United States Environmental Protection Agency

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

Pesticide Fact Sheet

Name of Chemical: Clothianidin
Reason for Issuance: Conditional Registration
Date Issued: May 30, 2003

1. DESCRIPTION OF CHEMICAL

Generic Name:	(E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine
Common Name:	Clothianidin
Trade Name:	Poncho 600
EPA Shaughnessy Code:	44309
Chemical Abstracts Service (CAS) Number:	205510-53-8 205510-92-5 210880-92-5
Year of Initial Registration:	2003
Pesticide Type:	Insecticide
Chemical Family:	Nitroguanidine subgroup of nicotinoids
U.S. Producer:	Bayer Corporation

2. USE PATTERNS AND FORMULATIONS

Application Sites:	Clothianidin is registered for seed treatment use on corn and canola.
Types of Formulations:	96% technical product 48% flowable concentrate end-use product

Types and Methods of Application:	For use in commercial liquid or slurry treaters by commercial treaters only.
Application Rates:	Application rates for canola are 150 grams to 400 grams active ingredient per 100 kilograms of seed, equivalent to 0.01 to 0.024 pounds of active ingredient per acre. For corn, application rates are 0.25 to 1.25 milligram active ingredient per kernel. Based on a maximum planting rate of 35,000 seeds (kernels) per acre, the application rate for corn would be 8.8 to 44 grams active ingredient per acre, or approximately 0.02 to 0.1 pounds active ingredient per acre.

3. SCIENCE FINDINGS

Summary Science Statements

Based upon a battery of acute toxicity studies, Poncho 600 is classified as Toxicity Category III. Clothianidin is classified as a "not likely" human carcinogen. There are no to low concerns and no residual uncertainties with regard to pre- and/or postnatal toxicity from clothianidin, and the FQPA 10X Safety Factor has been removed. However, due to evidence of effects on the rat immune system and that juvenile rats appear to be more susceptible to these effects, and due to the lack of a developmental immunotoxicity study, a 10X database uncertainty factor is applied to all dietary exposure endpoints.

Available data indicate that clothianidin on corn and canola should result in minimal acute toxic risk to birds. However, assessments show that exposure to treated seeds through ingestion may result in chronic toxic risk to non-endangered and endangered small birds (e.g., songbirds) and acute/chronic toxicity risk to non-endangered and endangered mammals. Clothianidin has the potential for toxic chronic exposure to honey bees, as well as other nontarget pollinators, through the translocation of clothianidin residues in nectar and pollen. Clothianidin should not present a direct acute or chronic risk to freshwater and estuarine/marine fish, or a risk to terrestrial or aquatic vascular and nonvascular plants.

The fate and disposition of clothianidin in the environment suggest a compound that is a systemic insecticide that is persistent and mobile, stable to hydrolysis, and has potential to leach to ground water, as well as runoff to surface waters.

Chemical Characteristics

Property	Technical	End-use
Physical State	Solid powder	Liquid suspension
Color	Colorless	
Odor	Odorless	Latex paint like odor
Melting Point	176.8°C	
Density	1.61 g/mL @ 20°C	1.2632 g/ml
Solubility (Water)	0.327 g/L at 20°C	
Vapor Pressure	1.3×10^{-10} Pa @ 25°C	
Octanol/Water Partition Coefficient	Log P_{ow} = 5 @ 25°C	
pH	6.24 @ 23°C	

Toxicology Characteristics

Acute Toxicity of Clothianidin Technical			
Guideline No.	**Study Type**	**Results**	**Toxicity Category**
870.1100	Acute Oral - rat	LD_{50} > 5000 mg/kg	IV
870.1100	Acute Oral - mouse	LD_{50} = 425 mg/kg	II
870.1200	Acute Dermal - rat	LD_{50} > 2000 mg/kg	III
870.1300	Acute Inhalation - rat	LC_{50} > 6.14 mg/L	IV
870.2400	Primary Eye Irritation - rabbit	Mild conjunctivitis cleared within 24 hours	IV
870.2500	Primary Skin Irritation - rabbit	No irritation or dermal changes for the 3 days observed.	IV
870.2600	Dermal sensitization - guinea pig	Not a dermal sensitizer	N/A

