at 216/298 mg/kg/day and 446/582 mg/kg/day for males/females. No evidence of developmental anomalies of the fetal nervous system were observed in the prenatal developmental toxicity studies in either rats, or

rabbits, at maternally toxic oral doses up to 25 and 32 mg/kg/day. In addition, there was no evidence of behavioral or neurological effects on the offspring in the two-generation reproduction study in rats.

Mutagenicity: Gene mutation assays in bacterial and mammalian cells, a mouse micronucleus assay and an *in vivo/in vitro* unscheduled DNA synthesis (UDS) assay in rats were negative. An *in vitro* unscheduled DNA synthesis assay-primary rat hepatocytes and a chromosome aberrations in human lymphocytes assay were positive. However, the negative results from the mouse bone marrow micronucleus assay support the lack of carcinogenic effect in the rat and mouse long-term feeding study.

Reference Dose: The Reference Dose (RfD) for cymoxanil is 0.013 mg/kg/day. This value is based on the NOEL of 4.08 mg/kg/day from a chronic feeding study in rats. The Uncertainty Factor of 300 was used to account for interspecies extrapolation, intraspecies variation and the enhanced sensitivity of infants and children.

A chronic exposure analysis was conducted using tolerance level residues and 100 percent crop treated data to estimate the Theoretical Maximum Residue Contribution (TMRC) for the general population and 22 subgroups. The chronic analysis showed that exposure from the proposed tolerance in or on potatoes and the use on tomatoes under the Section 18 emergency exemptions program resulted in a TMRC of < 1% of the RfD for the general U.S. population and 2% of the RfD for children 1-6 and 7-12.

The maximum estimated concentrations of cymoxanil in surface water and in ground water are less than EPA's levels of concern for cymoxanil in drinking water as a contribution to acute and chronic aggregate exposure. Therefore, EPA concluded with reasonable certainty that residues of cymoxanil in drinking water, when considered along with other sources of exposure for which EPA has reliable data, would not result in unacceptable levels of aggregate human health risk.

Tolerances are established for the residues of the fungicide cymoxanil [2-cyano-N-[(ethylamino)carbonyl]-2-(methoxyimino) acetamide] in or on potatoes at 0.05 ppm.

CHEMICAL CHARACTERISTICS

The physico-chemical characteristics of the cymoxanil technical (96.8%) are as follows.

Color:	Peach
Molecular Formula:	$C_7H_{10}N_4O_3$
Molecular Weight:	198.18
Physical State:	Solid
Melting Point:	159-160°C
Vapor Pressure:	1.5 x 10^{-4} Pa @ pH 5 and 20°C
Density:	1.32 g/cm^3

Dissociation Constant	
in Water:	pKa = 9.7 ± 0.2
Octanol/Water Partition	
Coefficient:	3.9 at pH 5, 4.7 at pH 7
Solubility:	
Water:	0.9 g/l, pH 5
	0.8 g/l, pH 7
Acetone:	62.4 g/l
Acetonitrile:	57.0 g/l
Dichloromethane:	133 g/l
Ethyl acetate:	28.0 g/l
Hexane:	0.037 g/l
Methanol:	22.9 g/l
Toluene:	5.29 g/l
Octanol:	1.43 g/l

The data provided fulfill all Product Chemistry data requirements for registration of cymoxanil, except for 1) Product chemistry data (required under OPPTS Series 830.7050) pertaining to UV/visible absorption for the PAI; 2) a revised enforcement method.

TOXICOLOGICAL CHARACTERISTICS:

Acute Testing

Curate 60 DF		Toxicity Category
1.	Acute Oral (Rat, 81-1)	
	LD_{50} = 418 mg/kg/day (males and females)	II (WARNING)
2.	Acute Dermal (Rabbit, 81-2)	
	LD_{50} = 5001.0 mg/kg/day (males and females)	III (CAUTION)
3.	Acute Inhalation (Rat, 81-3)	
	LC_{50} = 5.01 mg/l (males and females)	IV (CAUTION)
4.	Primary Eye Irritation (Rabbit, 81-4)	
	Not an ocular irritant	IV (CAUTION)
5.	Primary Skin Irritation (Rabbit, 81-5)	
	Not a dermal irritant	IV (CAUTION)
6.	Dermal Sensitization (Guinea pig, 81-6)	
	Not a sensitizer	N/A

