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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM **2/20/03**

Subject: EFED Risk Assessment for the Seed Treatment of Clothianidin 600FS on Corn and Canola (PC Code 044309; DP Barcode: D278110)

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Attached is the Environmental Fate and Effects Division's (EFED) environmental risk assessment of the Section 3 registration of the insecticide, clothianidin for seed treatment on corn and canola to control a host of insect pests (e.g., aphids, flea beetles, wireworms, chinch bugs, black cutworm, etc.). This registration is being conducted as a joint review between the regulatory agencies of Canada (PMRA), the United States (EPA), and Australia (NRA).

Based on laboratory and field studies submitted to the Agency, EFED has concluded that the proposed seed treatment use of clothianidin on corn and canola should result in minimal acute

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toxic risk to birds. However, our assessment also shows 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. The ingestion of treated seeds is a concern because several species of birds and mammals frequent corn and canola fields seeking forage and grit. This feeding strategy, raises a concern at the chronic level because only a few seeds may be necessary to cause reproductive and/or developmental effects (e.g., 1 - 2 corn seeds for small and medium size mammals). EFED is also concerned with the possibility of chronic toxic exposure to honey bees. Considering the toxicity profile and reported incidents of other neonicotinoids (e.g., imidacloprid), the proposed seed treatment with clothianidin has the potential for toxic risk to honey bees, as well as other pollinator insects. As a result of this concern, EFED is asking for additional chronic testing on bee hive activity (e.g., effects to queen, larvae, etc.). The results of our Tier I screening level exposure assessment also suggest that exposure to aquatic systems may occur through runoff after treated seed have been planted. Although this runoff should not result in toxic risk to fish (freshwater or estuarine/ marine), there is the possibility of acute toxic risk to aquatic invertebrates. However, with regard to plants, clothianidin does not appear to present 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. The high persistence of clothianidin (aerobic soil metabolism and terrestrial field dissipation half-lives ranging from half a year to several years) would cause accumulation of the chemical in soils with repeated uses.

Outstanding Data Requirements

OPPTS 850.1735: Whole Sediment Acute Toxicity Invertebrates, Freshwater. This is a 28 day test that measures survival, growth and emergence of *Chironomus riparius* that have been exposed to pesticide spiked sediment. EFED is requesting this acute sediment toxicity test because clothianidin is toxic to aquatic invertebrates, persistent in the environment, and binds to sediment over time.

Field Test for Pollinators (141-5): The possibility of toxic exposure to nontarget pollinators through the translocation of clothianidin residues that result from seed treatment (corn and canola) has prompted EFED to require field testing (141-5) that can evaluate the possible chronic exposure to honey bee larvae and queen. In order to fully evaluate the possibility of this toxic effect, a complete worker bee life cycle study (about 63 days) must be conducted, as well as an evaluation of exposure and effects to the queen.

Aerobic Aquatic Metabolism (162-4): 1) Although two studies were submitted for this requirement, the experimental design was not in compliance with guidelines (soil and water were pre-incubated before applying the test substance) and (2) aerobic conditions were not fully maintained during the course of the study as indicated by the low redox potential that developed in the sediment in another study, no sediment was used. A new study is required.

Seed Leaching Study: EFED believes that a seed leaching study would greatly increase certainty regarding a more realistic estimate of the amount of available clothianidin residues on the seed surface. This in turn would allow a refinement of exposure estimates and environmental concentration values (EECs).

Endangered Species

The Agency's level of concern for endangered and threatened birds, mammals and nontarget insects is exceeded for the proposed use of clothianidin on corn and canola. This concern to mammals and birds is based on chronic endpoints such as reproductive and developmental effects. The concern for nontarget insects is based on the uncertainty regarding potential chronic effects to honey bees and the toxicity profile and reported incidents to honey bees from seed treatment of other neonicotinoids (e.g., imidacloprid). The registrant must provide information on the proximity of Federally listed birds, mammals and nontarget insects to the proposed use sites. This requirement may be satisfied in one of three ways: 1) having membership in the FIFRA Endangered Species Task Force (Pesticide Registration [PR] Notice 2000-2); 2) citing FIFRA Endangered Species Task Force data; or 3) independently producing these data, provided the information is of sufficient quality to meet FIFRA requirements. The information will be used by the OPP Endangered Species Protection Program to develop recommendations to avoid adverse effects to listed species.

Uncertainty

Environmental Fate and Exposure

There is additional uncertainty with regard to aquatic photolysis of clothianidin where the half-life was calculated at < 1 day (core study) while a slow rate of dissipation was observed in field studies. The range of values given for surface water-source drinking water represents uncertainty with regard to the importance of photodegradation in the long-term fate of clothianidin in natural waters.

Clothianidin has the properties of a chemical which could lead to widespread ground-water contamination, but no ground-water monitoring studies have been conducted to date. Should the registrant request field uses involving direct application of clothianidin to the land surface, Prospective Ground-Water Monitoring Studies may be needed to evaluate fully the potential impact of such uses.

Ecological Effects

There is concern for the persistence of clothianidin in aquatic sediments, and uncertainty about effects on benthic organisms. Therefore, EFED requests submission of a sediment toxicity test on the midge, *Chironomus riparius*, as a condition of registration.

Other neonicotinoid compounds like imidacloprid (e.g., sunflower seed treatment) have resulted in incidents to honey bees. The National Union of French Beekeepers had concerns regarding imidacolprid (GAUCHO) seed treatment to sunflowers after beekeepers noted that honey bees were showing modifications of behavior that were reflected in foraging and orientation that eventually resulted in a drastic change in hive conditions and bee survival. Further research by the Le Centre Technique Interprofessional des Oleagineux (CETIOM) onfirmed imidacloprid toxic residue levels in the sunflower nectar. This action has prompted France to ban the use of imidacloprid for sunflower seed treatment. Since clothianidin has a similar toxicity profile as imidacloprid and is a member of the same family of compounds, there is uncertainty regarding the toxic risk to developing honey bee larvae, as well as the welfare of the queen from long term exposure to clothianidin residues that can be stored in the hive in honey and/or pollen.

There is uncertainty surrounding clothianidin's possible role as an endocrine disrupter as noted from mammalian developmental and avian reproductive effects. This issue is compounded by the fact that clothianidin is an analog of nicotine and that studies in the published literature suggest that nicotine, when administered, causes developmental toxicity, including functional deficits, in animals and/or humans that are exposed in utero. Mammalian data shows that exposure to clothianidin can result in developmental effects (rabbit) that include premature deliveries, decreased gravid uterine weights, and increase incidence of missing lung lobe in fetus. The mammalian data also suggests that chronic toxicity in mammals can be manifested as systemic effects that can include decreased body weight gains and delayed sexual maturation (males only); decreased absolute thymus weight in F1 pups (both sexes), and increased stillbirths (F1 and F2 litters). Reproductive effects were also noted for adult rats that included decreased sperm motility and increased number of sperm with detached heads. Although these effects did not reduce rat fecundity they do raise an uncertainty as to possible reproductive effects to other species that may have a more limited (less frequent) reproductive capability.

Label Recommendations

Manufacturing Use Product

Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

End Use Product

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.

This compound is toxic to birds and mammals. Treated clothianidin seeds exposed on soil surface may be hazardous to birds and mammals. Cover or collect clothianidin seeds spilled during loading.

This product is toxic to aquatic invertebrates. Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when disposing of equipment wash waters.

This compound is toxic to honey bees. The persistence of residues and the expression of clothianidin in nectar and pollen suggests the possibility of chronic toxic risk to honey bee larvae and the eventual stability of the hive.

Executive Summary

The registrant, Bayer Corporation, is submitting a proposal for clothianidin to be used as a seed treatment on corn and canola and to be considered as a Reduced Risk chemical at EPA. This registration is also being proposed for joint review between the regulatory agencies of Canada (PMRA), the United States (EPA), and Australia (NRA).

This compound is a member of the neonicotinoids (chloronicotinyl insecticides) that were developed as a chlorinated analog of nicotine. These compounds target the same receptor site (AChR) and activate post-synaptic acetylcholine receptors. Clothianidin, like other neonicotinoids, is an agonist of acetylcholine, the neurotransmitter that stimulates the nAChR. The fate and disposition of clothianidin in the environment shows a compound that is persistent, stable to hydrolysis, and mobile with the potential to leach to ground water and runoff to surface water. This proposed seed treatment use reduces the possibility of acute toxic risk to birds and mammals. However, EFED believes that this use pattern has the potential for chronic toxic risk to birds (≤ 0.178 kg) and mammals (0.15 - 0.035 kg) through seed ingestion during foraging in treated fields, as well as acute toxic risk to aquatic invertebrates from runoff. The possible chronic effects to birds (eggshell thinning) and mammals (reproductive, developmental) from ingestion of treated seeds suggest chronic toxic risk, Endocrine Disruption concerns, and Endangered Species triggers. These chronic effects in mammals can include decreased body weight gains and delayed sexual maturation (males only); decreased absolute thymus weight in F1 pups (both sexes), and increased stillbirths (F1 and F2 litters). Reproductive effects were also noted for adult rats that included decreased sperm mobility and increased number of sperm with detached heads. These effects could especially result in toxic risk to those species that have a limited reproductive capacity (e.g., few litters or broods, or those animals that reproduce only once per year). Although effects on sperm mobility may not effect the number of offspring in some cases, there can be an impact on the ratio of gender composition (e.g., more males produced as opposed to females) which will directly result in population reductions. Developmental effects were also noted in rabbits at 75 mg/kg/day (LOAEL = 75 mg/kg/day), and included premature deliveries, decreased gravid uterine weights, and increased litter incidence of missing lung lobe in the fetus. Although EFED does not develop a risk assessment on non target insects, information from standard tests and field studies, as well as incidents noted from the seed treatment application of other neonicotinoids (imidiacloprid), suggest an uncertainty regarding the potential for chronic toxic risk of this compound to honey bees and other beneficial insects. The persistence of residues and the expression of clothianidin in nectar and pollen suggests the possibility of chronic toxic risk to honey bee larvae that may eventually affect the stability of the hive. With regard to phytotoxicity, clothianidin does not appear to present a risk to terrestrial or aquatic vascular and nonvascular plants.

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I. Environmental Risk Conclusions

a. Proposed Use

The Bayer Corporation is submiting for registration a new neonicotinoid insecticide, clothianidin, to be used as a seed treatment on corn and canola. According to a previous agreement, this compound is being submitted for registration simultaneous to the regulatory agencies of Canada (PMRA), the United States (EPA), and Australia. Table 1 provides information on the proposed use patterns.

Table 1. Proposed clothianidin new usage patterns

Crop	Rate	Maximum Rate lbs ai/A	Number of applications
Corn	5.64 fl.oz/80,000 seeds	0.1	1
Canola	3.84 - 15.36 fl.oz/100 lbs seed	0.05	1

b. Major Risk Concerns

EFED's risk assessment suggests that the use of clothianidin as a seed treatment has the potential acute toxic risk to aquatic invertebrates from runoff and chronic toxic risk to terrestrial animals from possible ingestion of the treated corn and canola seeds after their application to a field. Although EFED does not do a risk assessment on nontarget insects, information from standard tests and field studies raise the uncertainty of possible toxic chronic risk to honey bees and other beneficial insects.

EFED has noted in its risk assessment that there is the potential for acute toxic risk to small and medium-sized birds (≤ 0.178 kg) for both crop scenarios (corn RQ = 0.1; canola RQ = 0.2), as well as acute toxic risk to mammals (corn RQ = 0.6, canola RQ = 0.8). However, the likelihood of these organisms reaching the lethal threshold of acute toxicity from seeds consumption is unlikely (e.g., about 285 corn seeds must be consumed by a 0.178 kg bird). However, clothianidin treated seed ingestion could result in chronic reproductive effects in birds (RQ = 6.3 - 8.6) and reproductive/developmental effects in mammals (RQ = 44 - 61) (e.g., about 1 -2 corn seeds have the potential for chronic effects to a mammal ≤ 0.035 kg). These chronic effects can be manifested as eggshell thinning in birds and in mammals, systemic, reproductive and developmental effects have been noted. The use of this compound as a seed treatment appears to present the possibility of chronic risk, as well as Endocrine Disruption, and Endangered Species concern for mammals and birds.

Acute toxicity studies on honey bees show that clothianidin has the potential to be highly toxic on both a contact and an oral basis (contact LD_{50} = 0.044 ug/bee; oral LD_{50} = 0.0037 ug/bee), while its degradates (e.g.,, TMG, MNG, TZMU, and TZNG) are moderately to practically non-toxic on an oral basis (LD_{50} = 3.9 - >153 ug/bee). One honey bee field study showed that mortality, pollen foraging activity, and honey yield were not affected by residues of clothianidin. However, the impact to honey bees from other neonicotinoids (imidacloprid sunflower seed treatment) suggests that there is uncertainty regarding the possible toxic risk to larvae and pupae inside the hives from stored pollen and honey that contains clothianidin residues.

EFED's risk assessment suggests that clothianidin should not present a direct acute or chronic risk to freshwater and estuarine/marine fish. However, based on a Tier I Screening Level assessment there is the possibility of acute toxic risk (RQ = 0.1) to freshwater invertebrates, via runoff. Because the clothianidin toxicity threshold is low for aquatic freshwater invertebrates on an acute basis, their vulnerability can represent acute risk from sediment exposure. As a dynamic trophic level, invertebrates add to the diversity and support of an aquatic system. Since clothianidin is persistent in the sediment, sediment toxicity testing will be needed to address the uncertainty of possible risk to the large communities of invertebrates that inhabit the sediment, as well as the indirect impact to fish that are dependent upon these organisms as a source of food.

c. Incidents

The EPA/OPP 6(a)(2) incident reporting data base currently does not contain incident reports for clothianidin since it is a new compound. However, other neonicotinoids compounds like imidacloprid have resulted in incidents to honey bees. The National Union of French Beekeepers had concerns regarding imidacolprid (GAUCHO) seed treatment to sunflowers. Beekeepers noted that bees were showing modifications of behavior that was reflected in foraging and orientation that eventually resulted in a drastic change in hive conditions and bee survival. Further research by the CETIOM confirmed imidacloprid toxic residue levels in the sunflower nectar. France has banned the use of imidacloprid for sunflower seed treatment.

d. Likelihood of Water Contamination

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

e. Monitoring and Modeling

The estimates for drinking water were performed using the model FIRST (Tier I Screening Level) for surface water and SCI-GROW for ground water and were based on a maximum application rate for corn (0.1 lbs ai/A) (with FIRST, similar results were obtained for canola even though the application rate was lower). The maximum expected concentration of clothianidin in surface waters is 3.97 ppb for acute risk calculations and 2.14 ppb for chronic risk and cancer risk calculations. Concentrations in ground water are not expected to exceed 0.91 ppb (Table 2).

Table 2. Estimated Tier 1 concentrations of clothianidin in drinking water.

Chemical	Surface Water (ug/L)		Groundwater (ug/L)
	Acute	Chronic	Acute and Chronic
Clothianidin	3.97	1.06 - 2.14	1.46

No Maximum Contaminant Levels (MCL) or Health Advisories (HA) have been established by the EPA for clothianidin.

All assessments have been based on the contamination potential with clothianidin parent, which appears to be the most significant contaminant of surface and ground waters; but we note that limited environmental fate data for the degradates indicates that some of these compounds may be mobile and persistent.

The range of values given for surface water-source drinking water represents uncertainty with regard to the importance of photodegradation in the long-term fate of clothianidin in natural waters. Additional data may be needed from the registrant to resolve these uncertainties.

II. Introduction

a. Mode of 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 symptoms appear rapidly as increased restlessness followed by violent convulsions and death. The advantage of clothianidin and other neonicotinoids over nicotine is that they are less likely to break down in the environment.

b. Degradation

Structures of clothianidin and its degradates are found in Appendix I. The major degradation products found in a variety of studies were *N*-(2-clorothiazol-5-ylmethyl)-*N*'-methylurea (TMZU), N-(2-chloro-5-thiazolyl methyl)- N'-nitroguanidine (TZNG; aka desmethyl TI435), N-(2-chlorothiazol-5-ylmethyl)- N'-methyl guanidine (TMG), N-methyl-N'-nitroguanidine (MNG), Nitroguanidine (NTG or NG), and CO_2.. Little degradation of parent occurred in each of the 10 soils used for aerobic metabolism investigation (54 to 95% of the parent compound remaining in the soil at the close of these studies) but there was still some evidence of accumulation of TZNG, MNG, and NTG in some of the test soils. TMG accumulated significantly in the aerobic aquatic studies (which were not strictly aerobic in the sediment where the TMG was found).

