United States
Environmental Protection
Agency

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

Pesticide Fact Sheet

Name of Chemical: Cyclanilide
Reason for Issuance: Registration
Date Issued: May 19, 1997

DESCRIPTION OF CHEMICAL

Generic Name:	1-(2,4-dichlorophenylaminocarbonyl)-cyclopropane carboxylic acid
Common Name:	cyclanilide
Trade Names:	Cyclanilide Technical FINISH® Harvest Aid for Cotton
EPA Chemical Code:	026201
Chemical Abstracts Service (CAS) Number:	113136-77-9
Year of Initial Registration:	1997
Pesticide Type:	Plant Growth Regulator
Chemical Family:	Malonanilate
U.S. and Foreign Producers:	Rhône-Poulenc Ag Company Rhône-Poulenc Secteur Agro

USE PATTERNS AND FORMULATIONS

Cyclanilide is a plant growth regulator used as a cotton harvest aid. It will be formulated as a suspension concentrate with ethephon (4.0 lb ethephon and 0.5 lb cyclanilide/gallon) and sold as FINISH® Harvest Aid for Cotton. FINISH® will be applied at the end of the cotton season to promote boll opening, defoliation and inhibition of terminal foliar regrowth. FINISH® will be applied by ground (10 gallons/ Acre spray volume) or air (2 gallons/Acre spray volume) at rates of 1 to 2 quarts/Acre (1 to 2 lb ethephon: 0.125 to 0.25 lb cyclanilide/Acre). The maximum use rate of FINISH® per acre per year is 2 quarts (2.0 lb ethephon, 0.25 lb cyclanilide per acre). Ethephon is currently registered for application to cotton in other products at equivalent application rates.

Cyclanilide Technical (RPA90946) is a 98.5% manufacturing use product.

SCIENCE FINDINGS

Summary Science Statements

Adequate chemistry, toxicological, ecological effects, and environmental fate data have been submitted and reviewed to support the conditional registration of Finish Harvest Aid for Cotton. The terms of the conditional registration will require Rhone-Poulenc to submit the following studies: Tier II Vegetative Vigor and Seedling Emergence Studies [GLN 123-1], a confirmatory Rat Unscheduled DNA Synthesis (UDS) Test [GLN 81-4], and Storage Stability Data for Field Dissipation Study [the stability data is currently awaiting EPA review].

The technical cyclanilide product is classified in toxicity category II [WARNING] based on acute oral toxicity and eye irritation studies. The formulated end use product is classified in toxicity category I [DANGER] based on the eye irritation study.

Cyclanilide was shown to be negative in assays for Salmonella Reverse Mutation (two studies) and for forward mutations in CHO/HGPRT cells. Structural Chromosomal Aberration assays were positive for inducing chromosomal aberrations assay in in vitro (CHO Cells) at cytotoxic concentration (two studies) but were negative for the induction of chromosomal aberrations in vivo (Mouse Micronucleus)(two studies). Since cyclanilide caused liver toxicity in several studies, a confirmatory rat unscheduled DNA synthesis (UDS) test needs to be conducted with cyclanilide.

Developmental toxicity studies in the rat and rabbit demonstrated no developmental effects. In the rat the No Observed Effect Level (NOEL) for maternal toxicity was 10 milligrams/kilogram(mg/kg)/day and for developmental toxicity was 30 mg/kg/day. In rabbit, the NOELs for maternal toxicity was 10 mg/kg/day and for developmental toxicity was 30 mg/kg. In a two-generation rat reproduction study, the systemic NOEL was less than 2.0 mg/kg/day for males and less than 2.4 mg/kg/day for females and the reproductive NOEL was 2.3 mg/kg/day.

In a 90-day rat dietary study the NOEL was 54.6 mg/kg/day for males and 62.4 mg/kg/day for females. In a 90-day mouse feeding study the NOEL was 38 mg/kg/day males and 43 mg/kg/day females). In a 90 day mammalian neurotoxicity study the NOEL was equal or greater than 78.6 mg/kg/day males and was 4.0 mg/kg/day females. In a 21-day rabbit dermal study the NOEL was equal or greater than 1000 mg/kg/day. In a 1-year dog chronic feeding study the NOEL was 5.3 mg/kg/day for males and 5.2 mg/kg/day for females and the LOEL was 21.2 mg/kg/day for males and 21.5 mg/kg/day for

females based on decreases in body weight gain, elevated enzymes, and gross and histopathological liver lesions.