Cymoxanil Technical Fungicide

		Toxicity Category
1.	Acute Oral (Rat, 81-1)	
	LD_{50} = 960 mg/kg/day (males and females)	III (CAUTION)
2.	Acute Dermal (Rabbit, 81-2)	
	LD_{50} > 2000 mg/kg	III (CAUTION)
3.	Acute Inhalation (Rat, 81-3)	
	LC_{50} > 5.06 mg/L (males and females)	IV (CAUTION)
4.	Primary Eye Irritation (Rabbit, 81-4)	
	Not an Ocular Irritant	IV (CAUTION)
5.	Primary Dermal Irritation (Rabbit, 81-4)	
	Mild or Slight Dermal Irritant	IV (CAUTION)
6.	Dermal Sensitization (Guinea Pig, 81-6)	
	Not a sensitizer	N/A

Subchronic Testing

1. 90-Day Oral Combined Toxicity/Neurotoxicity (Rat, 82-1)
   NOEL = 750 ppm for subchronic systemic toxicity
   (47.6 mg/kg/day in males; 59.9 mg/kg/day in females)
   LOEL = 1500 ppm
   (102 mg/kg/day in males; 137 mg/kg/day in females)

   NOEL = 3000 ppm for neurotoxicity
   (224 mg/kg/day in males; 333 mg/kg/day in females)
   LOEL - Not established for neurobehavioral and neuropathic effects

2. 90-Day Oral Toxicity (Mouse, 82-1)
   NOEL = 50 ppm (8.25 mg/kg/day) for males
   NOEL = 500 ppm (121 mg/kg/day) for females
   LOEL = 500 ppm (82.4 mg/kg/day) for males
   LOEL = 1750 ppm (433 mg/kg/day for females

3. 90-Day Oral (Dog, 82-1)
   NOEL - Not Established
   LOEL = 100 ppm (3 mg/kg/day for males and females)

4. 28-Day Dermal (Rat, 82-2)
   NOEL = 1000 mg/kg/day
   LOEL - not determined

5. Neurotoxicity (Rat, 82-7)
   See 90-Day Oral Combined Toxicity/Neurotoxicity (Rat, 82-1)

Chronic Testing

1. 2-Year Combined Chronic/Carcinogenicity Feeding (Rat, 83-1)
   Chronic Results:
      NOEL = 100 ppm (4.08 mg/kg/day for males, 5.36 mg/kg/day for females)
      LOEL = 700 ppm (30.3 mg/kg/day for males, 38.4 mg/kg/day for females)
   Carcinogenicity Results:
      No evidence of carcinogenic potential.

2. 2-Year Oral (Dog, 83-1)
   NOEL = 100 ppm (3.0 mg/kg/day for males, 3.1 mg/kg/day for females)
   LOEL = 200 ppm (5.7 mg/kg/day for males)
   LOEL - Not established for females.

3. Carcinogenicity (Rat, 83-5)
   See 2-Year Combined Chronic/Carcinogenicity Feeding, summarized above, 83-1.

   There was no demonstrated carcinogenic effect.

4. 80-Week Oral Carcinogenicity (Mouse, 83-5)
   NOEL = 30 ppm (4.19 mg/kg/day in males, 5.83 mg/kg/day in females)
   LOEL = 300 ppm (42 mg/kg/day in males, 58.1 mg/kg/day in females)

   There was no demonstrated carcinogenic effect.

5. Developmental Toxicity, by gavage (Rat, 83-3)
   Maternal NOEL = 10 mg/kg/day
   Maternal LOEL = 25 mg/kg/day

   Developmental NOEL = 10 mg/kg/day based upon overall malformations and delay in skeletal ossification.
   Developmental LOEL = 25 mg/kg/day

6. Developmental Toxicity, by gavage (Rabbit, 83-3)
   Maternal NOEL $\geq$ 16 mg/kg/day
   Maternal LOEL = Not determined

Developmental NOEL ≥ 16 mg/kg/day
Developmental LOEL = Not determined
There was no evidence of treatment-related maternal or developmental toxicity.