Degradates identified only in photolysis studies include 4-hydroxy-2-methylamino-2-imidazolin-5-one (HMIO), 7-methylamino-4H-imidazo[5,1-b][1,2,5]thiadiazin-4-one (MIT), formamide (FA), (MG), methyl urea (MU), urea, 3-methylamino-1*H*-imidazo [1,5-*c*]imidazole (MAI), and 2-chlorothiazol-5-ylmethanol (CTCA). Major photolytic products were MG, HMIO, MU, Urea, TMG, MAI, CTCA, and CO_2..

c. Use Characterization

Clothianidin is a systemic insecticide that is being proposed for registration as a seed treatment on corn and canola. This formulation (Clothianidin 600FS) is to be used in commercially available equipment designed for seed treatment only and not for use in hopper-box, slurry-box, or similar seed treatment applications used at planting.

d. Approach to Risk Assessment

EFED's approach to this risk assessment is based on exposure (chemistry, use, fate, etc.) and effects data (acute and chronic toxicity studies for terrestrial and aquatic organisms). The initial evaluation is focused on the development of a deterministic point estimate approach which is the ratio of model derived estimated environmental concentration (based on maximum application rate) of a compound to a worst case toxicity effects value (acute and chronic). The resulting Risk Quotients (RQ) are then compared to the Agency's Levels of Concern (LOC) which address the following risk presumption categories:

Risk Presumption Categories

Risk Presumption for Terrestrial Organisms	**LOC**
Acute High: high potential for acute risk for all non-target organisms	0.5
Acute Restricted Use: acute risk for all non-target organisms, but may be mitigated through restricted use classification	0.2
Acute Endangered Species: endangered species may be adversely affected by use	0.1
Chronic Risk: potential for chronic risk may warrant regulatory action	1
Risk Presumption for Aquatic Organisms	**LOC**
Acute High: high potential for acute risk for all non-target organisms	0.5
Acute Restricted Use: acute risk for all non-target organisms, but may be mitigated through restricted use classification	0.1
Acute Endangered Species: endangered species may be adversely affected by use	0.05
Chronic Risk: potential for chronic risk may warrant regulatory action	1

Currently the Agency does not perform assessments for chronic risk to plants, acute/chronic risks to non-target insects, or chronic risk from granular/bait formulations to birds and mammals.

In order to evaluate a Tier I assessment of clothianidin exposure to aquatic organisms, EFED has relied on the maximum EEC value generated through GENEEC2, while chronic values for fish and invertebrates reflected 56-day and 21-day GENEEC2 averages, respectively. Corn was modeled as a worst case scenario for aquatic exposure. Terrestrial risk was determined on an acute exposure scenario that estimates the quantity of seeds that an animal could ingest in one day (Nagy, 1987)[1] if the animal consumes only clothianidin treated seeds.

This approach defines a risk quotient (RQ) as follows:

$$RQ = Dose/LD_{50}$$

Dose is defined as the amount of clothianidin that an animal could receive by ingesting treated seeds in a 24-hour period per animal body mass (dose units in mg/kg). Acute high risk is assumed to occur with regard to RQ values ≥ 0.5, acute restricted use category for values ≥ 0.2, and acute endangered species concerns at ≥ 0.1.

The dose that an animal could receive by eating treated seeds can be approximated from the estimated amount of food that is consumed in a day. The dose can be described as

$$Dose = (FI)(C)(T)/M_{bird/mammal}$$

where FI = the food ingestion rate [kg/day]
C = active ingredient concentration on seed (mg/kg)
T = relevant duration time for food consumption (assumed to be 1 day in this assessment)
$M_{bird/mammal}$ = mass (wet) of animal [kg].

The calculations for chronic risk as noted by number of seeds consumed was as follows:

$$\text{Seed/mammal or bird} = \frac{(\text{LOAEL})(\text{animal wt})}{(\text{mg ai/seed})}$$

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[1]Nagy, K.A. (1987). Field metabolic rate and food requirement scaling in mammals and birds. *Ecol. Monogr.* 57:111-128.

III. Integrated Environmental Risk Characterization

a. Ecological Risk Summary

EFED has concluded that the available data on clothianidin show that the compound is persistent and mobile, stable to hydrolysis, and has potential to leach to ground water. In combination with the issue of persistence, our risk assessment suggests that the clothianidin proposed use pattern for seed treatment on corn and canola has the potential for chronic (RQ = 6.3 - 8.6) toxic risk to avian species, as well as mammalians (RQ = 44 - 61) from possible ingestion of treated seeds. This can be a greater toxic risk concern for mammals because they tend to cache food reserves (stockpile and store). Toxic risk to fish (freshwater and estuarine/marine) appears low, but there may be acute toxic risk to aquatic freshwater invertebrates (RQ = 0.1) through contamination of surface water via runoff. Although EFED does not do a risk assessment on non target insects, information from standard tests and field studies, as well as incident reports involving other neonicotinoids insecticides (e.g., imidacloprid) also suggest the potential for long term toxic risk to honey bees and other beneficial insects. Our risk assessment also shows toxic risk to Endangered Species (birds, mammals, and invertebrates). Risk to terrestrial and aquatic plants does not appear to be an issue of concern from this use pattern.

Although it was noted in EFED's risk assessment for terrestrial animals that there may be a potential for acute and chronic risk from treated seed ingestion, the prescribed agricultural practice of drilling seeds at planting should reduce exposure to these animals. We expect that foraging animals would have to consume a large number of seeds before an acute threshold could be realized (e.g., Bobwhite quail would need to eat 285 corn seeds before acute toxicity is a risk). However, the issue of chronic toxicity risk has raised uncertainty and concern. EFED believes that clothianidin treated seed ingestion has the potential for chronic reproductive effects in birds (RQ = 6.3 - 8.6) and mammals (RQ = 44 - 61). The chronic toxicity threshold for birds and mammals is low and could be possibly reached by the consumption of a fewer number of seeds (e.g., 1 - 2 seeds consumed by mammals in the small to medium range of ≤ 0.035 kg). Chronic risk to small mammals can be a special concern because the animals will cache food, seeking seeds and storing them. These chronic effects can be manifested as eggshell thinning in birds and systemic, reproductive and developmental effects in mammals. These chronic effects in mammals can include decreased body weight gains and delayed sexual maturation (males only); decreased absolute thymus weight in F1 pups (both sexes), and increased stillbirths (F1 and F2 litters). Reproductive effects were noted for adult rats that included decreased sperm motility and increased number of sperm with detached heads. These effects could especially result in toxic risk to those species that have a limited reproductive capacity (e.g., few litters or broods, those animals that reproduce only once per year, and Endangered Species). Although effects on sperm mobility may not effect the number of offspring in some cases, there can be an impact on the ratio of gender composition (e.g., more males produced as opposed to females) which can result in population reductions. Over time, developmental effects were noted in rabbits at 75 mg/kg/day, and included premature deliveries, decreased gravid uterine weights, and increased litter incidence of missing lung lobe in the fetus. The possibility of chronic risk suggests a Restricted Use compound, Endocrine Disruption candidate, as well as Endangered Species concern for mammals, birds, and invertebrates.

Although EFED does not do risk assessments on insects, there is a concern for the toxic residual exposure of clothianidin to honey bees. The compound is systemic and is expressed in the nectar and pollen of crops grown from treated seeds (canola). Our hazard assessment shows that clothianidin can result in acute toxicity to honey bees and is considered to be highly toxic on both a contact and an oral basis (contact LD_{50} = 0.044 ug/bee; oral LD_{50} = 0.0037 ug/bee), while its degradates (e.g.,, TMG, MNG, TZMU, and TZNG) are moderately to practically non-toxic on an oral basis (LD_{50} = 3.9 - >153 ug/bee). Although one honey bee field study showed that mortality, pollen foraging activity, and honey yield were not affected by residues of clothianidin, the study failed to address the issue of long term residues and their possible impact inside the hive. While acute contact should not be a major exposure route from the proposed seed treatment uses, there is uncertainty regarding the possible toxic risk (acute/chronic) to larvae and pupae from stored pollen and honey that contains clothianidin residues. This concern for toxic risk to honey bees has also been noted from the toxic actions of other neonicotinoid compounds like imidacloprid, where toxic impact to honey bees and hive activity have been noted.

EFED's Tier I Screening Level exposure assessment[2] suggests that clothianidin should not present a direct acute or chronic risk to freshwater and estuarine/marine fish. However, there is the possibility of acute toxic risk (RQ = 0.1) to freshwater invertebrates, via runoff. Because the clothianidin toxicity threshold is low for aquatic freshwater invertebrates on an acute basis, their vulnerability represents acute risk from sediment exposure. As a dynamic trophic level, invertebrates add to the diversity of an aquatic system. Since clothianidin is persistent in the sediment, sediment toxicity testing will be needed to address the uncertainty of possible risk to the large communities of invertebrates and fish that inhabit or come into contact with the sediment.

Corn

The planted acreage for **corn** in the USA amounts to 80, 227,000 acres with the highest production in the midwest and central states. The following states account for about 67% (53,752,090 acres) of the corn acreage (Figure 1): Iowa, 12 X 10^6 A; Illinois, 11 x10^6 A; Nebraska, 9 x 10^6 A; Minnesota, 7 x 10^6 A; Indiana, 6 x 10^6 A; Ohio, 3.6 x 10^6 A; Wisconsin, 3.8 x 10^6 A; Kansas, 2.85 x 10^6 A; South Dakota, 3.8 x 10^6 A; Missouri, 2.95 x 10^6 A (USDA, 2000). The proposed application rate for clothianidin use on corn is 0.1 lbs ai/A as a seed treatment and the exposure to aquatic and terrestrial organisms is reduced through the prescribed agricultural practice of drilling seeds at planting. However, several species of birds and mammals frequent corn fields seeking forage or grit, with the resulting ingestion of treated corn seeds possibly resulting in chronic toxic risk to these organisms. Since spring planting coincides with the reproductive patterns of several avian and mammalian species, the possibility of chronic toxic risk may increase. According to one scenario of EFED's calculations regarding terrestrial risk, the ingestion of about 1 - 2 corn seeds can result in chronic toxic risk to small and medium size mammals ($\leq$ 0.035 kg).

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[2]Tier I Screening Level exposure assessment assumes that 100% of the chemical was available for runoff. Since this is an uncertainty, this could be further refined with data from a seed leaching study (163-1).

Toxic risk to terrestrial organisms can be expanded to honey bees. Although corn is wind pollinated, the pollen is a source of protein that is utilized by honey bees. Corn pollen is 14% to 15% crude protein and is collected in large quantities for food that is initially consumed, as well as stored in the hive. The concern with clothianidin as a seed treatment on corn is the possibility of extended residual activity from pollen that is introduced into the hive. This scenario is reflected in similar situations of toxic impact to bee colonies from exposure to other insecticides (e.g., Penncap-M, Furadan) that also have extended residual time (8 - 14 days). After the French had banned the use of imidacloprid on sunflower seeds, bee populations appeared to still be experiencing toxic effects and imidacloprid laden corn pollen was suspected. This concern prompted a study by the National Institute of Research Agronomic (INRA) and the Centre for National Scientific Research (CNRS) to evaluate the effects of imidacloprid laden pollen to bees. Their findings confirm that the bees are still exposed to the molecule of Gaucho, imidacloprid, via corn pollen. Samples of the corn pollen taken from the entrance of hives contained 3.3 - 3.7 ppb imidacloprid.

About 70% of corn acreage is concentrated in the mid western states. This implies that the potential for clothianidin exposure to aquatic ecosystems will be primarily to lakes and rivers via runoff. EFEDs Tier I (GENEEC) risk assessment suggests that exposure of clothianidin to fish through the proposed use pattern on corn should not result in direct acute or chronic toxic risk. However, our model output suggest the possibility of runoff that can present sufficient exposure to cause acute toxic risk to aquatic invertebrates (RQ = 0.1).

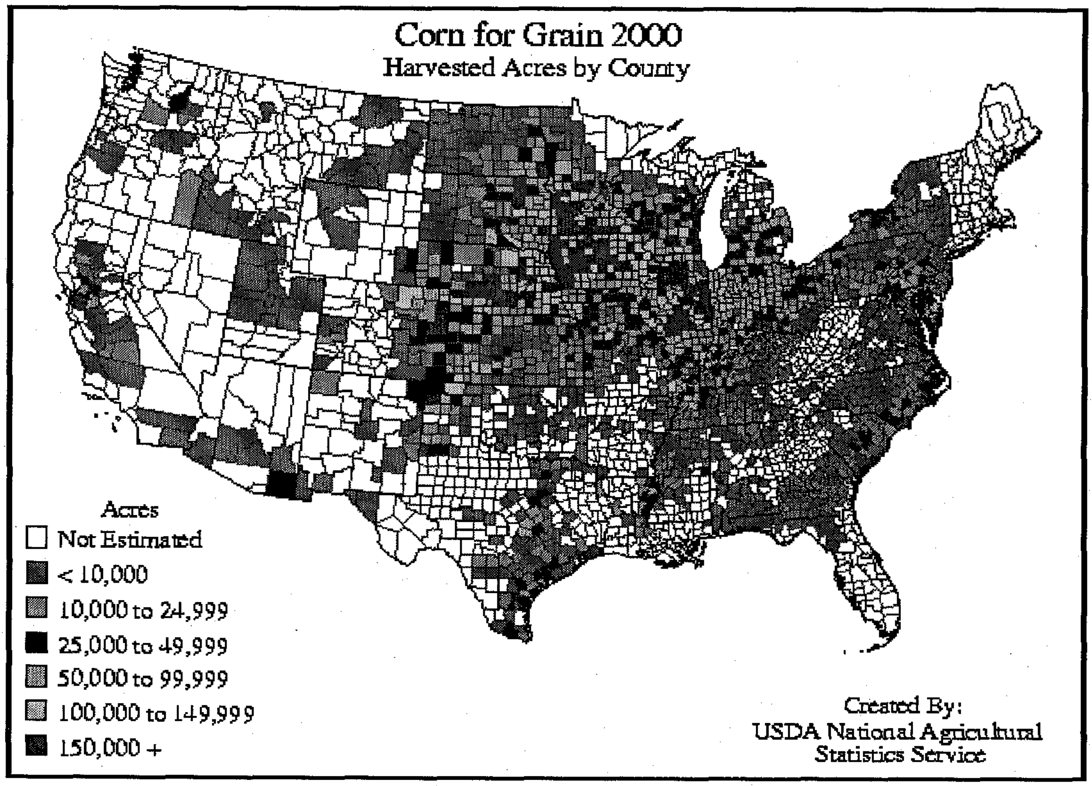

Figure 1. Corn acreage in the USA

Canola

The planted acreage for **canola** in the USA amounts to 1,513,000 acres with the highest production in the upper midwest and north central states. The following states account for about 90% (1,390,000 acres) of the canola acreage (Figure 2): North Dakota, 1.3 X 10^6 A; Minnesota, 90 x 10^3 A; other states, 73 x 10^3 A (USDA, 1992). The proposed application rate for clothianidin use on canola is 0.05 lbs ai/A as a seed treatment. Since several species of birds frequent canola fields seeking forage or grit, the ingestion of treated canola seeds can result in chronic toxic risk to these organisms. This risk may be a greater concern to species whose reproductive patterns coincide with spring planting. Mammals > 0.0015 kg are less likely to feed on canola seeds because of the small seed size.

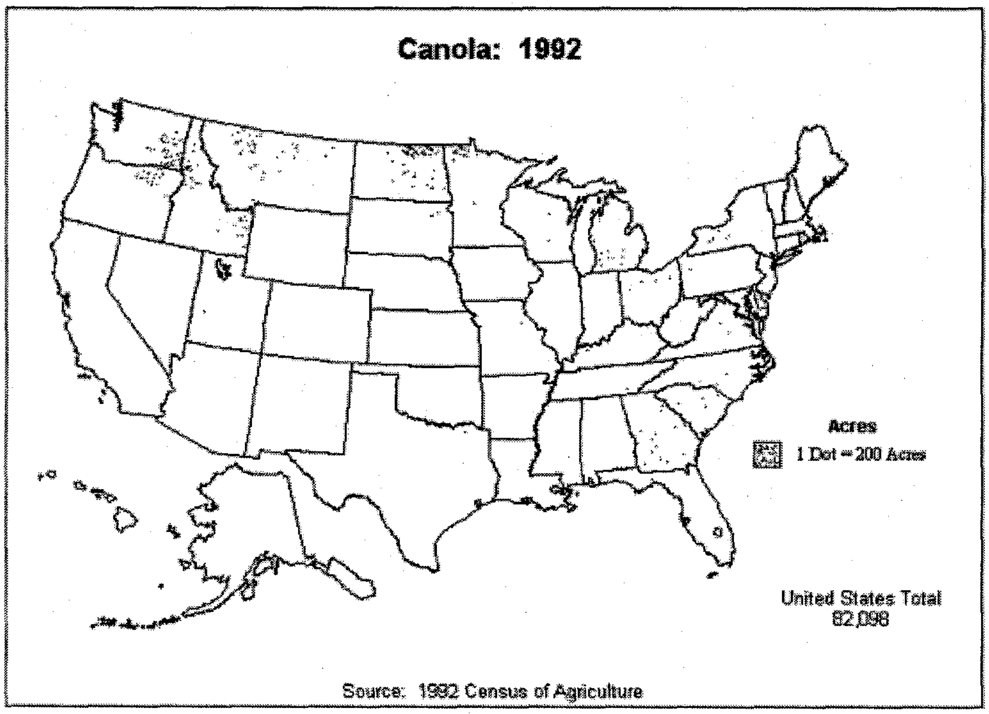

Figure 2. Canola acreage in the USA

Bees find canola blossoms very attractive and will travel several kilometers to forage for nectar and pollen in these fields. Canola pollen generally achieves high levels of protein (22 - 27%) and is readily used as immediate nourishment and/or stored in the hive. However, EFED has a concern for the possibility of extended clothianidin residual activity from pollen, as well as nectar, after these products are introduced into the hive. Studies have verified that pollination by honey bees is essential for a high production of hybrid canola seed. Honey bee pollination can be considered an essential agricultural component for maximum canola production.

b. Key Fate and Transport Conclusions

Clothianidin is highly persistent under most environmental conditions [aerobic soil half-lives were 148 to 1,155 days (10 soils) and field dissipation half-lives were 277 days to several years (5 sites)]. In the laboratory clothianidin undergoes very rapid photolysis in clear irradiated water (e.g.,, the measured aqueous photolysis half-life was <1 day), but the very slow rate of dissipation that was observed in field studies suggests that this route of degradation/dissipation may not be significant under most actual-use conditions. Degradation is also relatively rapid under anaerobic aquatic conditions (overall half-life of 27 days). Clothianidin is stable to hydrolysis at environmental pHs and temperatures. Clothianidin is mobile to highly mobile but only limited leaching has been confirmed in the available field studies; dedicated studies to investigate its leaching potential like the prospective ground-water monitoring study type have not been conducted. Volatilization is not expected to be a significant dissipation process. The drinking water and surface water exposure assessment herein is based on modeling results. The assumption of this Tier I Screening Level exposure assessment is that 100% of the applied chemical is expected to be available for runoff. Further refinement is possible with appropriate data from a seed leaching study that can help determine the actual percentage of chemical available for runoff.

c. Endangered Species

Clothianidin is expected to present acute/chronic toxicity risk to endangered/threatened birds and mammals via possible ingestion of treated corn and canola seeds. Endangered/ threatened pollinating invertebrates may be impacted via residue laden pollen and nectar. The potential use sites cover the entire USA because corn and canola are grown in the following states: AL, AZ, AR, CA, CO, CT, DE, FL, GA, ID, IL, IN, IS, KS, KY, LA, ME, MD, MA, MI, MN, MS, MO, MT, NE, NH, NJ, MN, NJ, NY, NC, ND, OH, OK, OR, PA, RI, SC, SD, TN, TX, UT, VT, VA, WA, WV, WI, WY. The registrant must provide information on the proximity of Federally listed birds, mammals, and invertebrates to the proposed use sites. This information may best be provided via the FIFRA Endangered Species Task Force (Pesticide Registration [PR] Notice 2000-2) 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 OPP's Field and External Affairs Division (FEAD) and EFED through the Endangered Species Protection Program to develop recommendations to avoid adverse effects to listed species.

d. Endocrine Disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disrupter Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific basis for including, as part of the program, the androgen- and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disrupter Screening Program (EDSP).