Acute Toxicity of Poncho 600			
Guideline No.	**Study Type**	**Results**	**Toxicity Category**
870.1100	Acute Oral - rat	2000 mg/kg > LD_{50} > 500 mg/kg	III
870.1200	Acute Dermal - rat	LD_{50} > 4000 mg/kg	III
870.1300	Acute Inhalation - rat	LC_{50} > 1.8 mg/L	III
870.2400	Primary Eye Irritation - rabbit	No observed ocular irritation	IV
870.2500	Primary Skin Irritation - rabbit	No observed dermal irritation	IV
870.2600	Dermal sensitization - guinea pig	Not a dermal sensitizer	N/A

Subchronic, Chronic, and Other Toxicity	
Guideline No./ Study Type	**Results**
870.3100 90-Day oral toxicity rodents (rats)	**NOAEL**: 27.9/34.0 mg/kg/day (male/female) **LOAEL**: 202.0/254.2 mg/kg/day (male/female: decreased body weight and body weight gain).
870.3150 90-Day oral toxicity in nonrodents (dogs)	**NOAEL**: 19.3/42.1 mg/kg/day (male/female) **LOAEL**: 40.9/61.8 mg/kg/day (thinness, decreased body weight, body weight gain and anemia (one male); decreased white blood cells, albumin, and total protein (female).
870.3200 21/28-Day dermal toxicity (rats)	**NOAEL**: 1000 mg/kg/day (highest dose tested) **LOAEL**: >1000 mg/kg/day
870.3700 Prenatal developmental in rodents (rats)	**Maternal NOAEL**: 10 mg/kg/day **Maternal LOAEL**: 40 mg/kg/day (decreased body weight gain and food consumption). **Developmental NOAEL**: 125 mg/kg/day **Developmental LOAEL**: cannot be established

Subchronic, Chronic, and Other Toxicity	
Guideline No./ Study Type	**Results**
870.3700 Prenatal developmental in nonrodents (rabbit)	**Maternal NOAEL**: 25 mg/kg/day **Maternal LOAEL**: 75 mg/kg/day (increased incidences of clinical signs (scant feces and orange urine), mortalities, decreased food consumption, early delivery, abortion, and decreased body weight gain) **Developmental NOAEL**: 25 mg/kg/day **Developmental LOAEL**: 75 mg/kg/day (premature deliveries, decreased gravid uterine weights, an increased litter incidence of a missing lobe of the lung and decreased litter average for ossified sternal centra per fetus).
870.3800 Reproduction and fertility effects (rat)	**Parental systemic NOAEL**: 31.2/36.8 mg/kg/day (male/female) **Parental systemic LOAEL**: 163.4/188.8 mg/kg/day (male/female) (decreased body weight, body weight gain and absolute and relative thymus weights). **Offspring systemic NOAEL**: 9.8/11.5 mg/kg/day (male/female) **Offspring systemic LOAEL**: 31.2/36.8 mg/kg/day (male/female: decreased body weight gains and delayed sexual maturation (male); decreased absolute thymus weights in F_1 pups of both sexes and an increase in stillbirths in both generations). **Reproductive NOAEL**: 31.2/188.8 mg/kg/day (male/female) **Reproductive LOAEL**: 163.4/not established mg/kg/day (male/female: decreased sperm motility, and increased number of sperm with detached heads in both generations).
870.4100 Chronic toxicity dogs	**NOAEL**: 46.4/40.1mg/kg/day (male/female) **LOAEL**: not established/52.9 mg/kg/day (male/female: clinical evidence of anemia in females). Note: dose-related decreases in ALT activity observed in mid- and high-dose males and females.
870.4200 Carcinogenicity mice	**NOAEL**: 171.4/65.1 mg/kg/day (male/female) **LOAEL**: 254.1/215.9 mg/kg/day (male/female: decreased body weight and body weight gain; decreased food consumption and food efficiency in males at the LOAEL). No evidence of carcinogenicity.