In the rat Chronic Feeding / Carcinogenicity study the NOEL was equal or greater than 43.1 mg/kg/day for males and was 8.1 mg/kg/day for females and the Lowest Observed Effect Level (LOEL) was greater than 43.1 mg/kg/day for males and equal to 25.5 mg/kg/day for females based on decreased body weight gains and histopathological changes in liver. The study was negative for oncogenicity. In the mouse dietary carcinogenicity study the NOEL was 41.8 mg/kg/day for males and 52.4 mg/kg/day for females and the LOEL was 168 mg/kg/day for males and 206 mg/kg/day for females based on decreased weight gain. The study was negative for oncogenicity.

Cyclanilide is classified as a "Not Likely" carcinogen "in at least two well conducted studies in two appropriate species without demonstrating carcinogenic effects".

The Reference Dose (RfD) for cyclanilide is 0.007 mg/kg/day. This value is based on the systemic LOEL of 30 ppm (2.0 mg/kg/day in males and 2.4 mg/kg/day in females) from the rat reproductive study. The NOEL was not achieved (less than 30 ppm the Lowest Dose Tested). Reduced body weights in young post-weaning F1 males and females and increased renal mineralization in adult F1 females were observed at this level. An Uncertainty Factor (UF) of 300 was applied to the LOEL based on an Uncertainty Factor of 100 to account for interspecies extrapolation and intraspecies variation and an additional Uncertainty Factor of 3 to account for the lack of a NOEL in the reproductive toxicity study.

Tolerances are established for the plant growth regulator, cyclanilide [1-(2,4-dichlorophenylaminocarbonyl)-cyclopropane carboxylic acid] determined as 2,4-dichloroaniline (calculated as cyclanilide) in or on the raw agricultural commodities cottonseed at 0.60 parts per million (ppm); cotton gin byproducts at 25.0 ppm; milk at 0.04 ppm; fat of cattle, goats, horses, hogs and sheep at 0.10 ppm; meat of cattle, goats, horses, hogs and sheep at 0.02 ppm; meat by-products (except kidney) of cattle, goats, horses, hogs and sheep at 0.20 ppm; and kidney of cattle, goats, horses, hogs and sheep at 2.0 ppm.

For the aggregate dietary exposures from food and drinking water, the percentage of the RfD utilized for non-nursing infants (the subgroup with the highest exposure) would be 91% of the Reference Dose (RfD). The exposure for the general U.S. population would be 21% of the RfD. The aggregate acute MOE for non-nursing infants (the subgroup with the highest exposure) would be greater than 8000. The acute MOE for the general U.S. population would be greater than 11,000. Even though these risks represent the worst-case scenario there appears to be no aggregate risk concern associated with the use of cyclanilide on

cotton.

The primary environmental fate process for cyclanilide is aerobic microbial degradation to 2,4-dichloroaniline which is further aerobically degraded in soil to carbon dioxide. Cyclanilide is moderately persistent in soil and is mobile under typical environmental conditions and photo-degrades moderately slowly. Cyclanilide does not bioaccumulate in aquatic organisms. A label Groundwater Advisory Statement is required.

Cyclanilide was shown to be of minimal toxicity to avian species, fish, aquatic invertebrates, estuarine and marine organisms, and honey bees. Cyclanilide can be toxic to non-target plants from movement off the treatment site. Environmental hazard precautionary statements are required. Since the vegetative vigor studies are invalid due to excess spray volumes and since the seedling emergence studies were rated supplementary due to phytotoxic symptoms which were not adequately described and an No Observed Effect Concentration was not determined for lettuce and cabbage, repeat Tier II vegetative vigor and seedling emergence studies are required.