When the appropriate screening and or testing protocols being considered under the Agency's Endocrine Disrupter Screening Program have been developed, clothianidin may be subjected to additional screening and or testing to better characterize effects related to endocrine disruption. Issues that have raised this concern include systemic, reproductive, and developmental effects in birds and mammals. These effects have been documented as egg shell thinning in birds and in mammals, delayed sexual maturation (males only); decreased absolute thymus weight in F1 pups (both sexes), and increased stillbirths (F1 and F2 litters), decreased sperm motility and increased number of sperm with detached heads, premature deliveries, decreased gravid uterine weights, and increased litter incidence of missing lung lobe in the fetus. EFED recommends that when current testing protocols being considered under the Agency's Endocrine Disrupter Screening Program (EDSP) have been validated, clothianidin may be subjected to more definitive testing to better characterize endocrine disrupter effects.

IV. Environmental Fate and Transport Assessment

a. Summary

Clothianidin appears to be a persistent compound under most field conditions. Based on analysis of the laboratory studies alone, the major route of dissipation for clothianidin would appear to be photolysis if exposure to sunlight occurs (e.g.,, the measured aqueous photolysis half-life was <1 day and aerobic half-lives were 148 to 1155 days) . Although photolysis appears to be much more rapid than other avenues of degradation/ dissipation of clothianidin in the laboratory studies, the very slow rate of dissipation that was observed in field studies suggests that photolysis probably is not significant under most actual-use conditions. Photolysis may be quite important in surface waters if residues have reached clear bodies of water and are in solution rather than bound to sediment. Degradation is also relatively rapid under anaerobic aquatic conditions (overall half-life of 27 days). Clothianidin is stable to hydrolysis at environmental pHs and temperatures, and metabolic degradation occurs very slowly in aerobic soil. Clothianidin is mobile to highly mobile in the laboratory [Soil organic carbon partition coefficients (Koc) values were 84 to 129 for all test soils except for a sandy loam soil which had a Koc value of 345], although only a modest amount of leaching was observed in the submitted field studies. Previous studies have confirmed that compounds with a similar combination of mobility and persistence characteristics have a potential to leach to ground water at some use sites. Volatilization is not expected to be a significant dissipation process.

b. Degradation and Metabolism

Metabolism in aerobic soil occurred very slowly. At 20°C, clothianidin degraded in two soils with a first-order half-life of 148 and 239 days (Hofchen and Laacher soil series), in seven soils ranging in texture from sand to silt loam with half-lives of 495 to 1,155 days (BBA 2.2, Quincy, Sparta, Crosby, Susan, Elder, and Howe soil series), and in a tenth soil with a half-life that was nominally calculated to be 6,931 days (Fugay soil series). Degradation was too little in the Fugay soil study to accurately calculate the degradation rate over the 1-year study period (r2 = .05).

Under anaerobic aquatic conditions, metabolic degradation occurred relatively quickly (half-life of 14 days in water; 37 days in sediment; 27 days overall). Clothianidin was <1% of the applied in the water at and after 120 days and was <2.0% in the silt loam sediment at and after 183 days. No major degradates were isolated; clothianidin was converted primarily to soil-bound residues.

Clothianidin photodegraded with half-lives of <1 day in sterile buffer solution in the laboratory and in natural water outdoors, and approximately 34 days in soil in the laboratory. The range of values (1 - 34 days) given for surface water-source drinking water represents uncertainty with regard to the importance of photodegradation in the long-term fate of clothianid in natural waters. In the laboratory, clothianidin photodegraded in sterile aqueous pH 7 buffer solutions with a half-life of 6.2-6.8 hours, based on a 12-hour light/12-hour dark cycle. Major degradates were *N*-(2-clorothiazol-5-ylmethyl)-*N*'-methylurea (TMZU), methylurea (MU), methylguanidine

(MG), 4-hydroxy-2-methylamino-2-imidazolin-5-one (HMIO), 7-methylamino-4H-imidazo[5,1-b][1,2,5]thiadiazin-4-one (MIT), formamide (FA), and CO_2. Outdoors, clothianidin degraded in nonsterile river water with a half-life of 25.1-27.7 hours under a cycle of approximately 9 hours sunlight/15 hours darkness. Major transformation products were MG, HMIO, MU, Urea, TMG, 3-methylamino-1*H*-imidazo [1,5-*c*]imidazole (MAI), 2-chlorothiazol-5-ylmethanol (CTCA), and CO_2. There was no degradation in the control samples held in the dark, which is consistent with clothianidin's observed stability to hydrolysis.

On moist soil, clothianidin photodegraded with a half-life of 8.2 days based on continuous irradiation (estimated to be equivalent to 34.2 solar summer days in Phoenix, AZ); degradation was not significant in the dark. At study termination (equivalent to 71 days solar summer days in Phoenix, AZ), 22.3% of the clothianidin remained undegraded. No degradates accumulated to significant levels during the study.

c. Soil sorption and mobility

In laboratory batch equilibrium studies, clothianidin had medium mobility in a US sandy loam soil and high mobility in US loamy sand and clay loam and German sand and sandy loam soils. In batch equilibrium studies using the same soils and similar conditions, MNG was very highly mobile, TZMU was highly to very highly mobile, TZNG was moderately mobile, and TMG was immobile or had low mobility. The mobility of clothianidin appeared to decrease as the length of time clothianidin was in contact with the soil increased; the longer clothianidin was aged in treated soil, the less likely it was to desorb from that soil.

d. Field dissipation

Clothianidin is expected to dissipate very slowly under terrestrial field conditions, based on the results of five bare ground field experiments conducted in the US and Canada. Half-lives of clothianidin, based on residues in the 0-15 cm soil depth, were 277 days (Wisconsin sand soil, incorporated), 315 days (Ohio silt loam soil, not incorporated), 365 days (Ontario silt loam soil, incorporated), and 1,386 days (North Dakota clay loam soil, not incorporated), and could not be determined at a fifth site due to limited dissipation during the 25-month study (Saskatchewan silty clay loam soil, incorporated). Incorporation did not appear to be a significant factor in determining the rate of dissipation. Clothianidin was generally not detected below the 45 cm soil depth except at one site, where it moved into the 45-60 cm depth. No degradates were detected at >10% of the applied, and degradates were generally only detected in the 0-15 cm soil layer. However, in many cases most of the parent remained untransformed at the close of the study; further accumulation of degradates could have occurred. Degradates that were increasing in concentration or at least continuing to persist towards the close of one or more field dissipation studies were: MNG (MRID 45422336) TZNG (MRID 45422335, 45422333), and TZMU (MRID 45422335).

Two studies were conducted to investigate leaching of clothianidin under field conditions (MRIDS 45422331 and 45422508). These studies were conducted in the Federal Republic of

Germany and were apparently designed to fulfill certain European regulatory requirements. In these monolith lysimeter studies, 42-59% of the applied remained in the soil approximately 3 to 4 years following the first of two applications, and residues were primarily undegraded clothianidin. The loss of radioactivity was attributed by the authors to mineralization of clothianidin, since ≤1% of the total residues were detected in the leachate. Clothianidin was not detected in the leachate. There was also a significant amount of TZNG and/ or MNG that remained in monolith lysimeters at the close of multi-year studies. In one study (MRID 45422331), analysis of the soil in the lysimeter three years after the original application of clothianidin revealed TZNG was present as about 5% of the applied clothianidin. When the soil was analyzed more than 4 years after application in another lysimeter study (MRID 45422508) about 3% of the applied was present as MNG and 2% was present as TZNG. The substantial amount of clothianidin parent remaining in the soil profile at the close of these studies indicates that further leaching of clothianidin may occur in following years if sufficient precipitation occurs.

V. Water Resources Summary (Drinking Water Assessment)

The registrant has not conducted any monitoring studies to support the registration of clothianidin and clothianidin has no previous registrations in the United States, hence no monitoring data are available from other sources. Consequently, the drinking water and surface water exposure assessment herein is only based on modeling results. The assumption of this Tier I Screening Level exposure assessment is that 100% of the applied chemical is expected to be available for runoff. Further refinement is possible with appropriate data from a seed leaching study. The range of values (1.1 - 34 days) given for surface water-source drinking water represents uncertainty with regard to the importance of photodegradation in the long-term fate of clothianid in natural waters. However, after running the GENEEC model using both values, EFED found that there was no significant difference in the final risk assessment RQ calculations.

a. Surface Water Monitoring and Modeling

The FIRST model (version 2) was used to estimate concentrations that might occur in vulnerable surface waters (Tables 3 and 5). FIRST is a screening model designed by EPA-OPP's Environmental Fate and Effects Division (EFED) to estimate the concentrations found in vulnerable drinking water sources (a reservoir adjacent to fields treated with the pesticide in question. Estimated Tier I concentrations of clothianidin in vulnerable drinking water were 3.97 ug/L for acute exposure and up to 2.14 ug/L for chronic exposure.

Table 3. Environmental Fate model input values used with FIRST. Use of clothianidin as a seed treatment

Using model version dated 08/05/01 and input selection guidance dated 02/28/02.			
Input	**Value**	**Source**	**Comments**
Run #	1 (corn) 2 (canola)	Reviewer's choice	

Input	Value	Source	Comments
Output File name	FIRST_CLOTHI2.TXT	Reviewer's choice	
Chemical name	Clothianidin	NA	Also known as TI-435.
Crop name	Corn	Proposed label	Seed treatment
	Canola		
Application rate (lb ai/acre)	0.1	Proposed label treatment rate of 1.25 mg ai/ corn seed	Based on seeding density of 90,000 seeds per hectare (MRID 45422423 - field toxicity effects on birds) - converts to 36,400 seeds per acre
	0.05	Proposed label maximum treatment rate of 0.6 kg ai/ 100 kg canola seed	Based on seeding rate of approximately 8 kg seed per hectare (MRID 45422424 - field toxicity effects on birds)
% Crop Treated	47 (Corn)	Input guidance	Estimated maximum percentage of watershed likely to be planted to corn.
	87 (Canola)	Input guidance	Default value based on maximum percent of watershed likely to be in agricultural production.
Soil aerobic metabolic half-life (days)	744	MRIDs 45422325 & 45422326	Calculated per guidance for n = 9. Fugay soil not included in calculation because too little degradation occurred to accurately calculate half-life.
Pesticide wetted in	No	NA	Not applicable to seed treatment
Method of application	Granular	NA	Seed treatment use is treated as granular for purposes of FIRST.
Incorporation depth (inches)	2	corn	Based on planting depth of 4-5 cm (MRID 45422423 - field toxicity effects on birds)
	0.5	canola	Based on planting depth of 1 cm (MRID 45422519 - laboratory toxicity effects on spiders)
Solubility (ppm)	300	MRID 45422317	Solubility stated as 300 mg/L
Aquatic metabolic half-life (days)	1488	MRID 45422324	2x aerobic soil half-life used since there was no acceptable aerobic aquatic study

Input	Value	Source	Comments
Aquatic photolysis half-life (days)	1.10 to 34[1]	MRID 45422323 (soil); 45422318, 45422320, & 45422322, 45422319, 45422321 (water)	Longest half-life of 34 days used instead of aqueous photolysis half-life because of demonstrated persistence in water and on soil surface exposed to sunlight. Lower value of 1.1 days used from natural water photolysis study. [2]

[1] The range of values given for surface water-source drinking water represents uncertainty with regard to the importance of photodegradation in the long-term fate of clothianidin in natural waters. Additional data may be needed from the registrant to resolve these uncertainties. [2] Refer to Appendix E.

b. Ground Water Monitoring and Modeling

Estimated acute and chronic exposure to clothianidin from vulnerable drinking water is **1.46** ug/L using the Tier I model SCI-GROW (Table 5); modeling input values are provided in Table 4. SCI-GROW provides an estimate of concentrations of pesticide likely to occur in highly vulnerable ground water (10 - 30 feet depth and overlain by sandy soils) under conditions that are likely to promote ground-water recharge.

While no ground-water monitoring studies have been conducted, the registrant did submit monolith lysimeter study results (discussed previously in the environmental fate section). In both studies (MRIDs 45422508 and 45422331) there was no parent clothianidin detected in the leachate. The degradates were detected in small quantities in the leachate. In one study MNG and NTG were detected in the leachate samples; in the other study none of the degradates in the leachate were identified. Clothianidin was extremely persistent and still potentially available for leaching at the close of the lysimeter studies (3 or 4 years after the first application), in both studies 42-59% of the applied radioactivity remained in the soil approximately 3 to 4 years following the first of two applications, and residues were primarily undegraded clothianidin. These results highlight the potential for very high persistence of clothianidin and some degradates and the possibility of leaching to ground water occurring even in soils of fairly low permeability several years after application of clothianidin.

Table 4. Environmental fate input parameters for clothianidin in SCI-GROW

Using model version dated 08/01/01 and input selection guidance dated 02/28/02		
Parameter	**Clothianidin**	**Source**
Application Rate (lbs ai.A)	0.1	Proposed label treatment rate of 1.25 mg ai /corn seed
Organic Carbon Partition Coefficient (Koc)	84	MRID 45422311. Minimum value calculated per guidance for pesticides with widely varying Kocs.

Parameter	Clothianidin	Source
Application Rate (lbs ai.A)	0.1	Proposed label treatment rate of 1.25 mg ai /corn seed
Aerobic Soil Metabolism Half-Life (days)	533	MRID 45422325 & 45422326. Median value calculated per guidance for pesticides with aerobic metabolism studies in more than 4 soils.

Table 5. Estimated Tier 1 concentrations of clothianidin in drinking water.

Chemical	Surface Water (ug/L)		Groundwater (ug/L)
	Acute	Chronic	Acute and Chronic
Clothianidin	**3.97**	**0.188 to 2.14**	**1.46**

c. Degradates in drinking water

The current exposure assessment is based solely upon the parent compound. Our understanding of the potential exposure to degradates of clothianidin in drinking water is constrained by the high persistence of clothianidin parent and the concomitant lack of significant accumulation of any specific products in most of the laboratory and field studies. Major degradates detected in one or more of the aqueous photolysis studies which might or might not be important under some actual use conditions are TZMU, TMG, MU, and MG (however, these studies were of very short duration and these degradates did not accumulate in the longer 17-day soil photolysis studies). TZMU was shown to be an important hydrolysis product in pH 9 solution at elevated temperature (No significant hydrolysis was observed at any pH at 25 C). Little degradation of parent occurred in each of the 10 soils used for aerobic metabolism investigation (54 to 95% of the parent compound remaining in the soil at the close of these studies) but there was still some evidence of accumulation of TZNG, MNG, and NTG in some of the test soils. TMG accumulated significantly in the aerobic aquatic studies (which were not strictly aerobic in the sediment where the TMG was found). In the anaerobic aquatic study, no degradate was found to accumulate significantly. In soil adsorption - desorption studies MNG and TZMU were shown to be extremely mobile in soil and could, if they form and persist in soil, be significant ground-water contaminants. All four of the degradates for which soil sorption was investigated (MNG, TZMU, TZNG, and TMG) could occur in runoff water if they form in significant amounts. No soil sorption studies were conducted for NTG. We conclude that degradates such as MNG, TZMU, TZNG, TMG, and NTG might potentially contaminate drinking water; however, because of the very long persistence of parent clothianidin (and relatively high soil mobility and low adsorption to soil and sediment) including the degradates in exposure modeling would not likely significantly increase the total exposure level estimates.