7. Developmental Toxicity, by gavage (Rabbit, 83-3)
Uncertainties regarding the source of the parental rabbits substantially reduce the confidence that any observed skeletal effects are solely related to treatment.

8. Developmental Toxicity, by gavage (Rabbit, 83-3)
Maternal NOEL = 4 mg/kg/day
Maternal LOEL = 8 mg/kg/day

Developmental NOEL = 4 mg/kg/day
Developmental LOEL = 8 mg/kg/day based on an increase in skeletal malformations of the cervical and thoracic vertebrae and ribs; and, at 32 mg/kg/day, cleft palate was observed.

9. Reproductive Toxicity (Rat, 83-4)
Parental Systemic Effects:
NOEL = 100 ppm (6.5 mg/kg/day in males, 7.9 mg/kg/day in females)
LOEL = 500 ppm (32.1 mg/kg/day in males, 40.6 mg/kg/day in females)

Reproductive Effects (Offspring):
NOEL = 100 ppm
LOEL = 500 ppm, based on decreased F1 pup viability on postnatal days 0-4 and on significant reduction in F2b pup weight.

10. Neurotoxicity Rat, 82-7)
See 90-Day Oral Combined Toxicity/Neurotoxicity (Rat, 82-1), summarized above.

The Agency will require a confirmatory developmental neurotoxicity study in rats as a result of a weight-of-evidence review of the database which suggested that neuropathological changes could result from long-term exposure to cymoxanil.

Mutagenicity Testing (84-2)

1. Gene Mutation/bacterial (Ames assay, *S. typhimurium*
Negative

2. Gene Mutation/Mammalian Cell (CHO/HPRT assay)
Negative

3. In vivo/vitro unscheduled DNA (UDS) synthesis-rats
Negative

4. In vitro UDS-primary hepatocytes-rats
   Positive from 5-500 mcg/mL, the tested concentration range
   Cytotoxicity seen at concentrations ≥ 500 mcg/mL

5. Chromosome aberrations in human lymphocytes
   Positive from 100-1500 mcg/mL
   Positive at 1250 and 1500 mcg/mL -S9
   Positive at 850-1500 mcg/mL +S9

The dominant lethal assay is required to determine if the effects noted in the reproduction, developmental subchronic, and chronic studies are associated with genetic damage to male germinal cells.

Metabolism (85-1)

In the rat metabolism study, radioactive cymoxanil administered by gavage as a single dose was readily absorbed through the intestines. The majority of the dose was excreted in the urine and to a lesser extent in the feces. The principal pathway for elimination of cymoxanil is via renal elimination. The proposed metabolic pathway involves hydrolysis of cymoxanil and then degradation to glycine, which is incorporated into natural constituents or further metabolized. Hydrolysis and subsequent glucuronide conjugation is proposed as the major metabolic pathway.

ECOLOGICAL CHARACTERISTICS

Avian Acute Oral Toxicity:
- Bobwhite Quail: LD_{50} > 2250 mg/kg
- Mallard Duck: LD_{50} > 2250 mg/kg

Avian Subacute Dietary Toxicity:
- Bobwhite Quail: LC_{50} > 5620 mg/kg
- Mallard Duck: LC_{50} > 5620 mg/kg

Avian Reproduction:
- Bobwhite Quail: NOEC = 300 ppm
  LOEC = 1200 ppm
- Mallard Duck: NOEC = 100 ppm
  LOEC = 300 ppm

Acute Mammal Toxicity (Data on laboratory rats substituted for wild mammal testing)
- Laboratory Rats: LD_{50} > 960 mg/kg

Nontarget Insect Acute Contact Toxicity:
- Honey Bee: LD_{50} > 25 μg/kg

Freshwater Fish Acute Toxicity:

Rainbow Trout: 96-hour LC_{50} > 61 ppm (95% CI - 47-79)
Bluegill Sunfish: 96-hour LC_{50} > 29 ppm (95% CI - 17-50)
Carp: 96-hour LC_{50} > 91 ppm (95% CI - 72-113)