Chemical Characteristics

Empirical Formula:	$C_{11}H_9Cl_2NO_3$
Molecular Weight:	274.1
Color:	white
Physical State:	powdery solid (20 C)
Odor:	no characteristic odor
Melting Point:	195.5 ± 1 C
Density at (20 C):	1.469-1.482 g/mL (20 C)
Solubility g/liter:	distilled water - 0.0037 g/100mL buffered pH 7 - 0.0048 g/100mL buffered pH 9 - 0.0048 g/100mL acetone - 5.29 g/100mL acetonitrile - 0.50 g/100mL dichloromethane - 0.17 g/100mL ethylacetate - 3.18 g/100mL hexane - < .0001 g/100mL

	methanol - 5.91 g/100mL 1-octanol - 6.72 g/100mL 2-propanol - 6.82 g/100mL
Vapor Pressure:	$<10^{-7}$ Torr (25 C) 6.3×10^{-8} Torr (50 C)
Dissociation Constant:	pKa = 3.5 ± 0.2 (22 C)
Octanol/Water partition coefficient:	Log P = 3.25 ± 0.4 (21 C)
pH:	3.8 (1% w/v water, 21 C)
Stability:	Stable in non-metallic packaging
Oxidizing/ Reducing Activity:	Unreactive with oxidizing/reducing agents
Explodability:	No danger of explosion
Flammability:	Not "highly flammable"
Storage Stability:	Stable for 14 days at 54 C Stable for 30 days at 50 C Stable for 90 days at 35 C Stable for 1 year at room temperature Stable for 14 days of continual exposure to artificial sunlight (23 C) Stable to metals over the range of 30-150 C (DSC) Degraded between 40 and 90 C in the presence of metal ions
Viscosity:	N/A - solid at room temperature
Miscibility:	N/A - no uses with petroleum solvents
Corrosiveness:	Not corrosive to non-metallic packing materials
Dielectric Breakdown Voltage:	Not applied around electrical equipment

Toxicology Characteristics

Finish Harvest Aid For Cotton
(End-Use Product)

Acute Oral Toxicity (rats):	LD50 > 5000 mg/kg (males) LD50 4063 mg/kg (females)
Toxicity Category:	III
Acute Dermal Toxicity (rabbits):	LD50 > 2000 mg/kg
Toxicity Category:	III
Acute Inhalation Toxicity (rats):	LC50 > 1.17 mg/L
Toxicity Category:	III
Primary Eye Irritation (rabbits):	Severe ocular reaction.
Toxicity Category:	I
Primary Skin Irritation (rabbits):	Erythema, edema and necrosis with resolution by day 10.
Toxicity Category:	II
Dermal Sensitization (guinea pigs):	Negative

Cyclanilide Technical
(manufacturing use product)

Acute Oral Toxicity (rats):	LD50 315 mg/kg males LD50 208 mg/kg females
Toxicity Category:	II

Acute Dermal Toxicity (rabbits):	LD50 > 2000 mg/kg
Toxicity Category:	III
Acute Inhalation Toxicity (rats):	LC50 > 2.64 mg/l
Toxicity Category:	IV
Primary Eye Irritation (rabbits):	Conjunctivitis and corneal with epithelial sloughing resolved by day 14
Toxicity Category:	II
Primary Skin Irritation (rabbits):	Slight erythema, resolved by 72 hours
Toxicity Category:	IV
Dermal Sensitization (guinea pigs):	Negative
Acute Oral Neurotoxicity (rat):	NOEL = 50 mg/kg LOEL = 150 mg/kg based on gait abnormalities, increased abdominal muscle tone, and slightly decreased motor activity test.
90-day dietary (rat):	NOEL = 54.6 mg/kg/day (males) NOEL = 62.4 mg/kg/day for (females) LOEL = 113.2 mg/kg/day for males and 121.4 mg/kg/day for females, based on reductions in body weight, body weight gain, and food consumption, clinical signs, and increased liver weight in males and females.
90-day dietary (mice):	NOEL = 38 mg/kg/day (males) NOEL = 43 mg/kg/day for (females) LOEL = 364 mg/kg/day for males and 416 mg/kg/day for females) based on mortality, elevated alkaline phosphatase, increase absolute, relative liver weights, focal