VI. Aquatic Exposure and Risk Assessment

a. Aquatic (Acute/Chronic Hazard Summary)

Clothianidin and its degradates (TMG, MNG, and TZNG) were shown to be practically non-toxic to freshwater fish (LC_{50} = 105 - 117 ppm), while clothianidin was shown to be slightly toxic to estuarine/marine fish (LC_{50} = 93.6 ppm) on an acute toxicity basis. Although chronic values were not determined for estuarine/marine fish, freshwater early life stage values (NOAEC/LOAEC) were shown to be 9.7/20 ppm, respectively, with significant reductions occurring in fish growth (length and dry weight). Clothianidin's acute toxicity values for aquatic invertebrates suggest that this compound ranges from very high toxicity to freshwater chironomids (EC_{50} = 0.022 ppm) to practically non-toxic to daphnids (EC_{50} = 100.8 - 119 ppm). Acute toxicity values for estuarine/marine invertebrates suggest that clothianidin is practically non-toxic to mollusks (EC_{50} = 129.1 ppm), yet very highly toxic to mysid species (LC_{50} = 0.051 ppm). Chronic exposure to aquatic invertebrates (mysid shrimp and *Daphnia*) showed significant reduction in the number of young/reproductive day (mysid: NOAEC/LOAEC = 0.0051/0.0097 ppm; Daphnia: NOAEC/LOAEC = 0.042/0.12 ppm).

b. Exposure (Surface and Ground Water Summary)

The GENEEC model (version 2) was used to estimate concentrations that might occur in vulnerable surface water (Appendix E; model inputs are provided in Table E-1). Ground water modeling with SCI-GROW is discussed in the "Water Resources Summary" section of this document. Tier 1 Screening Level exposure estimates (single seed planting) with GENEEC were 2.44 ppb (peak) and 2.11 to 2.37 ppb (chronic). This screening level assumes that 100% of the chemical on the seed is available for runoff.

EFED concludes that the available data on clothianidin shows that the compound is sufficiently mobile and persistent to contaminate surface and ground waters; the exposure modeling confirms this. Clothianidin is a persistent compound under most field conditions: Aerobic soil metabolism half-lives were 148 to 1155 days and field dissipation half-lives were 277 days to several years (at one of the five sites there was so little decline in clothianidin residues over 25 months that a dissipation half-life could not be calculated). Although photolysis appears to be much more rapid than other avenues of degradation/dissipation of clothianidin in the laboratory studies, the very slow rate of dissipation that was observed in field studies suggests that photolysis probably is not significant under most actual-use conditions. The range of values (1.1 - 34 days) given for surface water-source drinking water represents uncertainty with regard to the importance of photodegradation in the long-term fate of clothianid in natural waters. However, after running the GENEEC model using both values, EFED found that there was no significant difference in the final risk assessment RQ calculations. Degradation is also relatively rapid under anaerobic aquatic conditions (overall half-life of 27 days). Clothianidin is mobile to highly mobile in the laboratory [Soil organic carbon partition coefficients (Koc) values were 84 to 129 for all test soils except for a sandy loam soil which had a Koc value of 345]. Clothianidin is stable to hydrolysis and very water soluble (300 ppm). Previous studies have confirmed that compounds with a similar combination of mobility and persistence characteristics have a potential to leach to ground water at some use sites.

c. Ground-Water Monitoring and Modeling

Clothianidin has a high potential to contaminate ground water as discussed in the Water Resources Summary section of this document. The expected concentration in vulnerable ground water is 0.91 ug/L (results of modeling with SCI-GROW). The persistence of clothianidin is so high that there is a potential for clothianidin to accumulate in ground-water over many years of usage and there may be a long-term potential for adverse effects on organisms exposed to ground-water contributing to stream base flow, contaminated irrigation water, etc.

d. Risk to Aquatic Organisms (Acute/Chronic)

Tables 6 and 7 provide acute and chronic RQ values for clothianidin exposure to freshwater and estuarine/marine species relative to corn and canola use patterns. Our Tier I (GENEEC 2) risk assessment suggests that runoff exposure of this compound to fish (freshwater and estuarine/marine) through the proposed use patterns should not result in acute (RQ = 0.0) or chronic risk (RQ = 0.0). However, the same use patterns can result in acute risk (RQ = 0.1) to aquatic freshwater invertebrates, but not to estuarine/marine organisms (RQ = 0.0). Exposure from this scenario should not present a chronic concern for either freshwater or estuarine/marine organisms (RQ = 0.0 - 0.4). The GENEEC input parameters and output tables are provided as a separate attachment to this document (see Appendix D).

Clothianidin is very persistent in aerobic soil (aerobic soil metabolic half life = 744 days), and is subject to runoff. Relative to the use as seed treatment, soil runoff is the most likely mode by which clothianidin will reach aquatic environments. Laboratory studies have shown that clothianidin has medium to very high mobility in soils which increases its potential for leaching. Therefore, the combination of this high potential for runoff, as well as high mobility of clothianidin can increase the likelihood of exposure to aquatic systems. Once clothianidin reaches water, the compound appears stable to hydrolysis (pH 7) and does not degrade rapidly via anaerobic aquatic metabolism (half-lives of 14 days in the water phase, 37 days in the sediment phase, and 27 days overall in an anaerobic water:silt loam sediment (3:1, v:w) system at 20°C).

Because the clothianidin toxicity threshold is low for aquatic freshwater invertebrates on an acute basis, their vulnerability represents possible acute risk from sediment exposure[1]. As a dynamic trophic level, invertebrates add to the diversity of an aquatic system. Bioenergetics (the efficient utilization of resources) and the stability and maintenance of higher orders such as fish are dependent upon a stable and diverse invertebrate population. Since clothianidin is persistent in

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[1]Although clothianidin does not appear to be particularly strongly adsorbed to most soils / sediments, the degree of adsorption is variable (note that the K_{oc} was 345 in one test soil - Elder sandy loam, K^d = 4.14, MRID 45422311) and the registrant has previously contended in the prospective ground-water monitoring studies for a similar compound they have previously registered (imidacloprid), that the effective adsorption coefficient can increase significantly over time.

the sediment, sediment toxicity testing will be needed to address the uncertainty of possible risk to the large communities of invertebrates and fish that inhabit or come into contact with the sediment.

Table 6. Acute and chronic RQ's for evaluating toxic risk of clothianidin exposure to fish (freshwater and estuarine/marine). RQ's are based on the rainbow trout (*Oncorhynchus mykiss*) LC_{50} = 105.8 ppm, fathead minnow (*Pimephales promelas*) NOAEC = 9.7 ppm and sheepshead minnow (*Cyprinodon variegatus*) LC_{50} = >93.6.ppm. EEC values are generated from GENEEC.

Crop App. Rate (lbs ai/A; # App.)	Organism	LC_{50} (ppm)	NOAEC (ppm)	EEC Peak (ppm)	EEC 60-Day Ave. (ppm)	Acute RQ[1] (EEC/LC_{50})	Chronic RQ[2] (EEC/NOAEC)
Corn 0.1 (1)	Freshwater	105.8	9.7	0.002	0.002	**0**	**0**
	Estuarine/ Marine	93.6	ND	0.002	0.002	**0**	
Canola 0.05 (1)	Freshwater	105.8	9.7	0.002	0.002	**0**	**0**
	Estuarine/ Marine	93.6	ND	0.002	0.002	**0**	

[1] Acute restricted use (≥ 0.1)
[2] Chronic concern (≥ 1.0)
[3] Max 60 days average

Table 7. Acute and chronic risk RQ's for evaluating toxic risk of clothianidin exposure to aquatic invertebrates (freshwater and estuarine / marine). RQ's are based on midge (*Chironomus riparius*) EC_{50} = 0.022 ppm, waterflea (*Daphnia magna*) NOAEC = 0.042 ppm and the mysid shrimp (*Mysidopsis bahia*) LC_{50} = 0.051 ppm, NOAEC = 0.0051 ppm. EEC values are generated from GENEEC.

Crop App. Rate (lbs ai/A) # App. (days)	Organism	EC_{50} (ppm)	NOAEC (ppm)	EEC Peak (ppm)	EEC 21-Day Ave. (ppm)	Acute RQ[1] (EEC/ LC_{50})	Chronic RQ[2] (EEC/NOAEC)
Corn 0.1 (1)	Freshwater	0.022	0.042	0.002	0.0023	**0.1**	0
	Estuarine/ Marine	0.051	0.0051	0.002	0.0023	0	0.4
Canola 0.05 (1)	Freshwater	0.022	0.042	0.002	0.0023	**0.1**	0
	Estuarine/ Marine	0.051	0.0051	0.002	0.0023	0	0.4

[1] Acute restricted use (≥ 0.1)
[2] Chronic concern (≥ 1.0)

VII. Terrestrial Exposure and Risk

a. Terrestrial Hazard Summary

The available toxicity data are listed in Appendix B. Clothianidin appears to be moderate to slightly toxic to avian species on a subacute oral basis (Japanese quail LD_{50} = 423 mg/kg; mallard duck LD_{50} = 2,000 ppm) and practically non-toxic to avian species on a dietary basis (mallard duck LC_{50} > 5,040 ppm; Bobwhite quail LC_{50} > 5,230 ppm). However, chronic testing showed reductions in eggshell thickness for Bobwhite quail (NOAEC = 205 ppm).

Mammalian toxicity data suggest that clothianidin is practically non-toxic to small mammals on an acute oral basis (mouse LD_{50} = 389 - 465 mg/kg/day). However, systemic effects were noted during the rat reproductive test for F1 and F2 offspring. These effects included decreased body weight gains and delayed sexual maturation (males only); decreased absolute thymus weight in F1 pups (both sexes), and increased stillbirths (F1 and F2 litters). Reproductive effects were noted for adult rats at 2500 ppm and included decreased sperm motility and increased number of sperm with detached heads. Developmental effects also occurred in rabbits at 75 mg/kg/day.

Acute toxicity studies to honey bees show that clothianidin has the potential to be highly toxic on both a contact and an oral basis (contact LD_{50} = 0.044 ug/bee; oral LD_{50} = 0.0037 ug/bee), while its degradates (e.g.,, TMG, MNG, TZMU, and TZNG) are moderately to practically non-toxic on an oral basis (LD_{50} = 3.9 - >153 ug/bee). One honey bee field study (MRID # 45422435) showed that mortality, pollen foraging activity, and honey yield were negatively affected by residues of clothianidin; however, residues were not quantified in this study.

Subchronic invertebrate toxicity studies showed that clothianidin adversely affected earthworm mortality and body weight (LC_{50} = 15.5 ppm) and its degradates reduced body weight (LC_{50} = 982.6 ppm). There were no apparent effects of clothianidin on earthworm reproduction or population dynamics.

b. Risk to Avian and Mammalian Species (Acute/Chronic)

Tables 8, 9, 10, and 11 provide acute and chronic risk quotient (RQ) values for avian and mammalian consumption of clothianidin-treated seed. EFED's risk assessment suggests that there is a potential for acute toxic risk to non-endangered and endangered medium-sized songbirds (0.178 kg), as well as non-endangered and endangered mammalian species. Our calculations also show that exposure of avian and mammals to clothianidin-treated seeds could result in chronic risk (birds RQ = 16.1; mammal, RQ = 44 - 61). Chronic effects to birds include eggshell thinning. Chronic effects to mammals have been found to include developmental effects in rabbits (premature deliveries, decreased gravid uterine weights, and increased incidence of lung deformities in fetuses), reproductive effects in rats (decreased sperm mobility and an increase number of sperm with detached heads in F_1 and F_2 litters), and effects to F_1 and F_2 rat offspring (decreased body weight and delayed sexual maturation, as well as an increase in still births).

A major concern with this seed treatment use pattern is that birds and mammals may be exposed to clothianidin through the ingestion of treated seeds when foraging in the treated fields for food or grit even though soil incorporation may reduce overall species risk and/or access to the compound. The risk to birds is also based on an acute exposure scenario that estimates the quantity of seeds that an animal could ingest in one day if the animal eats only clothianidin-treated seeds. This approach defines a risk quotient (RQ) as

$$RQ = Dose/LD_{50}$$

where Dose = the amount of clothianidin that an animal could receive by ingesting treated seeds in a 24-hour period per animal body mass (dose units in mg/kg). Acute high risk is assumed to occur with regard to RQ values $\geq$ 0.5, acute restricted use category for values $\geq$ 0.2, and acute endangered species concerns at $\geq$ 0.1.

The dose that an animal could receive by eating treated seeds can be approximated from the estimated amount of food that is consumed in a day. The dose can be described as

$$Dose = (FI)(C)(T)/M_{bird}$$

where FI = the food ingestion rate [kg/day]
C = active ingredient concentration on seed (mg/kg)
T = relevant duration time for food consumption (assumed to be 1 day in this assessment)
M_{bird} = mass (wet) of bird [kg].

The rate of food consumption (FI) for a bird can be estimated by the method of Nagy (1987)[1]. For passerines, the Nagy relationship is $FI = 0.141 (M_{bird})^{0.850}$; for non-passerines the relationship is $FI = 0.054 (M_{bird})^{0.751}$; for mammals the relationship is $FI = 0.0687 (M_{mammals})^{0.822}$.

[1]Nagy, K.A. (1987). Field metabolic rate and food requirement scaling in mammals and birds. *Ecol. Monogr.* 57:111-128.

Table 8. Acute RQ calculations for birds consumption of clothianidin treated seeds (corn and canola)

Crop	Clothianidin Seed Concentration		Dose[1] (mg ai consumed /day /kg bird)	RQ = Dose/LD_{50}
	lb ai/kg seed	mg ai/kg seed	Quail[2] ([3]FI = 0.0148 kg/day)	Japanese Quail[4] (LD_{50} = 423 mg/kg)
Corn	0.0073	3300	274	**0.6**
Canola	0.01	4545	378	**0.9**

[1]Dose = (food intake)(clothianidin seed concentration)(1 day)/weight of bird ;
[2]Quail wt = 0.178 kg
[3]Food intake rate (FI) based on Nagy equation.
[4] Most sensitive avian species.

The risk quotients in Table 8 show that there is the potential for acute high risk to non-endangered and endangered medium-size birds (0.178 kg) for both crop scenarios (canola-treated seeds RQ = 0.9; corn treated seeds RQ = 0.6). However, additional calculations on estimating the number of seeds that will kill a bird (acute effect) suggest that the potential for acute risk to seed eating birds is low. The following calculation was used (Appendix C):

$$\text{Seeds/bird} = \frac{(LD_{50}\ \text{mg/kg})\ (\text{bird wt kg})}{(\text{mg ai/seed})}$$

Table 9. The number of clothianidin treated corn and canola seeds that would result in toxic risk to birds (acute effect).

Crop	mg ai/seed	Seeds/bird[1]
Corn	1.25	**285**
Canola	0.017	**20,941**

[1] Refer to Appendix C.

The likelihood of exclusively consuming such large numbers of seeds (corn at 285 seeds; canola at 20,941seeds) combined with the farming practice of drilling the seeds at planting, suggest the potential for acute toxic risk to birds but EFED concludes that the actual acute risk to these animals should be low because of minimal exposure.

In order to determine the chronic risk to birds from seed consumption, RQ values were calculated as follows: RQ = Concentration on Seeds/ NOAEC. RQ values (Table 10) for corn and canola (RQ = 16.1 and 22.2, respectively) suggest that seed consumption may present the potential for chronic risk. Combined with this potential for chronic risk, there is uncertainty regarding the critical point in the reproductive cycle where sublethal exposure may occur that might influence reproductive parameters (e.g., consumption of seed at the beginning of gestation may effect embryo development). Since the seeds are to be planted in the spring or early summer, chronic risk to birds is enhanced because of the corresponding breeding seasons.

Table 10. Chronic RQ calculations for birds consumption of clothianidin treated seeds (corn and canola)

Crop	Clothianidin Seed Concentration		RQ = Seed Concen./NOAEC
	lb ai/kg	mg ai/kg	Quail (0.178 kg) (NOAEC = 525 mg/kg)
Corn	0.0073	3300	**6.3**
Canola	0.01	4545	**8.6**

Calculations on the number of seeds that may result in toxic chronic risk to birds are noted in Table 11. Non passerines (e.g., Bobwhite quail) would require about 75 corn seeds and 5,497 canola seeds in order to trigger chronic toxicity, while passerines would need about 8 - 42 corn seed and 617 - 3,088 canola seeds. Assuming that 1% of drilled seed is unincorporated (170 - 330 corn seeds; 1,510 - 2,270 canola seed)[1] the likelihood of the non passerine birds consuming enough seed to result in chronic effects does not appear likely. However, passerine birds (e.g., sparrows, wrens, songbirds) require a fewer number of seed to reach a chronic threshold and could be at risk. Although there are uncertainties surrounding the amount of foraging that would consist of treated seed, as well as toxicokinetics considerations, EFED's weight of evidence suggest that chronic risk to passerine birds is a possibility from the ingestion of clothianidin treated seeds.