Subchronic, Chronic, and Other Toxicity	
Guideline No./ Study Type	**Results**
870.4300 Chronic feeding/Carcinogenicity rat	**NOAEL**: 82.0/32.5 mg/kg/day (male/female) **LOAEL**: 156.5/97.8 mg/kg/day (male/female, decreased body weight and food consumption and altered hepatocellular eosinophilic focus of the liver in both sexes; ovary interstitial gland hyperplasia and increased lymphohistiocytic infiltrate in females; and slightly increased incidences of pelvic mineralization and transitional cell hyperplasia in the kidney, mottled livers of males. No evidence of carcinogenicity.
870.5100 Gene Mutation bacterial reverse mutation assay Parent	Small, but significant increase in frequency of histidine revertants in TA1535 strain treated at 1500 and 5000 µg/plate +/-S9; still present but weaker in its absence. The positive response was only reproducible at 5000 µg/plate +/-S9. Clothianidin considered mutagenic under conditions of this test.
870.5100 Gene Mutation bacterial reverse mutation assay Parent	No mutagenic activity in bacteria (*Salmonella typhimurium* and *Escherichia coli*) under conditions of this assay.
870.5100 Gene Mutation bacterial reverse mutation assay Parent	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.
870.5100 Gene Mutation bacterial reverse mutation assay Parent	Only TA 1535 tested. No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.
870.5100 Gene Mutation bacterial reverse mutation assay BN0335E2 metabolite	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.

Subchronic, Chronic, and Other Toxicity	
Guideline No./ Study Type	**Results**
870.5100 Gene Mutation bacterial reverse mutation assay TZMU metabolite	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.
870.5100 Gene Mutation bacterial reverse mutation assay methyl guanidine intermediate	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.
870.5100 Gene Mutation bacterial reverse mutation assay TZNG metabolite	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.
870.5100 Gene Mutation bacterial reverse mutation assay TMG metabolite	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.
870.5100 Gene Mutation bacterial reverse mutation assay BN0230M metabolite	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.
870.5100 Gene Mutation bacterial reverse mutation assay MAI metabolite	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.

Subchronic, Chronic, and Other Toxicity	
Guideline No./ Study Type	**Results**
870.5100 Gene Mutation bacterial reverse mutation assay N-Methylnitroguanidin intermediate	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.
870.5100 Gene Mutation - bacterial reverse mutation assay TI 435-Triazan intermediate	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.
870.5100 Gene Mutation - bacterial reverse mutation assay TI 435-CCMT-Adduct	No mutagenic activity in bacteria (*Salmonella typhimurium*) under conditions of this assay.
870.5300 Gene Mutation - *in vitro* mammalian cell gene mutation test (L5178Y TK +/- mouse lymphoma cells) Parent	Increases in mutant frequency with and without S9 at dose levels that were cytotoxic. The observed response was primarily due to small colony formation, indicating clastogenic activity.
870.5300 Gene Mutation - *in vitro* mammalian cell gene mutation test (V79-HPRT Assay) Parent	No increase in mutant frequency under the conditions of the study.

Subchronic, Chronic, and Other Toxicity	
Guideline No./ Study Type	**Results**
870.5395 Cytogenetics - mammalian erythrocyte micronucleus test Parent	Clothianidin is considered to be neither clastogenic nor aneugenic under these test conditions.
870.5375 Cytogenetics - *in vitro* mammalian chromosome aberration test (CHL Cells) Parent	Significant increases in frequency of cells with structural aberrations. Predominant types were chromatid breaks and exchanges. There was, however, no clear indication of a dose-related response in either the presence or absence of S9 activation.
870.5500 Other Effects - DNA Repair Test in *Bacillus subtillis* Parent	No potential for DNA damage under these conditions.
870.5550 Other Effects - (UDS) in Mammalian Cells in Culture Parent	No evidence (or a dose related positive response) that UDS was induced.
870.6200 Acute neurotoxicity screening battery (rat)	**NOAEL**: not established **LOAEL**: 100 mg/kg (FOB: decreased arousal and decreased motor and locomotor activity).
870.6200 Subchronic neurotoxicity screening battery (rat)	**NOAEL**: 60.0/71.0 mg/kg/day (male/female) **LOAEL**: 177.0/200.1 mg/kg/day (male/female:slightly decreased food consumption, body weights and body weight gains).