	hepatocellular necrosis and handling inducted rigidity.
21-day dermal (rabbit):	NOEL 1000 mg/kg/day LOEL > 1000 mg/kg/day .
90-day mammalian neurotoxicity	NOEL 78.6 mg/kg/day (males) NOEL = 4.0 mg/kg/day (females) LOEL 78.6 mg/kg/day (males) LOEL = 35.8 mg/kg/day for females based on increased motor activity and decreased body weight.
Developmental Toxicity (rabbit):	Maternal NOEL = 10 mg/kg/day Maternal LOEL = 30 mg/kg/day based on wobbly gait, partial hindlimb paralysis and emaciation. Developmental NOEL = 30 mg/kg/day (Highest Dose Tested).
Developmental Toxicity (rat):	Maternal NOEL = 10 mg/kg/day Maternal LOEL = 30 mg/kg/day due to decreased body weight gain and food consumption. Developmental NOEL = 30 mg/kg/day (Highest Dose Tested)
Two Generation Reproduction (rat):	Systemic NOEL < 2.0 mg/kg/day (males) and < 2.4 mg/kg/day (females) Systemic LOEL = 2.0 mg/kg/day (males) based on reduced early post-weaning body weight gains and 2.4 mg/kg/day (females) based on reduce early post-weaning body weight gains and increased renal mineralization. Reproductive NOEL = 2.3 mg/kg/day Reproductive LOEL = 21.8 mg/kg/day based on decreased mean pup weight.
1 Year Chronic Feeding (dog):	NOEL = 5.3 mg/kg/day (males) and 5.2 mg/kg/day (females) LOEL = 21.2 (males) and 21.5 mg/kg/day (females) based on decreased body weight gain, elevated enzymes and gross and histopathological liver lesions.

Chronic Feeding/ Carcinogenicity (rat):	NOEL 43.1 mg/kg/day (males) and = 8.1 mg/kg/day (females) LOEL > 43.1 mg/kg/day (males) and = 25.5 mg/kg/day (females) based on decreased body weight gains and histopathological changes in liver. The study was negative for oncogenicity.
Carcinogenicity (mouse):	NOEL = 41.8 mg/kg/day (males) and 52.4 mg/kg/day (females) LOEL = 168 mg/kg/day (males) and 206 mg/kg/day (females) based on decreased weight gain. The study was negative for oncogenicity.
Carcinogenicity:	According to the new proposed guidelines for Carcinogen Risk Assessment (April, 1996), the appropriate descriptor for human carcinogenic potential of cyclanilide is "Not Likely". The appropriate subdescriptor is "has been evaluated in at least two well conducted studies in two appropriate species without demonstrating carcinogenic effects".
Gene Mutation:	Negative for Salmonella Reverse Mutation (two studies) Negative for forward mutations in CHO/HGPRT cells.
Structural Chromosomal Aberration:	Positive for inducing chromosomal aberrations assay in <u>in vitro</u> (CHO Cells) at cytotoxic concentration (two studies) Negative for the induction of chromosomal aberrations <u>in vivo</u> (Mouse Micronucleus)(two studies)

Since cyclanilide caused liver toxicity in several studies, a confirmatory rat unscheduled DNA synthesis (UDS) test needs to be conducted with cyclanilide.

Metabolism:	In the rat metabolism study radioactive cyclanilide was rapidly absorbed after oral administration. The principal route of elimination was by renal excretion of the parent compound and amino acid conjugates. Methylation was a minor metabolic pathway.

Ecological Characteristics

Avian Acute Toxicity:

Bobwhite Quail:	14-day LD_{50} = 240 mg ai/kg bw

Avian Dietary Toxicity:

Bobwhite Quail:	8-day LC_{50} = 2580 ppm
Mallard Duck:	8-day LC_{50} = 1740 ppm

Freshwater Fish Acute Toxicity:

Bluegill Sunfish	96-hr LC_{50} > 16 mg ai/l
Rainbow Trout:	96-hr LC_{50} > 11 mg ai/l

Fish Early Life Stage Test:

Fathead Minnow	MATC = 1.8 mg ai/l NOEC = 1.2 mg ai/l

Freshwater Invertebrate Toxicity:

Daphnia magna	48-hr EC50 = 5 mg ai/l (This is a conservative estimate base on supplemental data)

Aquatic Invertebrate Life Cycle:

Daphnia magna	NOEC = 12.6 mg ai/l

Estuarine and Marine Organisms Toxicity:

Sheepshead Minnow	96-hr LC50 = 49 mg ai/l
Eastern Oyster	96-hr EC50 = 19 mg ai/l
Mysid Shrimp	96-hr LC50 = 5 mg ai/l