Table 11. The number of clothianidin treated corn and canola seeds that would result in possible risk to birds (chronic effect).

Crop	mg ai/seed	Seeds/bird (passerines 0.020 - 0.1 kg)	Seeds/bird[1] (non passerine Bobwhite quail 0.178 kg)
Corn	1.25	**8 - 42**	**75**
Canola	0.017	**617 - 3,088**	**5,497**

[1] Refer to Appendix C.

Acute risk quotients were calculated for mammals as noted in Table 12. Consumption of treated corn seed has the potential for acute toxic risk to small (0.015 kg), medium (0.035 kg), and large (1 kg) mammals. Although our calculations suggest that canola seed consumption can result in acute risk to mammals, the seeds are too small for consumption by animals > 0.015 kg. However, canola treated seeds could account for acute toxic risk to mammals in the 0.015 kg range.

[1]Murray Hartman, Alberta Agriculture Food and Rural Development, Lacombe, Alberta, Canada

Table 12. Acute RQ calculations for mammalian consumption of clothianidin treated seeds (corn and canola)

Crop	Clothianidin Seed Concentration lb ai/kg seed mg ai/kg seed	Dose (mg/kg)[1] (mg ai consumed /day /kg mammal)			$RQ = Dose/LD_{50}$		
		0.015 kg ([2]FI = 0.0022 kg/day)	0.035 kg (FI = 0.0044 kg/day)	1kg (FI = 0.069 kg/day)	0.015 kg	0.035 kg	1kg
					([3]LD_{50} =389 mg/kg/day)		
Corn	0.0073 3300	484	415	228	**1.2**	**1.1**	**0.6**
Canola	0.01 4545	667	571	314	**1.7**	**1.5**	**0.8**

[1] Dose = (food intake)(clothianidin seed concentration)(1 day)/weight of mammal
[2]Food intake rate (FI) based on Nagy equation.
[3] Mouse LD_{50}

Chronic RQ values for mammals were calculated using the following equation: RQ = Concentration on Seeds / NOAEC. The developmental effects on rabbits (NOAEC/LOAEC = 25/75 mg/kg/day) was used as a worst case for all mammals. Risk Quotients for corn and canola (44 and 66, respectively; Table 13) show that mammalian consumption of treated seeds can potentially result in chronic risk. As noted with the possible chronic risk to birds, there is an uncertainty regarding the toxicokinetics (absorption, distribution, biotransformation, and excretion) of this compound in the whole organism.

Table 13. Chronic RQ calculations for mammalian consumption of clothianidin treated seeds (corn and canola)

Crop	Clothianidin Seed Concentration		RQ = Seed Concen./NOAEC
	lb ai/kg seed	mg ai/kg seed	Rabbit (NOAEC = 25 mg/kg/day)
Corn	0.0073	3300	**44**
Canola	0.01	4545	**61**

Calculations on the number of seeds that may result in toxic chronic risk to mammals are noted in Table 14. Mammals in the 0.015 - 0.035 kg range appear to be at greater acute and chronic risk that those in the 1.0 kg range. The number of seeds (corn) necessary for and acute effect on small and medium size mammals is about 4.7 - 10. The number that may cause a chronic effect is about 2 seeds.

Table 14. The number of clothianidin treated corn and canola seeds that would result in possible risk to mammals (acute and chronic effect).

Crop	mg ai/seed	Acute #Seeds/mammal (0.015 - 0.035 kg)	Chronic #Seeds/mammal (0.015 - 0.035 kg)	Chronic #Seeds/mammal[1] (1.0 kg)
Corn	1.25	**4.7 - 10**	**0.9 - 2.1**	**60**
Canola	0.017	**343 - 800**	**66 - 154**	**4,412**

[1] Refer to Appendix C.

c. Risk to Nontarget Insects and Terrestrial Invertebrates

Currently, EFED does not assess risk to nontarget insects or terrestrial invertebrates. However, it appears that clothianidin exposure to honeybees has the potential for high toxicity on both an acute contact and oral basis. The degradate TZNG also confers moderate toxicity to honeybees on an acute oral basis. Furthermore, in a field study (MRID = 45422435), clothianidin nectar and pollen residues appeared to adversely affect mortality, pollen foraging activity, and honey yield.

Subchronic invertebrate studies showed that clothianidin and its degradates (i.e., MNG and TZNG) are potentially toxic to earthworms. There appear to be no apparent toxic effects of clothianidin on earthworm reproduction or population dynamics.

d. Risk to Plants

Clothianidin does not appear to present a risk to terrestrial or aquatic vascular and nonvascular plants (RQ < 1.0, Table 15). The terrestrial plant EECs and RQ values were calculated using the TerrPlant Model, version 1.0 and aquatic plant EECs and RQ values were generated using GENEEC, version 2.0 (output for both models attached, see Appendix D). For the terrestrial plant model, the program (TerrPlant, ver. 1.0) estimated EECs from runoff conditions alone as if clothianidin were a granular pesticide and, so, only the toxicity value from the seedling emergence study was considered in calculating the RQs. Required input fields for the TerrPlant model were identical to those entered for the GENEEC modeling program.

Table 15. Acute and chronic RQ's for evaluating toxic risk of clothianidin exposure to non-target terrestrial and aquatic plants. RQ's are based on the freshwater green algae (*Selenastrum capricornutum*) EC_{50} = 64.0 ppm and the seedling emergence study (EC_{25}/NOAEC = 214).

Crop App. Rate (lbs ai/A; # App.)	Organism	EC_{50}/EC_{25} (ppm)	EEC	RQ (EEC/EC_x)
Corn 0.1 (1)	Terrestrial	EC_{25} = 214	0.0025-0.050 lb a.i./A	0
	Aquatic	EC_{50} = 64.0	0.002 ppm	0
Canola 0.05 (1)	Terrestrial	EC_{25} = 214	0.0025-0.050 lb a.i./A	0
	Aquatic	EC_{50} = 64.0	0.002 ppm	0

e. Endocrine Disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disrupter Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific basis for including, as part of the program, the androgen- and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects on wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects on wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disrupter Screening Program (EDSP).

When the appropriate screening and or testing protocols being considered under the Agency's Endocrine Disrupter Screening Program have been developed, clothianidin may be subjected to additional screening and or testing to better characterize effects related to endocrine disruption. The rationale for this consideration includes the following toxicity issues: chronic effects to birds that include eggshell thinning; chronic effects to mammals resulting in developmental effects in rabbits (premature deliveries, decreased gravid uterine weights, and increased incidence of lung deformities in fetuses); reproductive effects in rats (decreased sperm mobility and an increase number of sperm with detached heads in F_1 and F_2 litters); and, effects to F_1 and F_2 rat offspring (decreased body weight and delayed sexual maturation, as well as an increase in still births). Freshwater and estuarine/marine invertebrates reproductive effects (neonate production) were also noted.

Conclusions

The available data on clothianidin shows that the compound is relatively persistent to very persistent under most circumstances. Clothianidin is stable to hydrolysis at all pH's at environmental temperatures, moderately to highly stable under aerobic soil metabolism conditions (half-lives range from 148-6,900 days), and shows moderate stability under anaerobic aquatic metabolism (half-life of 27 days for the overall system). Laboratory data suggests that photolysis appears to play a role in the dissipation of the chemical (half-life of 14.4 hours in sterile water, 25.4 hours in natural water, and 34 days on soil). Clothianidin has medium to very high mobility in soils. The fact that the K_{OC}'s of four of the five soils were of similar order of magnitude (range 84-129) indicates that there may be a correlation of the mobility with the organic carbon content of the soil. Certain degradates appeared to accumulate in some soils under some conditions [e.g., TZNG MNG, NTG, (aerobic) and TMG (anaerobic)]; over the very long term significant contamination of soil and water with these products might occur. The terrestrial field dissipation studies confirm the findings in the laboratory studies. Clothianidin was found to be persistent in the field (half-lives of 277 days, 1,400 days, and too high to calculate). Based on the overall picture that the laboratory and field studies provided, EFED concluded that there is a very high likelihood that clothianidin would persist and accumulate from year to year after repeated uses. In addition, clothianidin shows a potential to leach to ground waters and, under certain circumstances, reach surface waters during runoff events. Clothianidin is not likely to bioaccumulate in fish.

In combination with the issue of persistence, our risk assessment suggests that the clothianidin proposed use pattern for seed treatment on corn and canola has potential for chronic toxic risk (RQ = 6.3 - 8.6) to avian species (passerines; e.g, songbirds), as well as chronic toxic risk (RQ = 44 - 61) to mammals (0.015 - 0.035 kg range). Considering the mode of agricultural practice of drilling seeds during planting, EFED believes that clothianidin seed treatment should result in minimal acute risk to these organisms. Toxic risk to fish (freshwater and estuarine/marine) appears low, but there may be acute toxic risk to aquatic freshwater invertebrates (RQ = 0.1) through a possible runoff scenario. Although EFED does not do a risk assessment on non target insects, information from standard tests and field studies, as well as incident reports involving other neonicotinoids insecticides (e.g., imidacloprid) also suggest the potential for long term toxic risk to honey bees and other beneficial insects. Our risk assessment also shows toxic risk to Endangered Species (birds, mammals, and invertebrates).

EFED's risk characterization to terrestrial animals was focused on the potential for acute and chronic toxic risk from the ingestion of treated seeds. We have noted that although there is a potential for acute toxic risk to small and medium-sized birds ($\leq$ 0.178kg) for both crop scenarios (corn RQ = 0.1; canola RQ = 0.2), this risk appears to be minimal because of the availability of the number of seeds needed for an acute effect. However, acute toxic risk from corn seed consumption (RQ = 0.6 - 0.8), to small (0.015 kg) and medium (0.035 kg) size mammals appears to present a concern. Our calculations also show that there is the potential for chronic toxicity risk, from clothianidin treated seeds ingestion (corn and canola) that could result in chronic reproductive effects in birds (RQ = 6.3 - 8.6) that may result in eggshell thinning. EFED also has a concern for chronic toxicity risk to mammals (RQ = 44 - 61) primarily from ingestion of treated corn seed. These chronic effects in mammals can be manifested as systemic, reproductive and developmental effects and can include decreased body weight gains and delayed sexual maturation (males only); decreased absolute thymus weight in F1 pups (both sexes), and increased stillbirths (F1 and F2 litters). Reproductive effects were noted for adult rats that included decreased sperm mobility and increased number of sperm with detached heads. Although effects on sperm mobility may not affect the number of offspring in some cases, there can be an impact on the ratio of gender composition (e.g., more males produced as opposed to females) which can result in population reductions. Developmental effects were noted in rabbits at 75 mg/kg/day, and included premature deliveries, decreased gravid uterine weights, and increased litter incidence of missing lung lobe in the fetus. The possibility of chronic risk suggest a Restricted Use compound, Endocrine Disruption candidate, as well as Endangered Species concern for mammals, birds, and invertebrates.

Since several species of birds and mammals frequent corn and canola fields seeking forage or grit, the ingestion of treated seeds can result in acute/chronic toxic risk to small and medium size mammals, as well as chronic risk to birds. Spring planting coincides with the reproductive patterns of several avian and mammalian species, and consumption of treated seeds can increases the possibility of acute/chronic toxic risk to small and medium size mammals and chronic risk to birds. According to one scenario of EFED's calculations regarding terrestrial risk, the ingestion of about 8 - 42 corn seeds may result in chronic toxic risk to songbirds (passerines). However, chronic toxic risk to small to medium size mammals (0.015 - 0.035 kg) appears to be greater with developmental effects possibly occurring in relation to the consumption of 1 - 2 corn seeds or 66 - 154 canola seeds. Small and medium size mammals are also at risk from acute exposure (e.g., consumption of 4.7 - 10 corn seeds needed for an acute effect).

EFED's risk assessment also suggests that clothianidin should not present a direct acute or chronic risk to freshwater and estuarine/marine fish. However, there is the possibility of acute toxic risk (RQ = 0.1) to freshwater invertebrates, via runoff. Because the clothianidin toxicity threshold is low for aquatic freshwater invertebrates on an acute basis, their vulnerability represents acute risk from sediment exposure. As a dynamic trophic level, invertebrates add to the diversity of an aquatic system. Since clothianidin is persistent in the sediment, sediment toxicity testing will be needed to address the uncertainty of possible risk to the large communities of invertebrates and fish that inhabit or come into contact with the sediment.

Appendix A : Environmental Fate and Transport; Results of Individual Studies

a. Degradation

Hydrolysis (161-1) - [Thiazolyl-^{14}C]clothianidin did not significantly hydrolyze in sterile pH 5, 7 and 9 buffer solutions at 25°C; ≥94% of the applied was undegraded at 33 days (study termination; MRID 45422317). Clothianidin did degrade quickly in pH 9 buffer solutions at 62°C and 74°C, with half-lives of 3.7 and 0.7 days, respectively. At pH 9 and the elevated temperatures, two significant degradates were formed. At 62°C, 2-chlorothiazol-5-ylmethylamine (ACT) and *N*-(2-chlorothiazol-5-ylmethyl)-*N*'-methylurea (TZMU) reached a maximum concentration of 53.6% and 14.7% of applied, respectively, at 7 days posttreatment. At 74°C, ACT and TZMU reached maximum concentrations of 59.2% and 22.6% of applied, respectively, at 1.9 days posttreatment.

Photolysis in water (161-2) - Nitroimino- and thiazolyl- [^{14}C]clothianidin photodegraded rapidly in sterile pH 7 buffer solution at 25°C under continuous irradiation; half-lives were 3.4 and 3.1 hours, respectively (MRIDs 454223-18, 20, 22). Less than 1% of the clothianidin remained undegraded after 24 hours of irradiation. No significant degradation occurred in the dark controls. The predicted environmental half-life was 14.4 hours (extrapolating from the actual study conditions assuming mid-summer sunny conditions in Phoenix, Arizona; based on continuous irradiation; 5.76 hours of irradiation were equivalent to 1 day of clear midday midsummer sunlight).

[Nitroimino-^{14}C]clothianidin degraded mainly to methylguanidine (MG), TZMU, 4-hydroxy-2-methylamino-2-imidazolin-5-one (HMIO) and methylurea (MU), with maximum concentrations of 34.7% (432 hours), 29.3% (24 hours), 26.6% (24 hours), and 11.0% (432 hours) of the applied, respectively. [Thiazolyl-^{14}C]clothianidin degraded mainly to TZMU, formamide (FA), 7-methylamino-4H-imidazol[5,1-b][1,2,5]thiadiazin-4-one (MIT), and CO_2, with maximum concentrations of 39.7% (24 hours), 16.1% (120 hours), 11.8% (24 hours), and 34.1% (432 hours) of the applied, respectively.

In nonsterile river water (pH 7.0-9.6) under sunlight, nitroimino- and thiazolyl-[^{14}C]clothianidin degraded with half-lives of 25.1 and 27.7 hours, respectively (MRIDs 454223-19, -21). Temperatures averaged approximately 25°C (range 21.5 to 31.3°C) and average daylight was 8.7 hours (range 0.7 to 14.4 hours). Clothianidin was <5% of the applied at and after 4 days posttreatment. No significant degradation occurred in the dark controls. This study suggests a longer transformation period than the sterile buffer study; however, variable conditions (temperature, pH, sunlight) make precise comparisons difficult.

In the river water, [nitroimino-^{14}C]clothianidin degraded mainly to MG, HMIO, and MU with maximum concentrations of 46.5% (696 hours), 28.0% (120 hours), and 12.0% (432 hours) of the applied, respectively. [Thiazolyl-^{14}C]clothianidin degraded mainly to CO_2, with a maximum concentrations of 28.5% (696 hours) of the applied; other major degradates were Urea, *N*-(2-clorothiazol-5-ylmethyl)-*N*'-methyguanidine (TMG), 3-methylamino-1*H*-imidazo [1,5-c]imidazole (MAI), and 2-chlorothiazol-5-lymethanol (CTCA) with maximum concentrations of 18.1% (264 hours), 17.2% (120 hours), 13.6% (120 hours), and 13.3% (432 hours) of the applied, respectively.

Photolysis on soil (161-3) - Clothianidin degraded with a half-life of 8.2 days in a sandy loam soil at 20°C, based on continuous irradiation; 5.76 hours of irradiation were equivalent to 1 day of clear midday midsummer sunlight at 40°N latitude (MRID 45422323). The equivalent environmental half-life calculated assuming 5.76 hours under study conditions equals one day under natural summer sunlight is 34 days. At study termination (17 days), 22.3% of the clothianidin remained undegraded. No significant degradation occurred in the dark controls. No degradates accumulated to significant levels during the study.

Aerobic soil metabolism (162-1) - Clothianidin degraded in two soils with a half-life of 148 and 239 days, in seven soils ranging in texture from sand to silt loam with half-lives of 495 to 1,155 days, and in a tenth soil (loamy sand, 0.35% OC) with a half-life of 6,932 days (MRIDs 45422325 and 45422326). In all cases, the data were extrapolated beyond the duration of the study and assumed that decay would continue at a first order rate.