Subchronic, Chronic, and Other Toxicity	
Guideline No./ Study Type	**Results**
870.6300 Developmental neurotoxicity (rat)	**Maternal NOAEL:** 42.9 mg/kg/day **Maternal LOAEL:** 142 mg/kg/day (decreased body weights, body weight gains, and food consumption) **Offspring NOAEL:** 12.9 mg/kg/day **Offspring LOAEL:** 42.9 mg/kg/day (decreased body weights and body weight gains)
870.7485 Metabolism and pharmacokinetics (rat)	Overall recovery: 95-100%. Readily absorbed and excreted within 96 hours following a single 2.5 mg/kg bw or repeated oral dose of 25 mg/kg bw, but at a dose of 250 mg/kg, absorption became biphasic and was saturated.
870.7485 Metabolism and pharmacokinetics (mouse)	Of the administered radioactivity, 98.7-99.2% was recovered. Readily absorbed and excreted within 168 hours following a single oral dose of 5 mg/kg body weight.
870.7600 Dermal Penetration - monkey	Dermal absorption as the sum of urinary and fecal excretion and Cage/Pan/Chair Wash, Debris was 0.24 ($\pm$ 0.11) as percent of dose. Adjustment of the direct absorption determination was not necessary because recovery from the dermal dose was >90%. A value of 1% dermal absorption was considered appropriate for use in risk assessment. This estimation takes into account any variability that would have likely occurred with testing several dose levels.
Special Study: Neurotoxicity and pharmacology mouse	**NOAEL**: 25 mg/kg/day (male/female) **LOAEL**: 50 mg/kg bw mg/kg/day (transient signs of decreased spontaneous motor activity, tremors, and deep respirations).

Toxicological Endpoints

The dose at which no adverse effects are observed (the NOAEL) from the toxicology study identified as appropriate for use in risk assessment is used to estimate the toxicological level of concern (LOC). However, the lowest dose at which adverse effects of concern are identified (the LOAEL) is sometimes used for risk assessment if no NOAEL was achieved in the toxicology study selected. An uncertainty factor (UF) is applied to reflect uncertainties inherent in the extrapolation

from laboratory animal data to humans and in the variations in sensitivity among members of the human population as well as other unknowns. An UF of 100 is routinely used, 10X to account for interspecies differences and 10X for intra species differences. EPA has concluded that the toxicology database for clothianidin is not complete. A 10X database uncertainty factor is to be applied to all dietary exposure endpoints for the lack of a developmental immunotoxicity study.

For dietary risk assessment (other than cancer) the Agency uses the UF to calculate an acute or chronic reference dose (acute RfD or chronic RfD) where the RfD is equal to the NOAEL divided by the appropriate UF (RfD = NOAEL/UF). Where an additional safety factors (SF) is retained due to concerns unique to the FQPA, this additional factor is applied to the RfD by dividing the RfD by such additional factor. The acute or chronic Population Adjusted Dose (aPAD or cPAD) is a modification of the RfD to accommodate this type of FQPA SF.

For non-dietary risk assessments (other than cancer) the UF is used to determine the LOC. For example, when 100 is the appropriate UF (10X to account for interspecies differences and 10X for intraspecies differences) the LOC is 100. To estimate risk, a ratio of the NOAEL to exposures (margin of exposure (MOE) = NOAEL/exposure) is calculated and compared to the LOC.

A summary of the toxicological endpoints for clothianidin used for human risk assessment is shown in the following table:

Toxicological Dose and Endpoints for Clothianidin for Use in Human Risk Assessment			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Acute Dietary (Females 13-50 years of age)	Developmental NOAEL = 25 UF = 1000[a] **Acute RfD** = 0.025 mg/kg	FQPA SF = 1 **aPAD** = $\frac{\text{acute RfD}}{\text{FQPA SF}}$ = 0.025 mg/kg	Developmental rabbit study Developmental LOAEL = 75 mg/kg/day based on an increased litter incidence of a missing lobe of the lung.
Acute Dietary (General population)	NOAEL = 25 UF = 1000[a] **Acute RfD** = 0.025 mg/kg	FQPA SF = 1 **aPAD** = $\frac{\text{acute RfD}}{\text{FQPA SF}}$ = 0.025 mg/kg	Special Neurotoxicity/Pharmacology Study in Mice and Rats LOAEL = 50 mg/kg based on transient signs of decreased spontaneous motor activity, tremors and deep respirations.

Toxicological Dose and Endpoints for Clothianidin for Use in Human Risk Assessment			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF* and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Chronic Dietary (All populations)	Offspring NOAEL= 9.8 UF = 1000[a] **Chronic RfD** = 0.0098 mg/kg/day	FQPA SF = 1 **cPAD** = chronic RfD / FQPA SF = 0.0098 mg/kg/day	2-Generation Reproduction Study Offspring LOAEL = 31.2 mg/kg/day based on decreased mean body weight gain and delayed sexual maturation, decreased absolute thymus weights in F_1 pups and an increase in stillbirths in both generations.
Cancer (oral, dermal, inhalation)	**Classification: Not Likely**		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose

[a] Additional 10x database uncertainty factor for lack of a developmental immunotoxicity study.