Non-Target Insects Toxicity:

Honey Bee Acute Contact	LD50 > 100 µg ai/bee

Seedling Germination and Vegetative Vigor for Cyclanilide Technical

Seedling Germination:

Cabbage, Corn, Cucumber,
Lettuce, Oat, Onion,
Perennial Ryegrass,
Soybean, Turnip,

Tomato	EC_{25} > 0.19 (lb ai/acre)

Seedling Emergence:

Corn, Oat, Onion Perennial Ryegrass	EC_{25} > 0.25 (lb ai/acre)
Cabbage	EC_{25} = 0.22 (lb ai/acre)
Cucumber	EC_{25} = 0.017 (lb ai/acre)
Lettuce	EC_{25} = 0.024 (lb ai/acre)
Soybean	EC_{25} > 0.22 (lb ai/acre)
Tomato	EC_{25} = 0.14 (lb ai/acre)
Turnip	EC_{25} = 0.05 (lb ai/acre)

Growth and Reproduction of Aquatic Plants:

Navicula pelliculosa	120-hr EC50 > 0.17 mg ai/l
Lemna gibba	14-day EC50 > 0.22 mg ai/l
Kirchneria subcapitata	120-hr EC50 = 1.0 mg ai/l
Skeletonema costatum	120-hr EC50 > 0.27 mg ai/l
Anabaena flos - aquae	120-hr EC50 = 0.08 mg ai/l

Seedling Emergency and Vegetative Vigor for End Use Product - FINISH® Harvest Aid for Cotton
(4.0 lb ethephon and 0.5 lb cyclanilide/gallon)

Seedling Emergence:

Cabbage, Corn, Perennial Ryegrass, Onion	EC_{25} > 6.4 (lb product/acre)
Cucumber	EC_{25} = 0.92 (lb product/acre)
Lettuce	EC_{25} = 1.7 (lb product/acre)
Oat	EC_{25} = 3.9 (lb product/acre)

Soybean EC_{25} = 3.0 (lb product/acre)

Tomato EC_{25} = 1.5 (lb product/acre)

Turnip EC_{25} = 0.76 (lb product/acre)

The vegetative vigor studies were invalid due to excess spray volume and the seedling emergence studies were rated supplementary due to phytotoxic symptoms which were not adequately described and an No Observed Effect Concentration was not determined for lettuce and cabbage. Repeat Tier II vegetative vigor and seedling emergence studies are required.

Cyclanilide was shown to be moderately to slightly toxic to aquatic and avian species. Based on the toxicity to non-target terrestrial and aquatic organisms and the modeled exposure data, the use of cyclanilide poses minimal acute risk to all aquatic organisms (fish, invertebrates, and plants) and to terrestrial animals, including birds, mammals and beneficial insects as well. Use of cyclanilide also poses minimal chronic risk to mammals, fish and invertebrates. Cyclanilide is a plant growth regulator and can have adverse growth effects on non-target terrestrial plants. Rhône-Poulenc is a member of the Spray Drift Task Force and is actively involved in work to address mitigation measures necessary to reduce the risk of off-site movement of products. Given the potential for adverse growth effects on terrestrial plants, adequate precautions should be taken when using cyclanilide to avoid off-site movement to nontarget plants.

The following statement 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." Standard label statements informing the user on methods to minimize spray drift should be used to reduce the risk to nontarget plants from aerial application as well.

Environmental Characteristics

Under aqueous buffered conditions at pH 5, 7, 9 in the dark, at a temperature of 25 C, cyclanilide is stable for 30 days. The half life of cyclanilide, in aqueous solutions (buffered pH 5, 7, and 9 and 25 C) under simulated sunlight is approximately 50-55 summer Florida days. Photodegradation is not a major dissipation pathway when cyclanilide is present on soil surfaces. In aerobic soil, at 0.25 ppm, the half life is 95 days. The major metabolite is 2,4-dichloroaniline which degrades slowly. Under anaerobic conditions in a water-sediment system, cyclanilide did not degrade. Cyclanilide is mobile to moderately mobile in soils, as demonstrated by adsorption K_{oc} values ranging from 194 to 565. Mobility of 2,4 - dichloroaniline is slightly less than cyclanilide, with adsorption K_{oc} values ranging from

349 to 883. In an aged leaching study, less than 3 percent of the applied radioactivity leached through soil columns. The majority of the radioactivity remained in the top six centimeters of the column; nearly all of the radioactivity was parent compound.