Freshwater Fish Chronic Toxicity:

Rainbow Trout: NOEC = 0.00098 ppm
LOEC = 0.0024 ppm

Freshwater Invertebrate Acute Toxicity:

Waterflea: 48-hour LC_{50}/EC_{50} = 27.0 ppm

Freshwater Invertebrate Life -Cycle (Chronic) Toxicity:

Waterflea: 21-day NOEC = 0.067 ppm
LOEC = 0.15 ppm

Estuarine/Marine Fish Acute Toxicity:

Sheepshead Minnow: 96-hour LC_{50} > 47.5 ppm

Estuarine Fish Early Life-Stage Toxicity Under Flow-through Conditions

Sheepshead Minnow: NOEC = 0.0942 ppm
LOEC = 0.178 ppm

Estuarine/Marine Invertebrate Acute Toxicity:

Eastern Oyster: 96-hour LC_{50} > 46.9 ppm
NOEC = 28.2 ppm
Mysid Shrimp EC_{50} > 44.4 ppm
NOEC = 17.6 ppm

Estuarine Aquatic Invertebrate Life Cycle (Chronic) Toxicity:

Mysid Shrimp 21- day NOEC = 1.70 ppm
LOEC = 3.77 ppm

Soil Invertebrates Acute Toxicity:

Earthworms LC_{50} = 2109 ppm

Plant Toxicity:

Lemna gibba:

A test concentration of 1.08 lb ai/A applied to a 6 inch water column resulted in no reduction in population growth.

Anabaena flosaquae:

EC_{50} = 231 ppb
NOEC = 65.2 ppb (95% CI of 182-294 ppb)

Selenastrum capricornutum

A test concentration of 1.5 lb ai/A applied to a 6 inch water column (1050 ppb) resulted in a 23.3% reduction in population growth over a 5 day period

Skeletonema costatum

A test concentration of 1.5 ai/A applied to a 6 inch water column (916 ppb) resulted in a l.6% reduction in population growth over a 5 day period.

Navicula pelliculosa

EC_{50} = 4.11 ppm

NOEC = 0.625 ppm (95% CI of 3.07-5.51 ppm)

Cymoxanil was shown to be practically nontoxic to avian species and bees, and minimally toxic to mammals. Cymoxanil was shown to be slightly toxic to freshwater fish, aquatic invertebrates, estuarine/marine fish, and estuarine/marine invertebrates. Cymoxanil is not expected to present a risk to nontarget or endangered species or aquatic plants.

ECOTOXICITY PRECAUTIONS

The following statements must appear in the Environmental Hazards section of the label:

"Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark."

The following spray drift management statements must appear in the Directions for Use section of the label:

"SPRAY DRIFT MANAGEMENT

The interaction of many equipment and weather-related factors determine the potential for spray drift. The applicator is responsible for considering all these factors when making decisions.

AVOIDING SPRAY DRIFT IS THE RESPONSIBILITY OF THE APPLICATOR.

IMPORTANCE OF DROPLET SIZE

The most effective way to reduce drift potential is to apply large droplets (> 150 - 200 microns). The best drift management strategy is to apply the largest droplets that provide sufficient coverage and control. The presence of sensitive species nearby, the environmental conditions, and pest pressure may affect how an applicator balances drift control and coverage. APPLYING LARGER DROPLETS REDUCES DRIFT POTENTIAL, BUT WILL NOT PREVENT DRIFT IF APPLICATIONS ARE MADE IMPROPERLY OR UNDER UNFAVORABLE ENVIRONMENTAL CONDITIONS! See **Wind, Temperature** and **Humidity**, and **Temperature Inversions.**

Controlling Droplet Size -General Techniques

- **Volume** - Use high flow rate nozzles to apply the highest practical spray volume. Nozzles with higher rated flows produce larger droplets.
- **Pressure** - Use the lower spray pressures recommended for the nozzle. Higher pressure reduces droplet size and does not improve canopy penetration. WHEN HIGHER FLOW RATES ARE NEEDED, USE A HIGHER-CAPACITY NOZZLE INSTEAD OF INCREASING PRESSURE.