***** The reference to the FQPA SF refers to any additional SF retained due to concerns unique to the FQPA.

Human Exposures and Risks

Acute risk

Acute dietary risk was calculated assuming that 100% of the corn and canola crops were treated and resulting crop residues are at tolerance levels. In addition, since clothianidin is a major metabolite of thiamethoxam (which has many registered uses and several pending uses), residues of clothianidin which would theoretically result from the metabolism of thiamethoxam were included in the analysis. The acute dietary exposure from food to clothianidin will occupy 7.3% of the aPAD for the U.S. population, 5.4% of the aPAD for females 13 years and older, 11% of the aPAD for all infants (less than one year old), and 16% of the aPAD for children one to two years old. In addition, there is potential for acute dietary exposure to clothianidin in drinking water. After calculating DWLOCs and comparing them to the EECs for surface and ground water, EPA does not expect the aggregate exposure to exceed 100% of the aPAD, as shown in the following table:

Aggregate Risk Assessment for Acute Exposure to Clothianidin					
Population Subgroup	aPAD (mg/kg)	% aPAD (Food)	Surface Water EEC (ppb)	Ground Water EEC (ppb)	Acute DWLOC (ppb)
General U.S. Population	0.025	7.3	3.97	1.46	810
All Infants (< 1 year old)	0.025	11	3.97	1.46	220
Children (1-2 years old)	0.025	16	3.97	1.46	210
Females (13 to 49 years old)	0.025	5.4	3.97	1.46	710
Adults (50+ years old)	0.025	6	3.97	1.46	820

Chronic risk

Chronic dietary risk was calculated assuming that 100% of the corn and canola crops were treated and resulting crop residues are at tolerance levels. In addition, since clothianidin is a major metabolite of thiamethoxam (which has many registered uses and several pending uses), residues of clothianidin which would theoretically result from the metabolism of thiamethoxam were included in the analysis. EPA has concluded that exposure to clothianidin from food will utilize 5.9% of the cPAD for the U.S. population, 9.8% of the cPAD for all infants (less than one year old) and 18% of the cPAD for children one to two years old. There are no residential uses for clothianidin that result in chronic residential exposure to clothianidin. In addition, there is potential for chronic dietary exposure to clothianidin in drinking water. After calculating DWLOCs and comparing them to the EECs for surface and ground water, EPA does not expect the aggregate exposure to exceed 100% of the cPAD, as shown in the following table:

Aggregate Risk Assessment for Chronic Exposure to Clothianidin					
Population Subgroup	aPAD (mg/kg)	% aPAD (Food)	Surface Water EEC (ppb)	Ground Water EEC (ppb)	Acute DWLOC (ppb)
General U.S. Population	0.0098	5.9	2.14	1.46	320
All Infants (< 1 year old)	0.0098	9.8	2.14	1.46	88
Children (1-2 years old)	0.0098	18	2.14	1.46	80
Females (13 to 49 years old)	0.0098	4.6	2.14	1.46	280
Adults (50+ years old)	0.0098	4.9	2.14	1.46	320

Occupational Risk

Clothianidin is intended for use as a seed treatment for corn and canola. For canola, the proposed use rate would be 150 g to 400 g a.i./100 kg seed. The application rate would be approximately 0.01 to 0.024 lb ai/acre based on a seeding rate of 6 lb. seeds/acre. For corn, the treatment rate is 0.25 or 1.25 mg ai/kernel. Based on a maximum planting rate of 35,000 seeds (kernels)/acre, the application rate would be 8.8 or 44 g ai/acre (approximately 0.02 or 0.1 lb ai/acre). Application using hopper-box, slurry-box, or similar seed treatment applications used at planting is prohibited. In addition, the proposed label specifically prohibits on-farm seed treatment, which would likely use the least efficient equipment and result in higher exposures per lb ai handled.

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted to the Agency in support of the registration of clothianidin. Instead, the registrant (Bayer) submitted surrogate studies using the chemicals Oftanol (isofenphos) and Baytan (triadimenol). Bayer Corp. also submitted two exposure assessments which used these seed treatment exposure studies as surrogates for exposure to clothianidin.