The kinetics of cyclanilide dissipation under field conditions are complicated by an autumn application. Based on supplemental information at applications of 0.25 pound a.i./acre, degradation rates (half-lives) range from 35 to 114 days. Degradation rates are slow during dry and cooler autumn and winter months but increased with increasing moisture and warmth during Spring and Summer months. Residues of cyclanilide were predominately contained in the upper 15 cm of soil. Based on the assumption of one application aerially at the maximum application rate 0.25 lb a.i./A, a GENEEC model was used to calculate that the peak (acute) concentration in runoff water adjacent to the application area to be 8.4 ppb and the chronic (56-day) concentration to be 7.7 ppb.

Since cyclanilide will be mobile on many soils and has a potential to contaminate ground water but because cyclanilide is a new chemical and no detections have been reported, the following Groundwater label Advisory Statement is required:

> This chemical has properties and characteristics associated with chemicals detected in ground water. The use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in ground water contamination.

Based on a general knowledge of the leaching and runoff of agri-chemicals and the specific chemical characteristics of this compound, EPA expects that the maximum concentrations of cyclanilide in ground water will not exceed the maximum concentrations predicted for surface water.

Aerial Spray Drift Management Statements

The following spray drift management statements appear on the FINISH® brand Harvest Aid for Cotton label. These statements are based upon requirements from the Ethephon Reregistration Eligibility Decision, because FINISH® contains ethephon.

SPRAY DRIFT

Avoid spray drift. Do not apply when weather conditions may cause drift. Do not allow this product to drift on to non-target areas. Drift may result in illegal residues or injury to adjacent crops and vegetation, in the form of leaf yellowing and defoliation. To avoid spray drift, DO NOT apply aerially when wind speed is greater than 10 mph or during periods of

temperature inversions. Use of larger droplet size will also reduce spray drift.

AVOID SPRAY DRIFT AT THE APPLICATION SITE IS THE RESPONSIBILITY OF THE APPLICATOR.

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.

The following drift management requirements must be followed to avoid off-target movement from aerial applications to agricultural field crops. These requirements do not apply to forestry applications, public health uses or to applications using dry formulations.

The distance of the outer most nozzles on the boom must not exceed ¾ the length of the wingspan or rotor.

Nozzles must always point backward parallel with the air stream and never be pointed downwards more than 45 degrees.

Where states have more stringent regulations, they should be observed.

The applicator should be familiar with and take into account the information covered in the Aerial Drift Reduction Advisory below:

AERIAL DRIFT REDUCTION ADVISORY

[This section is advisory in nature and does not supersede the mandatory label requirements.]

INFORMATION ON DROPLET SIZE

The most effective way to reduce drift potential is to apply large droplets. The best drift management strategy is to apply the largest droplets that provide sufficient coverage and control. Applying larger droplets reduces drift potential, but will not prevent drift is applications are made improperly, or under unfavorable environmental conditions (See Wind, Temperature and Humidity, and Temperature Inversions.)

CONTROLLING DROPLET SIZE

Volume - Use high flow rate nozzles to apply the highest practical spray volume. Nozzles with higher rated flows produce larger droplets.

Pressure - Do not exceed the nozzle manufacturer’s recommended pressures. For many nozzle types lower pressure produces larger

droplets. When higher flow rates are needed, use higher flow rate nozzles instead of increasing pressure.

Number of nozzles - Use the minimum number of nozzles that provide uniform coverage.

Nozzle Orientation - Orienting nozzles so that the spray is released parallel to the airstream produces larger droplets than other orientations and is the recommended practice. Significant deflection from horizontal will reduce droplet size and increase drift potential.

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. Solid stream nozzles oriented straight back produce the largest droplets and the lowest drift.

BOOM LENGTH

For some use patterns, reducing the effective boom length to less than ¾ of the wingspan or rotor length may further reduce drift without reducing swath width.