- **Nozzle Type** - Use a nozzle type that is designed for the intended application. With most nozzle types, narrower spray angles produce larger droplets. Consider using low-drift nozzles.

Controlling Droplet Size - Aircraft

- **Number of Nozzles** - Use the minimum number of nozzles with the highest flow rate that provide uniform coverage.

- **Nozzle Orientation** - Orienting nozzles so that the spray is emitted backwards, parallel to the airstream will produce larger droplets than other orientations.

- **Nozzle Type** - Solid stream nozzles (such as disc and core with swirl plate removed) oriented straight back produce larger droplets than other nozzle types.

- **Boom Length** - The boom length should not exceed 3/4 of the wing or rotor length - longer booms increase drift potential.

- **Application Height** - Application more than 10 ft. Above the canopy increases the potential for spray drift.

BOOM HEIGHT

Setting the boom at the lowest labeled height (if specified) which provides uniform coverage reduces the exposure of droplets to evaporation and wind. For ground equipment, the boom should remain level with the crop and have minimal bounce.

WIND

Drift potential is lowest at wind speeds of 3 mph (due to inversion potential) or more than 10 mph. However, many factors, including droplet size and equipment type determine drift potential at any given wind speed. AVOID GUSTY AND WINDLESS CONDITIONS

Note: Local terrain can influence wind patterns. Every applicator should be familiar with local wind patterns and how they effect spray drift.

TEMPERATURE AND HUMIDITY

When making applications in hot and dry conditions, set up equipment to produce larger droplets to reduce effects on evaporation.

TEMPERATURE INVERSIONS

Drift potential is high during a temperature inversion. Temperature inversions restrict vertical air mixing, which causes small suspended droplets to remain close to the ground and move laterally in a concentrated cloud. Temperature inversions are characterized by increasing temperature with altitude and are common on nights with limited cloud cover and light to no wind. They begin to form as the sun sets and often continue into the morning. Their presence can be indicated by ground fog; however, if fog is not present, inversions can also be identified by the movement of smoke from ground source or an aircraft smoke generator. Smoke that layers and moves laterally in a concentrated cloud (under low wind conditions) indicates an inversion, while smoke that moves upward and rapidly dissipates indicates good vertical air mixing.

SHIELDED SPRAYERS

Shielding the boom or individual nozzles can reduce the effects of wind. However, it is the responsibility of the applicator to verify that the shields are preventing drift and not interfering with uniform disposition of the product.

AIR ASSISTED (AIR BLAST) FIELD CROP SPRAYERS

Air assisted field crop sprayers carry droplets to the target via a downward directed air stream. Some may reduce the potential for drift, but if a sprayer is unsuitable for the application and/or set up improperly, high drift potential can result. It is the responsibility of the applicator to determine that a sprayer is suitable for the intended application, is configured properly, and that drift is not occurring.
Note: Air assisted field sprayers can affect product performance by affecting spray coverage and canopy penetration. Consult the application equipment section of this label to determine if use of an air assisted sprayer is recommended.

ENVIRONMENTAL CHARACTERISTICS

Degradation and Metabolism

Cymoxanil degrades rapidly in the environment. It hydrolyzes under aqueous conditions at neutral and alkaline pHs and it also photodegrades in water. In soils, cymoxanil biodegrades very quickly under both aerobic and anaerobic conditions. Though cymoxanil has a low K_d

values and would be expected to leach to ground water or runoff to surface water, EPA believes that because the chemical has very short half-lives in the environment, it will not likely pose a threat to ground or surface waters.

In addition to CO_2 (the primary soil degradate), eight degradates have been identified in laboratory studies. In an acceptable aerobic soil metabolism study, no single degradate, other than CO_2 exceeded 10% of the amount applied at any of the test intervals. It appears that in soils, cymoxanil is eventually mineralized to CO_2.

Cymoxanil hydrolysis is pH dependent. At pH 5, the chemical is relatively stable. However, in neutral and alkaline waters, it hydrolyzes quickly (pH 7 half life: 34 hours, pH 9 half-life 31 minutes). Of the three major degradates observed, the most persistent, declined to an average of 27% of the applied at day 30.