All of the soils were studied at 20°C with a moisture content of 75% of 1/3 bar except for the Laacher Hof silt loam and Hofchen silt soils from Germany, which were studied at a moisture content of 40% of maximum water holding capacity. Since all studies were conducted at 20°C, clothianidin might have been less persistent than if the studies had been conducted at 25°C, the temperature of most laboratory soil metabolism studies. The Hofchen, Laacher Hof, and BBA 2.2 soils were treated with [nitroimido-^{14}C]clothianidin. The remaining soils were treated with [thiazolyl-^{14}C]clothianidin.

Summary of aerobic soil metabolism study for clothianidin, presented in order of ascending half-lives.

Soil	% OC	pH in water /0.01 M CaCl2	% Remaining at end of study	Extrapolated half-life, days
Hofchen silt from Germany (MRID 45422325)	2.66	7.8/7.2	54.3% at 120 days	148
Laacher Hof (AII) silt loam from Germany (MRID 45422325)	0.86	8.1/7.3	68.6% at 120 days	239
Loamy sand (BBA 2.2) from Germany (MRID 45422325)	2.5	6.0/6.3	57.8% at 365 days	495
Quincy loamy sand (MRID 45422326)	0.4	6.8/---	80.8% at 181 days	533
Sparta sand (MRID 45422326)	0.73	6.22/5.31	79.5% at 181 days	533
Crosby silt loam (MRID 45422326)	1.37	6.74/6.01	60.3% at 379 days	578

Soil	% OC	pH in water /0.01 M CaCl2	% Remaining at end of study	Extrapolated half-life, days
Susan silt loam (MRID 45422326)	3.27	6.66/5.91	78.3% at 181 days	693
Howe sandy loam (MRID 45422325)	1.12	6.7/6.7	75.8% at 365 days	990
Elder loam (MRID 45422326)	1.41	6.67/5.84	87.5% at 181 days	1155
Fuguay loamy sand (MRID 45422326)	0.35	6.67/5.84	95.3% at 181 days	6932

Residue analysis. Residues were analyzed using thin-layer chromatography (TLC) in multiple solvent systems and radiographic imaging. In MRID 45422325, clothianidin and four nonvolatile degradates [N–methyl-N'-nitroguanidine (MNG); nitroguanidine (NTG); N-(2-chlorothiazol-5-ylmethyl)-N'-nitroguanidine (TZNG); and N-(2-chlorothiazol-5-ylmethyl)-N'-methylurea (TZMU)] were identified by comparison to reference standards. In MRID 45422326, clothianidin, TZNG, and TZMU were identified by comparison to reference standards and LC/MS. There were no unidentified extractable degradation products.

MNG, a degradate originating from the nitroimino moiety, was a maximum 0.7 and 9.5% of the applied in the Laacher Hof and Hofchen soils and 5.9% in the BBA 2.2 soils (MRID 45422325). The maximum concentrations were measured either at the final sampling interval or, if measured prior to the final interval, showed no pattern of decline through study termination. In sandy loam and silt loam Laacher Hof soils and the Hofchen silt soil at 20°C and 50% of maximum water holding capacity, MNG degraded with half-lives of 65-116 days (MRID 45422327).

NTG, a degradate originating from the nitroimino moiety, was a maximum 3.7-6.7% of the applied; in all three soils the maximum was measured at the final sampling interval (MRID 45422325).

TZNG was a maximum 5.1-9.1% of the applied in the Laacher Hof, Hofchen, and BBA 2.2 soils and 2.5% in the Howe sandy loam soil at the final sampling interval (MRID 45422325). In all other soils, the maximum was ≤0.5% of the applied (MRID 45422326). In sandy loam and silt loam Laacher Hof soils and the Hofchen silt soil at 20°C and 50% of maximum water holding capacity, TZNG degraded with half-lives of 53-122 days (MRID 45422328).

TZMU was ≤2.4% of the applied in all soils (MRIDs 45422325 and 45422326).

The maximum concentrations of MNG and TZNG in the soils are probably limited by the relatively rapid rate of degradation of these compounds compared to the slower rate of degradation of clothianidin. No additional information was submitted on the rate of degradation of NTG, so it is not certain if significant additional accumulation would occur. TZMU is most likely a minor degradate under all conditions.

CO_2 was a major transformation product in soils in several soils in which significant degradation occurred prior to study termination (MRIDs 45422325 and 45422326).

Anaerobic soil metabolism (162-2) - No anaerobic soil metabolism study has been conducted; however, an anaerobic aquatic soil metabolism study was conducted in lieu of this study.

Anaerobic aquatic metabolism (162-3) - Clothianidin degraded in with half-lives of 14 days in the water phase, 37 days in the sediment phase, and 27 days overall in an anaerobic water:silt loam sediment (3:1, v:w) system at 20°C (MRID 45422330). Clothianidin was <1% of the applied in the water phase at and after 120 days and was <2.0% in the sediment at and after 183 days. No major degradates were isolated and no minor degradates were identified, in large part because the majority of the residues were not extracted from the sediment at later sampling intervals despite the use of more harsh extraction procedures.

Aerobic aquatic metabolism (162-4) - No acceptable aerobic aquatic metabolism studies have been conducted. Although two studies were submitted by the registrant under this guideline, the experimental designs of both were inadequate to define the pattern of decline of clothianidin under aerobic aquatic conditions (MRIDs 45422324 and 45422329). The experimental design was not in compliance with guidelines (soil and water were pre-incubated before applying the test substance) and aerobic conditions were not fully maintained during the course of the study as indicated by the low redox potential that developed in the sediment

b. Mobility

Mobility/Adsorption/Desorption (163-1) - Clothianidin has medium to very high mobility in soils ranging from sand to clay loam, with Freundlich adsorption coefficients ranging between 0.52 and 4.14 (MRID 45422311). Soil organic carbon partition coefficients (Koc) values were 84 to 129 for all test soils except the US sandy loam soil, which had a Koc value of 345. For all five test soils, Freundlich desorption coefficients and soil desorption carbon coefficients were slightly higher than those obtained for adsorption.

Freundlich adsorption and desorption constants of clothianidin in the soils.

Soil	Adsorption				Desorption			
	K_d	1/n	r^2	K_{oc}	K_d	1/n	r^2	K_{oc}
Quincy loamy sand	0.52	0.8351	0.9952	129	0.62	0.8068	0.9982	154
BBA 2.1 sand	0.59	0.8648	0.9974	119	0.85	0.8843	0.9966	170
Crosby clay loam	1.48	0.8216	0.9992	123	1.67	0.8240	0.9987	139
Laacher Hof sandy loam	1.77	0.8146	0.9998	84	1.99	0.8136	0.9981	95
Elder sandy loam	4.14	0.8088	0.9997	345	4.58	0.8115	0.9987	382

The mobility of four clothianidin degradates (MNG, TZMU, TZNG, and TMG) was also studied in the three US and two German soils using batch equilibrium experiments. The mobilities of the degradates varied from very highly mobile to immobile. **MNG** had very high mobility in the five test soils, with Freundlich adsorption coefficients between 0.0199 and 0.3736, and soil organic carbon partition coefficients ranging from 5.2 to 34.3 (MRID 45422313). **TZMU** had high to very high mobility, with Freundlich adsorption coefficients ranging between 0.1764 and 1.0445, and corresponding soil organic carbon partition coefficients between 46.4 and 95.8 (MRID 45422315). **TZNG** was moderately mobile in the test soils, with Freundlich adsorption coefficients ranging between 0.6274 and 4.7137 and corresponding soil organic carbon partition coefficients between 204.5 to 432.5 (MRID 45422314). **TMG** was immobile or had low mobility in the test soils; Freundlich adsorption coefficients were between 2.4381 and 39.4584 and corresponding soil organic carbon partition coefficients were 525.0 to 6159.4 (MRID 45422316). Freundlich desorption coefficients and soil organic carbon partition coefficients (when calculated) for the four degradates were higher than those obtained for adsorption, except were lower for MNG in the US silt loam soil.

Freundlich adsorption and desorption constants of clothianidin degradates MNG, TZMU, TZNG, and TMG in three US and two German soils.

Soil	Adsorption				Desorption			
	K_d	1/n	r^2	K_{oc}	K_d	1/n	r^2	K_{oc}
MNG								
Quincy sand	0.0514	1.1012	0.9726	21.4	Not calculated			
BBA 2.1 sand	0.0199	0.7017	0.8920	5.2	Not calculated due to low adsorption			
Crosby silt loam	0.1928	0.9249	0.9983	16.5	0.1520	0.8764	0.9812	13.0
Laacher Hof AXXa sandy loam	0.2584	0.9005	0.9999	25.3	0.3561	0.8907	0.9998	34.9
Elder sandy loam	0.3736	0.9083	0.9988	34.3	0.4795	0.9697	0.9993	44.0
TZMU								
Quincy sand	0.1280	0.9276	0.9999	53.3	0.1511	0.8463	0.9995	63.0
BBA 2.1 sand	0.1764	0.8695	0.9999	46.4	0.2604	0.8659	0.9999	68.5
Crosby silt loam	0.6547	0.8645	0.9999	56.0	0.8329	0.8716	1.0000	71.2
Laacher Hof AXXa sandy loam	0.5867	0.8804	0.9996	57.5	0.7832	0.8781	0.9996	76.8
Elder sandy loam	1.0445	0.8430	0.9996	95.8	1.3390	0.8554	0.9998	122.8
TZNG								
Quincy sand	0.6274	0.9010	0.9963	261.4	0.8309	0.8975	0.9958	346.2
BBA 2.1 sand	0.7772	0.8059	0.9994	204.5	1.0290	0.7923	0.9988	270.8

Soil	Adsorption				Desorption			
	K_d	1/n	r^2	K_{oc}	K_d	1/n	r^2	K_{oc}
Crosby silt loam	2.8387	0.8070	0.9999	242.6	3.2321	0.8059	0.9999	276.2
Laacher Hof AXXa sandy loam	2.4072	0.8003	0.9999	236.0	2.8622	0.7924	0.9999	280.6
Elder sandy loam	4.7137	0.7832	0.9997	432.5	5.7460	0.7924	0.9997	527.2
TMG								
Quincy sand	14.7825	0.7798	0.9984	6159.4	21.6317	0.7858	0.9982	9013.2
BBA 2.1 sand	2.4381	0.8256	1.0000	641.6	2.9727	0.8214	1.0000	782.3
Crosby silt loam	15.7889	0.7803	0.9997	1349.5	18.5460	0.7859	0.9994	1585.1
Laacher Hof AXXa sandy loam	5.3550	0.8493	0.9990	525.0	6.1451	0.8094	0.9998	602.5
Elder sandy loam	39.4584	0.7297	0.9977	3620.0	54.4096	0.7348	0.9976	4991.7

In addition to the above-mentioned studies, the desorption of aged clothianidin was studied using Laacher Hof AXXa sandy loam and Laacher Hof AIII silt loam soils from Germany, adjusted to 40% of the maximum water holding capacity, dosed at 0.13 or 1.35 mg a.i./kg, and incubated at 20 ± 1°C for up to 99 days (MRID 45422312). After aging, the soils were equilibrated for 24 hours. Clothianidin comprised approximately 57% of the applied in the soil at 99 days. Clothianidin has low to moderate mobility in the soils after aging. Freundlich desorption coefficients and soil organic carbon partition coefficients (Koc) increased over time in the low-dose soils.

Freundlich desorption constants of clothianidin in the low-dose soils.

Soil	Days of Aging Prior to Desorption						
	0	2	7	14	27	55	99
Sandy loam							
K_d	2.09	2.51	3.99	3.26	3.65	4.86	5.94
K_{oc}	205	246	391	319	357	477	582
Silt loam							
K_d	1.17	1.40	2.37	2.01	2.23	3.34	4.05
K_{oc}	120	143	242	205	228	341	413

Similar results were observed in the high-dose soils aged for 99 days. Freundlich adsorption coefficients increased from 1.56 to 3.30 for the sandy loam soil and from 0.96 to 3.05 for the silt loam soil after 99 days; corresponding increases in soil organic partition coefficients were 153 to 323 and 98 to 311. The study author attributed the increasing Koc values to changes in the sorption process, leading to stronger adsorption to soil and diffusion processes into less accessible sorption sites.

c. Accumulation

Accumulation in Laboratory Fish (165-4)– This data requirement has been waived. Octanol/water partitioning (Kow) data provided in an aerobic aquatic metabolism study indicates a low potential for clothianidin to accumulate (Kow for clothianidin = 1.12 at pH 7; MRID 45422329).

d. Field Dissipation

Terrestrial field dissipation (164-1). Terrestrial field dissipation studies of clothianidin applied to bare soil have been submitted from Wisconsin (MRID 45422332), Ohio (MRID 45422333), North Dakota (MRID 45422334), Ontario (MRID 45422335) and Saskatchewan (MRID 45422336). Clothianidin was applied as a broadcast spray using the test formulation TI-435 FS 600 (a seed treatment for corn and canola seeds) in all five studies. The application rate in the field studies was 243 or 660 g a.i/ha, approximately two and six times the maximum proposed label rate (corn; 1.5 mg/seed, equivalent to 122 g a.i./ha).

Half-lives of clothianidin, based on residues in the 0-15 cm soil depth, ranged from 277 days (Wisconsin test site, sand soil) to 1,386 days (North Dakota test site, clay loam soil); a half-life could not be determined for the Saskatchewan (clay loam soil) test site due to limited dissipation during the study. DT90 values ranged from 980 days to 2,780 days and could not be determined for the Saskatchewan test site. No degradates were detected at >10% of the applied, with the exception of a single detection of TZMU at 10.1% of the applied the Ohio test site. Clothianidin was generally not detected below the 45 cm soil depth, except in the Wisconsin sand soil at a maximum depth of 45-60 cm. Degradates were generally only detected in the 0-15 cm soil layer.

Dissipation of clothianidin in five field studies following a single application of TI-435 FS 600 to bare soil.

Geographic location	Soil texture (0-15 cm)	Application rate (target)	Incorporated	Time 0 or maximum conc.[1]	Conc. at study termination[1]	Half-life[2]	DT90[3]	Major degradates
Wisconsin, USA	Sand	660 g a.i./ha	Yes, depth not reported	0.319 mg/kg (7 days)	0.030 mg/kg (823 days)	277 days ($r^2 = 0.80$)	1,330 days	None at >10% of the applied TI-435
Ohio, USA	Silt loam	660 g a.i./ha	No	0.235 mg/kg (7 days)	0.0305 mg/kg (735 days)	315 days ($r^2 = 0.85$)	980 days	None at >10% of the applied TI-435
North Dakota, USA	Clay loam	243 g a.i./ha	No	0.124 mg/kg (15 days)[4]	0.0353 mg/kg (864 days)	1,386 ($r^2 = 0.10$)	2,780 days	None at >10% of the applied TI-435
Ontario, Canada	Silt loam	660 g a.i./ha	Yes, 5 cm	0.278 mg/kg (7 days)	0.0576 mg/kg (798 days)	365 days ($r^2 = 0.51$)	1,160 days	None at >10% of the applied TI-435
Saskatchewan, Canada[5]	Silty clay loam	243 g a.i./ha	Yes, 5 cm	0.0811-0.0985 mg/kg (day 0)[6]	0.0638-0.0796 mg/kg (775 days)	Could not be determined[7]	Could not be determined[7]	None at >10% of the applied TI-435

[1] Concentration in the 0-15 cm soil layer.
[2] Reviewer-calculated, based on residues in the 0-15 cm soil layer.
[3] Registrant-calculated, based on residues in all soil layers.
[4] Excludes outlier at 842 days posttreatment (TI-435 detected at 0.146 mg/kg, mean of three replicates).
[5] Two trials were conducted at the Saskatchewan test site.
[6] Day 0 (post-incorporated values). The maximum concentration of TI-435 observed in trials 1 and 2 occurred at 61 days (0.122 mg/kg) and 678 days (0.0916 mg/kg), respectively.
[7] A half-life could not be determined at the Saskatchewan test site due to limited dissipation during the study.

In lysimeter studies conducted in the Federal Republic of Germany (FRG), clothianidin was applied to the same sandy loam soil (0-10 cm depth: 70.8% sand, 20.7% silt, 8.6% clay, pH 7.2, 1.8% organic carbon; Appendix 5, p. 45) in Monheim, FRG. In the first study, [nitroimino-^{14}C]clothianidin, formulated as TI-435 200 SC, was applied twice (10 months apart) at approximately 160 g a.i./ha/application to an enclosed plot (1 m^2 x 1.3 m depth) of sandy loam soil planted with turf (MRID 45422508). In the second study, [Thiazolyl-^{14}C]clothianidin, formulated as TI-435 70 WS, was applied twice (400 days apart) as a seed treatment at approximately 100 g a.i./ha and 138 g a.i./ha, respectively, to an enclosed plot (1 m^2 x 1.3 m depth) of sandy loam soil (MRID 45422331).

In the MRID 45422508 study, approximately three years following the first application, 42-45% of the applied was detected in the soil and approximately 1% was detected in the leachate; the loss of radioactivity, approximately 54-56%, was attributed to mineralization of clothianidin. Grass clippings were not analyzed separately. Approximately 39.5-40.4% of the applied was detected within the top 0-30 cm of soil, with clothianidin accounting for the majority of the extracted radioactivity (maximum of 18.02 µg/kg soil in the 0-10 cm soil layer). The degradates MNG, TZNG and NTG were detected at maximum concentrations of 1.57 µg/kg soil, 3.05 µg/kg soil and 0.77 µg/kg soil, respectively, in the 10 cm soil layer. MNG and NTG were also detected in the leachate samples; clothianidin was not detected in any leachate samples.