APPLICATION HEIGHT

Applications should not be made at a height greater than 10 feet above the top of the target plants unless a greater height is required for aircraft safety. Making applications at the lowest height that is safe reduces exposure of droplets to evaporation and wind.

SWATH ADJUSTMENT

When applications are made with a cross wind, the swath will be displaced downwind. Therefore, on the up and downwind edges of the field, the applicator should compensate for this displacement by adjusting the path of the aircraft upwind. Swath adjustment distance should increase, with increasing drift potential (higher wind, smaller drops, etc.).

WIND

Drift potential is lowest between wind speeds of 2-10 mph. However, many factors, including droplet size and equipment type determine drift potential at any given speed. Application should be avoided below 2 mph due to variable wind direction and high inversion potential. NOTE: Local terrain can influence wind patterns. Every applicator should be familiar with local wind patterns and how they affect spray drift.

TEMPERATURE AND HUMIDITY

When making applications in low relative humidity, set up equipment to produce larger droplets to compensate for evaporation. Droplet evaporation is most severe when conditions are both hot and dry.

TEMPERATURE INVERSIONS

Applications should not occur during a temperature inversion because drift potential is high. Temperature inversions restrict vertical air mixing, which causes small suspended droplets to remain in a concentrated cloud. This cloud can move in unpredictable directions due to the light variable winds common during inversions. Temperature inversions are characterized by increasing temperatures 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 a 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.

SENSITIVE AREAS

The pesticide should only be applied when the potential for drift to adjacent sensitive areas (e.g., residential areas, bodies of water, known habitat for threatened or endangered species, non-target crops) is minimal (e.g., when wind is blowing away from the sensitive areas).

Where states have more stringent regulations, they should be observed.

The following studies are needed to complete the ecological risk assessments on cyclanilide:

1. Tier II Vegetative Vigor and Seedling Emergence Studies [GLN 123-1],

2. Storage Stability Data for Field Dissipation Study [GLN 164-1] - the stability data is currently awaiting EPA review.

TOLERANCE ASSESSMENT

Tolerances are established for the plant growth regulator, cyclanilide [1-(2,4-dichlorophenylaminocarbonyl)-cyclopropane carboxylic acid] determined as 2,4-dichloroaniline (calculated as cyclanilide) in or on the raw agricultural commodities cottonseed at 0.60 parts per million (ppm); cotton gin byproducts at 25.0 ppm; milk at 0.04 ppm; fat of cattle, goats, horses, hogs and

sheep at 0.10 ppm; meat of cattle, goats, horses, hogs and sheep at 0.02 ppm; meat by-products (except kidney) of cattle, goats, horses, hogs and sheep at 0.20 ppm; and kidney of cattle, goats, horses, hogs and sheep at 2.0 ppm.

AGGREGATE EXPOSURES

In examining aggregate exposure, 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

The Reference Dose (RfD) for cyclanilide is 0.007 mg/kg/day. This value is based on the systemic LOEL of 30 ppm (2.0 mg/kg/day in males and 2.4 mg/kg/day in females) from the rat reproductive study. The NOEL was not achieved (less than 30 ppm the Lowest Dose Tested). Reduced body weights in young post-weaning F1 males and females and increased renal mineralization in adult F1 females were observed at this level. An Uncertainty Factor (UF) of 300 was applied to the LOEL based on an Uncertainty Factor of 100 to account for interspecies extrapolation and an additional Uncertainty Factor of 3 to account for the lack of a NOEL in the reproductive toxicity study.

A DRES chronic exposure analysis was conducted using tolerance level residues and 100 percent crop treated information to estimate the Theoretical Maximum Residue Contribution (TMRC) for the general population and 22 subgroups. The chronic analysis showed that exposure from the tolerances in or on cottonseed, cotton gin trash, milk, and meat for non-nursing infants (the subgroup with the highest exposure) would be 76.7% of the Reference Dose (RfD). The exposure for the general U.S. population would be 14.9% of the RfD.

The analysis for cyclanilide is a worst case estimate of dietary exposure with all residues at tolerance levels and 100 percent of the commodities assumed to be treated with cyclanilide. Even without refinements, the chronic dietary exposure to cyclanilide appears to be minimal.