Cymoxanil photodegrades quickly in aqueous media. A half-life of 1.8 days was observed in a pH 5 buffer. Of the two major degradates observed, the most persistent, decreased slowly to 25% at day 15. In contrast, cymoxanil photodegrades slowly on soils, with a half-life of 25.3 days.

Mobility

Cymoxanil appeared to be mobile in the four soils tested with Freundlich adsorption (K_{ads}) values of 0.29 in the Sassafras sandy loam soil (1.3% OM), 2.86 in the Fargo clay loam soil (4.5% OM), 1.38 in the Mississippi silt loam soil (1.0% OM), and 0.79 in the Tama silt loam soil (1.3% OM). In addition, in unaged columns 22-25% of the applied radioactivity was recovered in the eluent. The major components in the eluent were cymoxanil (2.76-3.05% of the applied and two degradates (7.55-7.94%, 1.94-3.37%).

Bioaccumulation

The low octanol/water partition coefficient (K_{ow}) for cymoxanil (3.9-4.7) indicates a very low potential for cymoxanil to bioaccumulate in fish.

Field Dissipation

The low persistence predicted by laboratory studies was confirmed in the field (the observed half-life of cymoxanil in Elkton, MD was < 1 day; the calculated half-lives averaged 8.7 days in Madera, CA). No detections of cymoxanil were observed below the 0-15 cm soil depth. Although no degradates were monitored in these studies, the major degradates observed in the hydrolysis and photolysis water studies were not observed in large amounts in the aerobic soil metabolism study. Therefore, EPA believes that cymoxanil degradates will not persist in the environment.

Spray Drift

No cymoxanil-specific studies were reviewed. Droplet size spectrum (201-1) and drift field evaluation (202-1) studies are required since cymoxanil may be applied aerially. The registrant, E.I. DuPont de Nemours is a member of the Spray Drift Task Force (SDTF). The SDTF has completed and submitted to the Agency its series of studies which are intended to characterize spray droplet drift potential due to various factors, including application methods, application equipment, meteorological conditions, crop geometry, and droplet characteristics. The Agency is currently evaluating these studies. After its review of the new studies submitted by the SDTF, the Agency will determine whether a reassessment is warranted of the potential risks from the application of cymoxanil to nontarget organisms.

TOLERANCE ASSESSMENT

Tolerances are established for the residue of the fungicide cymoxanil in or on potatoes at 0.05 ppm.

HUMAN AGGREGATE EXPOSURES

In examining aggregate exposure, the Food Quality Protection Act (FQPA) directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary non-food sources of exposure the Agency looks at include drinking water (whether from groundwater or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

1. From Food and Feed Uses

Acute Toxicity-Females 13+: To assess acute dietary exposure for the sub-population of concern, the Agency used a NOEL of 4 mg/kg/day from prenatal developmental toxicity studies in rabbits based on an increase in skeletal malformations of the cervical and thoracic vertebrae and ribs at 8 mg/kg/day. The Agency determined that the 10x factor to account for enhanced sensitivity of infants and children (required by FQPA) should be reduced to 3x. An MOE of 300 is required for the acute dietary assessment to protect the sub-population of concern, "Females 13+," due to neuropathological lesions seen in the chronic toxicity study in rats and the need for an additional developmental neurotoxicity study. The MOE for the sub-population (Females 13+) is 5000.

Chronic Dietary Toxicity: The Reference Dose (RfD) for cymoxanil is 0.013 mg/kg/day. This value is based on the NOEL of 4.08 mg/kg/day from a chronic feeding study in rats. The Uncertainty Factor of 300 was used to account for interspecies extrapolation, intraspecies variation and the enhanced sensitivity of infants and children.

A chronic exposure analysis was conducted using tolerance level residues and 100 percent crop treated data to estimate the Theoretical Maximum Residue Contribution (TMRC) for the general population and 22 subgroups. The chronic analysis showed that exposure from the proposed tolerance in or on potatoes and the current use on tomatoes under the Section 18 emergency exemptions program resulted in a TMRC of < 1% of the RfD for the general U.S. population and 2% of the RfD for children 1-6 and 7-12. This analysis used a worse case estimate of dietary exposure. Even without refinement, the chronic dietary exposure to cymoxanil appears to be minimal.