None of the baseline seed treater estimates exceed the HED level of concern (all MOEs were greater than 100). Because the Oftanol and Baytan study subjects were wearing long sleeved shirts, long pants, and chemical resistant gloves, the "baseline" risk estimates assume the same level of protection. The baseline total dermal and inhalation MOEs ranged from 380 to 960 for loader/applicators in large commercial facilities The small/medium facility estimates reflect the addition of bagger exposure data from the Baytan study, which was from a medium sized facility. The lowest handler MOE was 110 for seed baggers in small/medium sized facilities. This exposure estimate is driven nearly equally by dermal and inhalation exposure.

The postapplication exposure scenario for seed treatment consists of the farmer purchasing bags of treated seed, placing the seed in hopper, and planting seed in fields. The MOEs for loading and planting seed were all greater than 100 (ranging from 15,000 to 26,000) and therefore, did not exceed HED's level of concern. These estimates are believed to be sufficiently conservative to be protective of all workers.

Environmental Characteristics

STUDY TYPE	HALF LIFE/OTHER
Hydrolysis	Stable
Photolysis in Water	Less than 1 day
Photolysis on Soil	34 days
Aerobic Soil Metabolism	148 to 1,155 days
Anaerobic Aquatic Metabolism	27 days
Mobility-Leaching	Mobile to highly mobile
Terrestrial Field Dissipation	277 days to 1,386 days in the 0-15 cm soil depth; generally not detected below the 45 cm soil depth

Potential to Contaminate Groundwater

Based on laboratory and field studies, the available data on clothianidin show that the compound is persistent and mobile, stable to hydrolysis, and has potential to leach to ground water and be transported via runoff to surface water bodies.

Ecological Characteristics

Terrestrial

Clothianidin is practically non-toxic to the bobwhite quail on an acute basis (LD_{50} > 2000 mg/kg) and practically non-toxic to the mallard duck and the bobwhite quail on a sub-acute basis (5-day LC_{50} > 5040 ppm and 5230 ppm, respectively). However, exposure to treated seeds through ingestion may result in chronic toxic risk to birds (exposure of 525 ppm adversely affected eggshell thickness for Bobwhite quail).

Clothianidin is moderately toxic to small mammals on an acute oral basis (LD_{50} > 389 mg/kg). Chronic exposure to treated seeds through ingestion may result in reproductive and/or developmental effects.

Clothianidin is highly toxic to honey bees on an acute contact basis (LD_{50} > 0.0439 µg/bee). It has the potential for toxic chronic exposure to honey bees, as well as other nontarget pollinators, through the translocation of clothianidin residues in nectar and pollen. In honey bees, the effects of this toxic chronic exposure may include lethal and/or sub-lethal effects in the larvae and reproductive effects in the queen.

Aquatic - Freshwater

Clothianidin is practically non-toxic to the blue-gill sunfish (96-hour LC_{50} = 117 ppm) and practically non-toxic to the rainbow trout (96-hour LC_{50} = 105 ppm). It ranges from very highly toxic to *Chironomus riparius* (48-hour EC_{50} = 0.022 ppm) to practically non-toxic to *Daphnia magna* (48-hour EC_{50} = 100.8 - 119 ppm).

Aquatic - Estuarine/Marine

Clothianidin is slightly toxic to the sheepshead minnow (96-hour LC_{50} > 93.6 ppm). It is practically non-toxic to the eastern oyster (96-hour EC_{50} = 129.1 ppm) and very highly toxic to the mysid shrimp (96-hour LC_{50} = 0.051 ppm).

Plants

Clothianidin does not appear to present a risk to terrestrial plants (seedling emergence EC_{25} > 214 ppm; vegetative vigor EC_{25} > 218 ppm). In addition, it does not appear to present a risk to aquatic vascular plants (*Lemna gibba* EC_{50} > 121 ppm) or aquatic nonvascular plants (*Selenastrum capricornutum* EC_{50} averages 70 ppm).

Endangered Species

Clothianidin is expected to present acute and/or chronic toxicity risk to endangered/threatened birds and mammals via possible ingestion of treated corn and canola seeds. Endangered/threatened non-target insects may be impacted via residue laden pollen and nectar. The potential use sites cover the entire U.S. because corn is grown in almost all U.S. states. The registrant must provide information on the proximity of Federally listed birds, mammals, and non-target insects to the proposed use sites. This information may best be provided via the FIFRA Endangered Species Task Force, but may be produced independently, providing the information is of sufficient quality to meet FIFRA and Endangered Species Act requirements. The information will be used by the EPA to develop specific recommendations to avoid adverse effects to listed species.