An acute dietary analysis was conducted to determine the Margin of Exposure from how close the high end exposure comes to the lowest observed effect level of 150 mg/kg/day in the rat acute oral neurotoxicity study. Generally acute dietary margins of exposure greater than 100 tend to cause no dietary concern. The high end MOE for cyclanilide for all population subgroups was

greater than 5000 and is above the acceptable level and demonstrates no acute dietary concerns.

2. From Potable Water

As a worst case screen, upper bound estimates (acute/chronic) of the concentration of cyclanilide that might be found in surface water have been calculated with the GENEEC screening model program. For cotton, based on the assumption of one application aerially at the maximum application rate 0.25 lb a.i./A), GENEEC calculates the peak (acute) concentration in runoff water adjacent to the application area to be 8.4 ppb and the chronic concentration to be 7.7 ppb. Based on the estimated exposures to cyclanilide from drinking water, the percentage of the RfD utilized for non-nursing infants (the subgroup with the highest exposure) would be 10% of the Reference Dose (RfD). The exposure for the general U.S. population would be 6% of the RfD. There is no established Maximum Concentration Level or Health Advisory Level for cyclanilide under the Safe Drinking Water Act.

The Acute MOE for drinking water is estimated to be greater than 47,000 for all population subgroups. The acute dietary MOE greater than 100 indicates that there is not acute dietary risk concern from acute drinking water cyclanilide exposure.

For the aggregate dietary exposures from food and drinking water, the percentage of the RfD utilized for non-nursing infants (the subgroup with the highest exposure) would be 91% of the Reference Dose (RfD). The exposure for the general U.S. population would be 21% of the RfD. The aggregate acute MOE for non-nursing infants (the subgroup with the highest exposure) would be greater than 8000. The acute MOE for the general U.S. population would be greater than 11,000. Even though these risks represent the worst-case scenario there appears to be no aggregate risk concern associated with the use of cyclanilide on cotton.

3. From Non-Dietary Uses

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

4. Cumulative Exposure to Substances with Common Mechanism of Toxicity

For cyclanilide, 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 for 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 cyclanilide. Cyclanilide appears to be the only know pesticide member of its class of chemistry and here are no reliable data to indicate that this chemical is structurally or toxicologically similar to existing chemical substances at this time. Therefore it appear unlikely that cyclanilide bears a common mechanism of activity with other substances.

DETERMINATION OF SAFETY FOR INFANTS AND CHILDREN

FQPA provides that EPA shall apply an additional safety factor for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the data base, unless EPA determines that such an additional factor is not necessary to protect the safety of infants and children. An additional Uncertainty Factor to account for possible increased sensitivity of children to cyclanilide was not used because 1) the experimental data provided no indication of increased sensitivity of fetal animals to in utero exposure to cyclanilide or of neonates to pre-weaning exposure to cyclanilide; 2) the endpoint upon which the RfD was set, decreased body weight gain in young post-weaning rats, was observed in young, growing animals and therefore already considered the increased sensitivity of young animals in the determination for the LOEL; and 3) treatment related effects seen in other animals did not indicate potential pre or post-natal effects of concern to infants or small children.

OCCUPATIONAL EXPOSURE

Since the available toxicological data does not indicate an evidence of significant toxicity, EPA did not require a short-term or intermediate-term occupational risk assessment. An occupational chronic risk assessment is not appropriate since worker exposure from application to cotton at harvest does not occur often enough to be considered a chronic exposure i.e. a continuous exposure that occurs for at least several months.

SUMMARY OF DATA GAPS

1. A confirmatory Rat Unscheduled DNA Synthesis (UDS) Test [GLN 84-4]

2. Repeat Tier II Vegetative Vigor and Seedling Emergence Studies [GLN 123-1],

3. Storage Stability Data for Field Dissipation Study [GLN 164-1] - the stability data is currently awaiting EPA review.

PUBLIC INTEREST FINDING

For cotton cyclanilide will provide a harvest aid that is comparable in efficacy to the major registered standard tank mix combinations of products but at a cost substantially less that standard tank mix combinations. Rhone-Poulenc claims that Finish will give more consistent performance over a wider range of conditions and with earlier defoliation and boll opening which will allow earlier harvest. However, these claims were not statistically supported. Registration of cyclanilide would provide an important aid for the harvest of cotton.

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