2. From Drinking Water

EPA estimated surface water exposure using the Generic Expected Environmental Concentration (GENEEC) model, a screening level model for determining concentrations of pesticides in surface water. GENEEC uses the soil/water partition coefficient , hydrolysis half life, and maximum label rate to estimate surface water concentration. In addition, the model contains a number of conservative underlying assumptions. Therefore, the drinking water concentrations derived from GENEEC for surface water are likely to be overestimated. Surface water estimates derived from GENEEC assumed 7 applications of 0.12 lbs. active ingredient/acre would be applied. The model indicated that cymoxanil in surface water could reach 4.13 parts per billion (ppb) (peak concentration) and 0.19 ppb (average 56 day concentration).

EPA calculated DWLOC for acute exposure by using the acute toxicity endpoint. The acute dietary food exposure (from the DRES analysis) was subtracted from the ratio of the acute NOEL (used for acute dietary assessments) to the "acceptable" MOE for aggregate exposure to obtain the acceptable acute exposure to cymoxanil in drinking water.

EPA has calculated drinking water levels of concern (DWLOCs) for acute exposure to cymoxanil in drinking water for females (13+ years old) to be 380 ppb. The maximum estimated concentrations of cymoxanil in surface and ground water are below EPA's levels of concern for cymoxanil in drinking water as a contribution to acute aggregate exposure. Therefore, EPA concludes with reasonable certainty that residues of cymoxanil in drinking water do not contribute significantly to the aggregate acute human health risk.

Chronic (non-cancer), drinking water levels of concern are 450 ppb for U.S. population and 130 ppb children (1-6 years old). The estimated average concentrations of cymoxanil in surface and ground water are less than EPA's levels of concern for cymoxanil in drinking water as a contribution to chronic aggregate exposure. Therefore, EPA concludes with reasonable certainty that residues of cymoxanil in drinking water do not contribute significantly to the aggregate chronic human health risk.

3. From Non-Dietary Uses

There are no non-food uses of cymoxanil registered. No non-dietary exposures are expected for the general population.

4. Cumulative Exposure to Substances with Common Mechanism of Toxicity

For cymoxanil, EPA has not conducted a detailed review of common mechanism yet to determine whether it is appropriate, or how to include this chemical in a cumulative risk assessment. After EPA develops a methodology to apply common mechanism of toxicity issues to risk assessments, the Agency will develop a process (either as part of the periodic review of pesticides or otherwise) to reexamine these tolerance decisions. The Agency has determined that there are no metabolites of toxicological concern associated with cymoxanil. Cymoxanil is structurally related to metazachlor, dimethenamid and amiphos. Of these pesticides, only dimethenamid is currently registered for use in the United States. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, cymoxanil does not appear to produce a toxic metabolite produced by other substances. Therefore, EPA has not assumed that cymoxanil has a common mechanism of toxicity with other substances.

OCCUPATIONAL EXPOSURE

The available toxicological data does not indicate any evidence of dermal or systemic toxicity, therefore a short-term or intermediate term risk assessment was not required. A risk assessment was conducted for inhalation exposure and all handler inhalation MOE's were found not to exceed the Agency's level of concern.

SUMMARY OF DATA GAPS

1. A developmental neurotoxicity study
2. A rat dominant lethal assay
3. Product chemistry data pertaining to UV/visible absorption for the PAI (OPPTS series 830.7050).

PUBLIC INTEREST FINDING

The Agency has determined that the use of cymoxanil on potatoes is in the public interest since cymoxanil has been used on potatoes in the U.S. since 1995 under Section 18 emergency exemptions. A time-limited tolerance of 0.05 ppm for residues of cymoxanil in or on potatoes was established under 40 CFR §180.503(b) in connection with the Agency's granting of emergency exemptions in the states of AL, CA, CO, DE, FL, ID, IN, MA, ME, MI, MN, MT, NE, NV, NJ, NY, NC, ND, OR, PA, VA, WA, and WI.

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