To address ecological concerns, labeling will be required that mandates treated seed bags be printed with advisory language regarding hazards to wildlife and will include specific instructions to cover or collect clothianidin treated seeds that are spilled during loading. In order to fully evaluate the possibility of chronic exposure to honey bees, a complete worker bee life cycle study will be required, as well as an evaluation of exposure and effects to the queen. Sediment toxicity testing will be required to address the uncertainty of possible risk to communities of invertebrates and fish that inhabit or come into contact with sediment from fields planted with treated seed.

Mechanism of Pesticidal Action

Although nicotine has been used as a pesticide for over 200 years it degraded too rapidly in the environment and lacked the selectivity to be very useful in large scale agricultural situations. However, in order to address this problem, the neonicotinoids (chloronicotinyl insecticides) were developed as a substitute of nicotine, targeting the same receptor site (AChR) and activating post-synaptic acetylcholine receptors but not inhibiting AChE. Clothianidin, like other neonicotinoids, is an agonist of acetylcholine, the neurotransmitter that stimulates the nAChR. In insects, neonicotinoids cause symptoms similar to that of nicotine. The advantage of clothianidin and other neonicotinoids over nicotine is that they are less likely to break down in the environment.

4. SUMMARY OF REGULATORY POSITION AND RATIONALE

Available data provide adequate information to support the conditional registration of Poncho 600 for seed treatment use on corn and canola.

Use, Formulation, Manufacturing Process or Geographic Restrictions

Environmental Hazards

This product is toxic to aquatic invertebrates. Clothianidin has properties and characteristics associated with chemicals detected in ground water. Contain any product spills or equipment leaks and dispose of wastes according to disposal instructions on this label. Do not contaminate water when disposing of equipment washwaters.

Use Directions - General Precautions

For use by commercial treaters only. Not for use in agricultural establishments in hopper-box, slurry-box, or similar on-farm seed treatment applicators used at planting. This product is to be used in commercial liquid or slurry treaters.

All seed treated must be conspicuously coloured at the time of treatment. An appropriate colorant must be added during application to seed to distinguish and prevent subsequent inadvertent use as a food for man or feed for animals.

Treated seed must be labeled in accordance with the requirements of the Federal Seed Act.

Required Labeling for Treated Seed Bags

Seeds are treated with clothianidin as an insecticide.

Treated seeds exposed on soil surface may be hazardous to wildlife. Cover or collect treated seeds spilled during loading.

Areas planted with treated seed may be replanted immediately with corn, rapeseed, and canola. These areas may also be replanted after 30 days with cereal grains, grasses, nongrass animal feeds, soybeans, and dried beans. Do not plant any other crop in the treated area for at least one year after treated seeds are planted.

Do not use treated seed for feed, food or oil processing.

Rapeseed greens and seed grown or harvested from treated seed must not be used for feed or human consumption.

Store away from feeds and other foodstuffs.

Wear long-sleeved shirt, long pants, and waterproof gloves when handling treated seed.

Dispose of all excess treated seed. Left over treated seed may be doublesown around the headland or buried away from water sources in accordance with local requirements. Do not contaminate water bodies when disposing of planting equipment washwaters.

Dispose of seed packaging in accordance with local requirements.

5. SUMMARY OF DATA GAPS

Toxicology:
- Developmental immunotoxicity study
- Additional analysis of test materials used in mutagenicity studies

Residue Chemistry:
- Rotational crop residue field trials with mature soybeans

Environmental Fate Data:
- Aerobic aquatic metabolism
- Seed leaching study

Ecological Effects Data:
- Whole sediment acute toxicity to freshwater invertebrates
- Field test for pollinators

6. CONTACT PERSON AT EPA

Daniel C. Kenny
Product Manager 01
Insecticide-Rodenticide Branch
Registration Division (7505C)
Office of Pesticide Programs
Environmental Protection Agency
Aerial Rios Building
1200 Pennsylvania Ave., NW
Washington, DC 20460

Office Location and Telephone Number

Room 229, Crystal Mall Building #2
1921 Jefferson Davis Highway
Arlington, VA 22202
(703) 305-7546