In the MRID 45422331 study, winter barley seeds were treated and sown for the first application and winter wheat seeds were treated and sown for the second application; the lysimeter was cropped with untreated winter wheat during the third year of the study. Approximately three years following the first application, 59% of the applied was detected in the soil, 3% was detected in the harvested crops and 0.3% was detected in the leachate; the loss of radioactivity, approximately 37%, was attributed to mineralization of clothianidin. Approximately 57% of the applied was detected within the top 0-30 cm of soil, with clothianidin accounting for the majority of the extracted radioactivity (maximum of 25.4 µg/kg soil in the 0-10 cm soil layer). The only degradate detected was TZNG, at a maximum concentration of 5.21 µg/kg soil in the 10 cm soil layer. Clothianidin and TZNG were detected in the harvested crops, with the majority of the radioactivity being detected in the hulls/straw and chaff. Four unknown degradates were detected in the leachate samples; clothianidin was not detected in any leachate samples.

Ancillary studies - The extraction efficiency of two analytical methods to determine clothianidin and its degradates TZNG, MNG, TZMU and TNG was compared in two aged German soils (MRID 45422604). Radiolabeled test substances were applied to the two soils (a sandy loam and a silt loam) at a concentration equivalent to 300 g a.i./ha and maintained in the dark at 20 ± 1 °C and at 75% of 1/3 bar moisture under static aerobic conditions for 92 days. For the "lab method", 100 g soil samples were extracted four times with acetonitrile and once with water by shaking; following centrifugation, extracts were filtered and analyzed by TLC. For the "field method", 20 g soil samples were mixed with 4 g hydromatrix and extracted using an Accelerated Solvent Extractor with acetonitrile:water:acetic acid:guanidine hydrochloride (200:800:0.8:8, v:v:v:w) at a temperature of 140°C and a pressure of 140 bar; extracts were analyzed by TLC. Both total radioactive residues extracted and extraction efficiencies for each individual test substance were generally greater with the field method as compared to the lab method. The study author speculated that the lower recoveries for the lab method may have been a result of the higher metabolism/mineralization capacity of the 100 g soil samples used in the lab method as compared to the 20 g soil samples used in the field method; however, neither bound residues nor CO_2 were measured.

Soil	Lab method		Field method	
	Total extracted ^{14}C	Total identified ^{14}C	Total extracted ^{14}C	Total identified ^{14}C
Sandy loam				
TI-435	105.3	76.5	102.9	82.2
TZNG	89.3	52.4	90.1	69.9
MNG	89.4	56.0	90.4	66.8
TZMU	35.8	20.2	61.0	41.6
TMG	73.3	62.1	83.5	78.9
Silt loam				
TI-435	100.2	70.3	109.4	81.9
TZNG	85.1	50.1	89.5	61.4
MNG	86.6	44.4	79.5	49.0
TZMU	20.9	13.4	34.6	20.8
TMG	64.3	58.2	84.6	80.7

In a storage stability study, no significant degradation of clothianidin and the degradates TZNG, TZMU, TMG, and MNG was observed in frozen samples of Howe soil fortified with parent and degradates at approximately 50 µg/kg and stored frozen for 12 months at temperatures between -18 and -25°C (MRID 45422612). Following storage, clothianidin and the degradates were extracted from soil with acetonitrile:water:acetic acid:guanidine hydrochloride (200:800:0.8:8, v:v:v:w) using an Accelerated Solvent Extractor (ASE). After extraction, an internal standard solution was added and the volume adjusted with acetonitrile:water (1:4, v:v). Extracts were analyzed by LC-MS/MS. Isotopically labeled internal standards (d_3-TI-435; ^{13}C, ^{15}N-TZNG; d_3-TZMU; d_3-MNG and d_3-TMG) were used to compensate for possible matrix effects in the MS/MS detector. Mean recoveries of TI-435 were 106% at day 0, 98.4% at 118 days, 96.1% at 180 days, and 91.2% following 356 days of storage. Mean recoveries of TZNG were 94.6% at day 0, 101% at 118 days, 98.6% at 180 days, and 92.4% following 356 days of storage. Mean recoveries of TZMU were 104% at day 0 and 118 days, 95.6% at 180 days, and 93.7% following 356 days of storage. Mean recoveries of TMG were 95.6% at day 0, 82.3% at 118 days, 94.4% at 180 days, and 83.4% following 356 days of storage. Mean recoveries of MNG were 95.7% at day 0, 96.1% at 118 days, 110% at 180 days, and 101% following 356 days of storage. The study "is still running for at least one more year."

e. Special Field Studies

Small-Scale Prospective Ground-Water Monitoring Studies (164-1). No small-scale prospective ground-water monitoring studies have been submitted.

Appendix B: Ecological Hazards Assessment

Overview

The toxicity testing required does not test all species of birds, fish, mammals, invertebrates, and plants. Only two surrogate species for birds (Bobwhite quail and mallard ducks) are used to represent all bird species (over 900 in the US), three species of freshwater fish (rainbow trout, bluegill sunfish and fathead minnow) are used to represent all freshwater fish species (over 900 in the US), and one estuarine/marine fish species (sheepshead minnow) is used to represent all estuarine/marine fish (over 300 in the US). The surrogate species for terrestrial invertebrates is the honey bee, for freshwater invertebrates the surrogate species is usually the waterflea (*Daphnia magna*) and for estuarine/marine invertebrates the surrogate species are mysid shrimp and eastern oyster. These five species are used to represent all invertebrates species (over 10,000 in the US). For plants, there are ten surrogate species used for all terrestrial plants and five surrogate species used for all aquatic plants. There are over 20,000 plant species in the US which includes flowering plants, conifers, ferns, mosses, liverworts, hornworts and lichens with over 27,000 species of algae worldwide.

The surrogate species testing scheme used in this assessment assumes that a chemical's mechanism of action and toxicity found for avian species is similar to that in all reptiles (over 300 species in the US). The same assumption applies to amphibians (over 200 species in the US) and fish; the tadpole stage of amphibians is assumed to have the same sensitivity as a fish. Therefore, the results from toxicity tests on surrogate species are considered applicable to other member species within their class and are extrapolated to reptiles and amphibians. The US species numbers noted in this section were taken from: http://www.natureserve.org/summary (NatureServe: An online encyclopedia of life [web application].2000) and the worldwide species number from Ecological Planning and Toxicology, Inc.1996.

a. Toxicity to Terrestrial Animals

i. Birds, Acute and Subacute

An acute oral toxicity study using the technical grade of the active ingredient (TGAI) is required to establish the toxicity of clothianidin to birds. The preferred test species is either mallard duck (a waterfowl) or Bobwhite quail (an upland gamebird). The data that were submitted show that the LD_{50} is >2,000 mg/kg for Bobwhite quail. A study conducted on a non-guideline species, Japanese quail, showed that the LD_{50} is 423 mg/kg. Based on these results, clothianidin is categorized as ranging from practically non-toxic to moderately toxic to avian species on an acute oral basis; the guideline (71-1) is fulfilled (MRID #45422417).

Table B-1 :Avian Acute Oral Toxicity

Species	% a.i.	5-day LD_{50} (mg/kg)	Toxicity Category	MRID No. Author, Year	Study Classification
Bobwhite quail *(Colinus virginianus)*	96.0	>2,000	Practically non-toxic	45422417 Johnson, 1998	Core
Japanese quail (*Coturnix coturnix japonica)*	97.6	423	Moderately toxic	45422418 Gallagher *et al.*, 2000	Supplemental

Two subacute dietary studies using the TGAI are required to establish the toxicity of clothianidin to birds. The preferred test species are mallard duck and Bobwhite quail. The data that were submitted show that the LC_{50} is >5,000 ppm; therefore, clothianidin is categorized as practically non-toxic to avian species on a subacute dietary basis. The guideline (71-2) is fulfilled (MRID #45422419; MRID #45422420).

Table B-2: Avian Subacute Dietary Studies

Species	% a.i.	5-Day LC_{50} (ppm)	Toxicity Category	MRID No. Author, Year	Study Classification
Northern Bobwhite quail *(Colinus virginianus)*	96	>5,230	Practically non-toxic	45422419 Johnson, 1998	Core
Mallard duck *(Anas platyrhynchos)*	96	>5,040	Practically non-toxic	45422420 Johnson, 1997	Core

ii. Birds, Chronic

Avian reproduction studies using the TGAI are required for clothianidin because birds may be subject to repeated or continuous exposure to the pesticide, especially preceding or during the breeding season. Clothianidin is highly stable in terrestrial environments (e.g., half-life of 744 days aerobic soil metabolism) to the extent that potentially toxic amounts may persist in animal feed. The preferred test species are mallard duck and Bobwhite quail. The submitted data show that clothianidin exposure of 525 ppm adversely affected eggshell thickness for Bobwhite quail, but did not result in chronic effects during reproduction for mallard duck; the guideline (71-4) is fulfilled (MRID #45422421; MRID #45422422).

Table B-3: Avian Reproduction

Species	% a.i.	NOAEC/LOAEC (ppm)	LOAEC Endpoints	MRID. No. Author, Year	Study Classification
Northern Bobwhite quail *(Colinus virginianus)*	97.6	205/525	Eggshell thickness	45422421 Gallagher *et al.*, 2000	Core
Mallard duck *(Anas platyrhynchos)*	97.6	525/ >525	No effect on reproduction	45422422 Gallagher *et al.*, 2000	Supplemental

iv. Birds, Effect

Non-guideline acute dietary toxicity studie was submitted which showed no effect on mortality or body weight of the domestic pigeon after exposure to maize seed treated with 50g clothianidin/50,000 seeds. However, without proper controls there is not enough information to support the conclusions of aversion. In a similar mode, study authors stated in the Japanese quail study that there was a treatment-related decrease in seed intake (aversion response). However, without proper controls, there is not enough information to make this statement.

Table B-4: Avian Acute Avoidance (Treated Seed) Studies

Species	a.i. (g/L)	Endpoints Affected	MRID. No. Author, Year	Study Classification
Domestic pigeon *(Columba livia-f. domestica)*	50 g ai/50,000 seeds	No mortalities or treatment effects on body weight	45422516 Barfknecht, 1998	Supplemental
Japanese Quail *(Coturnix coturnix)*	1.67 L product/ 100 kg seed	no symptoms of intoxication or behavioral changes reported.	45422515 Barfknecht, 1998	Supplemental

v. Mammals, Acute and Chronic

Wild mammal testing is required on a case-by-case basis, depending on the results of lower tier laboratory mammalian studies, intended use pattern and pertinent environmental fate characteristics. In most cases, rat or mouse toxicity values obtained from the Agency's Health Effects Division (HED) substitute for wild mammal testing. These toxicity values are reported below.

Table B-5: Mammalian Acute and Chronic Toxicity

Species	% a.i.	Test Type	Toxicity	Affected Endpoints	MRID No. Author, Year
Rat (*Rattus norvegicus*)	96	Acute	LD_{50} =5,000 mg/kg/day	Mortality	45422621 Gardner, 1997
Mouse (*Mus musculus*)	96	Acute	LD_{50} = 389-465 mg/kg/day	Mortality	45422622 Gardner, 1997
Rat (*Rattus norvegicus*)	96	2nd-Generation Reproduction	NOAEL (M/F) = 9.8/11.5 mg/kg/day (150/500 ppm) LOAEL (M/F) = 31.2/36.8 mg/kg/day (500/500 ppm) NOAEL (M) = 31.2 mg/kg/day (500 ppm) LOAEL (M)= 163.4 mg/kg/day (2500 ppm)	Offspring systemic[1] Reproduction[2]	4522714-16 and 45422825-26, 2000 and 2001
Rabbit (*Sylvilagus* sp.)	96	Developmental	NOAEL/LOAEL = 25/75 mg/kg/day	Development[3]	45422712 and -13, 1998

[1] Decreased body weight gains and delayed sexual maturation (males only); decreased absolute thymus weight in F1 pups (both sexes), and increased stillbirths (F1 and F2 litters).
[2] Decreased sperm mobility and increased number of sperm with detatched heads (F1 and F2 litters).
[3] Premature deliveries, decreased gravid uterine weights, and increased litter incidence of missing lobe of the lung per fetus.

The results indicate that clothianidin is categorized as practically non-toxic to small mammals on an acute oral basis (LD_{50} = 389->5,000 mg/kg/day).

In the 2nd generation rat reproduction study, offspring systemic toxicity was detected for males and females at 500 ppm and reproductive toxicity was detected in males at 2500 ppm. The NOAEL for offspring systemic toxicity was 150 and 500 ppm for males and females, respectively, and the NOAEL for reproduction was 500 ppm. In the rabbit developmental study, toxicity was observed at 75 mg/kg/day; the NOAEL was 25 mg/kg/day.

vi. Terrestrial Insects, Acute

Insect Acute Contact

A honey bee acute contact study using the TGAI is required for clothianidin because its outdoor seed treatment use will result in honey bee exposure. The acute contact LD_{50}, using the honey bee, *Apis mellifera*, is an acute contact, single-dose laboratory study designed to estimate the quantity of toxicant required to cause 50% mortality in a test population of bees. The TGAI is administered by one of two methods: whole body exposure to technical pesticide in a nontoxic dust diluent; or, topical exposure to technical pesticide via micro-applicator. The median lethal dose (LD_{50}) is expressed in micrograms of active ingredient per bee (µg a.i./bee). Results of this test are tabulated below (Table B-7). Toxicity category descriptions for honey bee acute contact toxicity are the following (Atkins, 1981):

If the LD_{50} is *less than 2* µg a.i./bee, then the test substance is *highly toxic.*
If the LD_{50} is *2 to less than 11* µg a.i./bee, then the test substance is *moderately toxic.*
If the LD_{50} is *11* µg a.i./bee or *greater*, then the test substance is *practically nontoxic*

The five (5) acute oral toxicity studies are categorized as supplemental because the submission of honey bee acute oral toxicity studies is not a guideline requirement and the core classification is reserved for guideline studies that fulfill guideline requirements. The acute contact and acute oral bee studies submitted for clothianidin received the same MRID No. (45422426) however only the acute contact study for the TGAI formulation is considered to be a Core study. The acute contact LD_{50} for clothianidin is 0.0439 µg a.i./bee and it is, therefore, classified as highly toxic to bees on a contact exposure basis. The guideline (141-1) is fulfilled (MRID No. 45422426). The Office of Pesticide Programs (OPP) does not have a categorization scheme for acute oral toxicity to honey bees. However the following acute oral toxicity categorization scheme based on ICBB (1985) categorization is provided for informational purposes:

If the LD_{50} is greater than 100 µg a.i./bee, then the test substance is Virtually non-toxic.
If the LD_{50} 10-100 µg a.i./bee, then the test substance is Slightly toxic.
If the LD_{50} 1-10 µg a.i./bee, then the test substance is Moderately toxic.
If the LD_{50} less than 1.0 µg a.i./bee, then the test substance is Highly toxic.

Table B-7: Honey bee Acute Contact and Oral Toxicity

Species/Study Duration	% ai	LD50 (µg ai/bee)	Toxicity Category	MRID # Author/Year	Study Classification
Honey bee Acute Contact Toxicity - Clothianidin					
Honey bee (Apis mellifera)/48 hour	96	0.0439	highly toxic	45422426/Weyman, G.S./1998	Core
Honey bee Acute Oral Toxicity - Clothianidin					
Honey bee (Apis mellifera)/48 hour	96	0.0037	not applicable[1]	45422426/Weyman, G.S./1998	Supplemental
Honey bee Acute Oral Toxicity - Clothianidin Metabolite -TMG					
Honey bee (Apis mellifera)/48 hour	96	≥152	not applicable[1]	45422427/Wilkins, P./2000	Supplemental
Honey bee Acute Oral Toxicity - Clothianidin Metabolite - MNG					
Honey bee (Apis mellifera)/48 hour	99.2	>153	not applicable[1]	45422428/Wilkins, P./2000	Supplemental
Honey bee Acute Oral Toxicity - Clothianidin Metabolite - TZMU					
Honey bee (Apis mellifera)/48 hour	98.8	>113	not applicable[1]	45422429/Wilkins, P./2000	Supplemental
Honey bee Acute Oral Toxicity - Clothianidin Metabolite - TZNG					
Honey bee (Apis mellifera)/48 hour	98.6	3.95	not applicable[1]	45422430/Wilkins, P./2000	Supplemental

1. OPP does not categorize honey bee acute oral toxicities

Insect Residual Contact

A honey bee toxicity of residues on foliage study is required on an end-use product for any pesticide intended for outdoor application when the proposed use pattern indicates that honey bees may be exposed to the pesticide and when the formulation contains one or more active ingredients having an acute contact honey bee LD_{50} which falls in the moderately toxic or highly toxic range. The purpose of this guideline study is to develop data on the residual toxicity to honey bees. Bee mortality determinations are made from bees exposed to treated foliage harvested at various time periods after treatment. Clothianidin, as indicated in the acute toxicity test in Table B-6, is highly toxic to honey bees on a contact basis. Usually pesticides toxic to honey bees require bee precautionary labeling on all end-use formulations and registrants are required to submit data in accordance with Guideline 141-2 - Honey Bee Toxicity of Residues on Foliage. However, because the proposed use patterns for clothianidin (seed treatment uses on canola and corn) are not likely to result in honey bee contact exposure from the application of clothianidin, a honey bee toxicity of residues on foliage study (guideline 141-2) is not required for clothianidin at this time but is being reserved for future, possible submission. Should the proposed use pattern of clothianidin be revised in future registration actions such that the direct exposure to bees from clothianidin applications is likely, then honey bee precautionary labeling is required and the submission of Guideline 141-2 - Honey Bee Toxicity of Residues on Foliage is required.

Insect Mortality, Reproduction, and Feeding Capacity

Two (2) studies were submitted to show acute effects of corn (MRID No. 45422520) and summer rape (MRID No. 45422521) seeds treated with TI 435 FS600 (formulated product) on carabid beetles (*Poecilus cupreus*) under extended laboratory test conditions. The goal of these studies was to evaluate whether or not exposing carabid beetles to clothianidin treated corn or rape seeds increased mortality or decreased feeding rate compared to the controls. About one third of the adult carabid beetles exposed to the treated corn seeds at a seed treatment rate of 0.45 lb ai/A showed abnormalities (undescribed signs of intoxication). There was also a significant increase in mortality in the treatment groups compared to the controls. Rape seed treated with clothianidin at an application rate of 0.095 lb ai/A caused behavioral impacts (intoxication) to 63 % of adult carabid beetles in the treatment group. The feeding rate of beetles in the treatment group was significantly reduced. There was also a significant difference in mortality (13.3 %) of the treatment group compared to the control. These studies were scientifically sound and classified as Supplemental.

Three studies (MRID Nos. 45422524, 45422522, & 45422523) were submitted to show effects of clothianidin on the life cycle of rove beetles (*Aleochara bilineata*) under extended laboratory conditions. The first study (MRID No. 45422524) was designed to evaluate the effects clothianidin would have on the beneficial ground beetles exposed to the pesticide in treated soil. Study endpoints were adult mortality and reproduction (total number of progeny produced). In this study, there were no significant differences observed between the control and clothianidin treatment groups for adult mortality. Reproductive performance (as indicated by decreased number of progeny) was affected in the two highest clothianidin treatment groups (200 and 250 µg a.i./kg soil). The goal of final two (2) rove beetle studies (MRID Nos. 45422522 & 45422523) was to evaluate whether or not exposure of rove beetles to corn seeds (MRID No. 45422522) treated at a rate of 0.55 lb ai/A and to rape seeds (MRID No. 45422523) treated at a rate of 0.095 lb ai/A (10 g a.i./kg TI 435 FS 600) would result in significantly increased mortality of parent beetles and whether or not the offspring production rate would be adversely affected. The beetles exposed to the treated corn seed experienced a significant increase in mortality but no significant reproductive difference when compared to the controls. The reproductive performance of the rove beetles was determined by counting the number of rove beetles which emerged from the host pupae between days 39 and 77 after treatment. Rove beetles exposed to the treated rape seed experienced an increase in mortality and a reduced parasitization capacity. The number of offspring that emerged (reproductive performance) in the rape seed treated test groups was not significantly lower than the control group. These studies were scientifically sound and classified as Supplemental.

Insect Field Testing

Six honey bee field studies (Table B-8) were reviewed and determined to be scientifically sound and classified as Supplemental. The studies were not required but were voluntarily submitted by the registrant in compliance with a European Union directive (91/414/EEC). These studies were reviewed under OPP's guideline 141-5, Field Testing for Pollinators, and were categorized as supplemental because these studies were conducted without a prior agreed upon protocol between the registrant and the Agency as required by guideline 141-5.

These field studies evaluated the effects to small honey bee colonies hived on clothianidin rape seed treated and untreated (control) plots. Colonies were placed on the treated and untreated plots during the rape bloom stage approximately two months after the rape crops were planted and monitored for short periods of time to determine if the bees were being adversely affected by the clothianidin exposure as a result of the systemic activity demonstrated by clothianidin. All of the studies provided clothianidin residue levels in various bee related commodities as a result clothianidin's seed treatment use to canola (rape) seeds. Residues of clothianidin ranged from 1.0 μg ai/kg found in the nectar sampled from beehives and rape flowers to 8.6 μg ai/kg from nectar sampled from forage bees honey stomachs. Residues of clothianidin were also found in forage bees, rape flowers, pollen taken from foraging bees and pollen from beehives. These residues were a result of the clothianidin seed treatments performed approximately 60 days prior to sampling the commodities. Two (2) studies (MRID Nos. 45422436 & 45422437) also tested for the clothianidin metabolites, TZMU and TZNG, but residues of these metabolites were not found in the nectar and pollen samples analyzed. Although residues of clothianidin were found in numerous samples collected, none of the studies indicated the exposed bees were adversely affected when compared to the controls. Parameters such as bee mortality, foraging (nectar or pollen) activity, and honey production were monitored for effects.

These studies were limited in value because the length of time the bees were monitored for adverse effects was brief and the studies failed to use replication in the treatments and controls. Field exposure to the test substance and bee observation period were too brief (< 30 days) to fully evaluate the impact the exposure levels of clothianidin would have had on the bee colonies tested. The complete life cycle for an individual worker bee during the time period tested would be approximately 63 days.[2] Statistical analyses could not be conducted on any of these honey bee field studies, due to only one replicate hive per treatment and control being used in the studies.

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2 Egg stage through pupae stage ≈ 21 days; adult house bee stage ≈21 days; and adult forager ≈ 21 days.

Table B-7: Clothianidin (TI-435) (044309) Honey Bee Field Studies

MRID #	Study Classification	Clothianidin Seed Treatment Crop	Study Location & Plant Date of Treated Seed	Chemical Application Rate	Sample Date(s)	Commodity Sampled	Clothianidin Residues Found (µg ai/kg)
45422431	Supplemental	canola (rape)	Borlunda-Skelinge, Sweden 4/28/98	<u>Clothianidin</u> 8.6 g a.i./kg seed or 8.62 lb ai/1000 lb seed or 0.038 lb ai/acre	1st week of July '98	forage bees	1.4
					1st week of July '98	nectar in bees	8.6
					7/3/98 and 7/2/98	nectar from rape flowers	1.2 and 7.2
					1st week of July '98	rape flowers	4.1
45422432	Supplemental	canola (rape)	Elm Farm., United Kingdom 3/28/98	<u>Clothianidin</u> 10.4 lb ai/1000 lb seed or 0.046 lb ai/acre	6/22-6/24/98	rape flowers	3.3
					6/22-6/24/98	forage bees	none detected
45422433	Supplemental	canola (rape)	Conches in Northern France 3/19/98	<u>Clothianidin</u> 10.4 lb ai/1000 lb seed or 0.046 lb ai/acre	6/15-6/18/98	pollen taken from forage bees	1.7
45422435	Supplemental	canola (rape)	Ontario, Canada 5/3/00	<u>Clothianidin</u> 6 lb ai/1,000 lb seed or 0.04 lb ai /A	6/26-7/20/00	pollen from bee hives	3.0 (61 days after application)
							1.6 (68 days after application)
						nectar from bee hives	3.7 (61 days after application)
							0.9 * (68 days after application)
			Minnesota, US 5/16/00		6/28-7/28/00	pollen from bee hives	2.3 (50 days after application)
							2.8 (57 days after application)
						nectar from bee hives	1.1 (50 days after application)

Table B-7: Clothianidin (TI-435) (044309) Honey Bee Field Studies

MRID #	Study Classification	Clothianidin Seed Treatment Crop	Study Location & Plant Date of Treated Seed	Chemical Application Rate	Sample Date(s)	Commodity Sampled	Clothianidin Residues Found (µg ai/kg)
							1.0 (57 days after application)
45422436	Supplemental	canola (rape)	Monheim, Germany 5/2/00	**Clothianidin** 1056 g a.i./100 kg seed or 1 lb ai/100 lb seed or 0.025 lb ai/A	7/6/00 and 7/7/00	nectar from rape flowers	2.8 and 3.0
45422437	Supplemental	canola (rape)	Burscheid, Germany 4/28/00	**Clothianidin** 1056 g a.i./100 kg seed or 1 lb ai/100 lb seed or 0.025 lb ai/A	6/30/00 and 7/6/00	nectar from rape flowers	5.4 and 1.0
					combs sampled 7/12/00; forage bees sampled on 7/2 and 7/18/00	pollen from combs/forage bees	1.9 to 2.5

* <Level of Quantification (LOQ) =1.0 µg/kg and Level of Detection (LOD) = 0.3 µg/kg

A seventh honey bee field study (MRID No. 45422440), reviewed under guideline 141-5 evaluated the effects to small colonies of honey bees fed various concentrations of clothianidin treated pollen. One small beehive (about 500 bees) per treatment and control was tented on oat plots in cages and fed treated maize pollen with a total of five colonies (3 treatment levels and 2 control colonies) used in the study. Pollen treated with clothianidin at a measured concentration level up to 19.7 µg ai/kg produced no significant adverse effects to the parameters measured in this study based upon the visual inspection of the data. The parameters measured included mortality, foraging activity (including honey and pollen collection), comb production, honey storage behavior, population growth (including egg, larvae, pupae, and adult growth stages) and behavioral anomalies. Since there was only one replicate hive per treatment level, a statistical analysis could not be made of the data provided. MRID No. 45422440 was determined to be scientifically sound and classified as Supplemental.

Spider Mortality and Feeding Capacity

Two extended laboratory studies (MRID Nos. 45422518 & 45422519) to evaluate the effects of clothianidin treated seed on the wolf spider, *Pardosa* spp. (Araneae, Lycosidae) were reviewed. The goal of these studies was to evaluate whether or not exposing wolf spiders to treated corn and rape seeds increased mortality or decreased feeding rate compared to the controls. The seed treatment rate for the corn seeds was 48.8 g a.i./Unit (1 Unit = 50,000 seed) with 2 corn seeds per 1170 cm^2 test box equivalent to 0.15 lb ai/A. The seed treatment rate for the rape seeds was 10 g a.i./kg TI 435 FS 600 with 4 rape seeds per 178 cm^2 test box equivalent to 0.06 lb ai/A. The studies' results indicated that the wolf spider mortality and feeding capacity in the clothianidin treatments were not significantly different from the controls. These studies were scientifically sound and classified as Supplemental.

Earthworm Acute and Chronic

Five acute/chronic earthworm studies were reviewed for clothianidin and its metabolite/transformation products. These studies were classified as supplemental since earthworm studies are not a guideline requirement under FIFRA. These studies were conducted in compliance with the Organization for Economic Cooperation and Development (OECD) guidelines for testing of chemicals and were reviewed, by EFED, under EPA Ecological Effects Test Guidelines (U.S. EPA Ecological Effects Test Guidelines, April, 1996). EFED does not have a toxicity categorization for earthworms. The clothianidin earthworm LC50 (conc. in soil) was determined to be 15.5 mg/kg (MRID No. 45422511) with the metabolite, MNG, and transformation product, TZNG, being less toxic to earthworms than the parent compound. Clothianidin exhibits no apparent effect to earthworms at application rates equal to or greater than 0.08 lb ai/A (MRID No. 45422526). The results of these studies are in Table B-8.

Table B-8: Earthworm Acute and Chronic Toxicity - Clothianidin Technical and TEP

Species/Study Duration	% ai	LC50/ EC50 (nominal/ measured) (mg/kg in dry soil or lb ai/A)	Toxicity Category	NOAEC/ LOAEC (nominal/ measured) (mg/kg in dry soil or lb ai/A)	Endpoints	MRID# Author/Year	Study Classification
Earthworm (*Eisenia foetida)*/14 days	96	15.5 mg/kg (nominal)	not applicable	< 10.0 mg/kg (nominal)	mortality	45422511/Weyman, G/1998	Supplemental
Earthworm (*Eisenia fetida)*/56 days	48	> 0.054 lb ai/A[1] (nominal)	not applicable	≥ 0.054 lb ai/A[1] (nominal)	mortality, body weight, or number of offspring per surviving adult	45422525/Meisner, P./2000	Supplemental
Earthworm *(Lumbricus terrestris, L.rubellus, L. castaneus, Apporrectodea caliginosa, Allolobophora chlorotica,* and *Aporrectodea terrestris longa)*/1 year	47.8	> 0.08 lb ai/A[2] (measured)	not applicable	≥ 0.08 lb ai/A[2] (measured)	number and biomass of earthworms	45422526/Heimbach,F./2000	Supplemental

Table B-8: Earthworm Acute and Chronic Toxicity - Clothianidin Technical and TEP

Species/Study Duration	% ai	LC50/ EC50 (nominal/ measured) (mg/kg in dry soil or lb ai/A)	Toxicity Category	NOAEC/ LOAEC (nominal/ measured) (mg/kg in dry soil or lb ai/A)	Endpoints	MRID# Author/Year	Study Classification
Clothianidin Metabolite - MNG							
Earthworm (*Eisenia fetida)*/14 days	99.2	> 1,000 mg/kg (nominal)	not applicable	320.0 mg/kg (nominal)	reduction in body weights (NOAEC)	45422512/Noack, M./2000	Supplemental
Clothianidin Transformation Product - TZNG							
Earthworm (*Eisenia fetida)*/14 days	99	982.0 mg/kg (nominal)	not applicable	125.0 mg/kg (nominal)	mortality (LC50) (reduction in body weights (NOAEC)	45422513/Noack, M./2000	Supplemental

1 Equivalent to >500,000 clothianidin dressed corn seeds/ha

MRID No. 45422525 - Earthworm

$$\frac{6.62\text{ g formulation} * 48\%\text{ ai / formulation}}{\text{kg corn seed}} = \frac{3.18\text{ g ai}}{2.2\text{ lb corn seed} * 1{,}200\text{ corn seed / lb}} = \frac{3.18\text{ g ai}}{2{,}640\text{ corn seed}} = \frac{0.00701\text{ lb ai}}{2{,}640\text{ corn seed}} = \frac{2.7 \times 10^{-6}\text{ lb ai}}{\text{corn seed}}$$

MRID No. 45422525 - Earthworm (continued)

$$\frac{2.7 \times 10^{-6}\text{ lb ai}}{\text{corn seed}} * \frac{500{,}000\text{ seed}}{\text{HA}} = \frac{1.33\text{ lb ai}}{\text{HA}} = \frac{0.054\text{ lb ai}}{\text{Acre}}$$

2 Equivalent to > 91.4 g a.i./ha

MRID No. 45422526 - Earthworm

$$\frac{91.4\text{ g ai}}{\text{ha}} = \frac{0.2015\text{ lb ai}}{2.47\text{ Acre}} = \frac{0.08\text{ lb ai}}{\text{Acre}}$$

b. Toxicity to Freshwater Aquatic Animals

i. Freshwater Fish, Acute

Two freshwater fish toxicity studies using the TGAI are required to establish the acute toxicity of clothianidin to fish. The preferred test species are rainbow trout (a coldwater fish) and bluegill sunfish (a warmwater fish). The acute studies that were submitted that tested the parent compound showed that clothianidin is practically non-toxic to freshwater fish (LC_{50} >105.8 -117 ppm). Studies on degradates (TMG, MNG, and TZNG) indicated a similar practically non-toxic profile (LC_{50} >105 ppm). EFED will use the worst case value (LC_{50} >105.8 ppm) for evaluating acute toxic exposure to freshwater fish. The guideline (72-1) is fulfilled (MRID #45422407; MRID# 45422406).

Table B-9: Freshwater Fish Acute Toxicity

Species	% a.i.	96-hour LC_{50} (ppm)	Toxicity Category	MRID No. Author, Year	Study Classification
Bluegill sunfish *(Lepomis macrochirus)*	97.6	>117	Practically non-toxic	45422407 Palmer *et al.*, 2000	Core
Rainbow trout *(Oncorhynchus mykiss)*	96	>105.8	Practically non-toxic	45422406 Wilhelmy *et al.*, 1998	Supplemental
Rainbow trout *(Oncorhynchus mykiss)*	95.1 TMG	>110	Practically non-toxic	45422408 Dorgerloh, 2000	Supplemental
Rainbow trout *(Oncorhynchus mykiss)*	99.0 MNG	>105	Practically non-toxic	45422409 Dorgerloh, 2000	Supplemental
Rainbow trout *(Oncorhynchus mykiss)*	99.0 TZNG	>116	Practically non-toxic	45422410 Dorgerloh, 2000	Supplemental

ii. Freshwater Fish, Chronic

A freshwater fish early life-stage test using the TGAI is required for clothianidin because the end-use product may be transported to water from the intended use site (i.e., corn and canola), and the following conditions are met: (1) clothianidin is intended for use such that its presence in water is likely to be continuous or recurrent regardless of toxicity; (2) studies on aquatic invertebrates showed reproductive effects (daphnid 21-day LOAEC = 0.12 ppm) and (3) clothianidin is persistent in water (e.g., half-life of 744 days aerobic soil metabolism).

A chronic early life stage study conducted on the fathead minnow showed that exposure of 20 ppm has the potential to affect length and dry weight of freshwater fish. The NOAEC of 9.7 ppm will be used for risk assessment purposes. The guideline (72-4) is fulfilled (MRID #45422413).

Table B-10: Freshwater Fish Early Life-Stage Toxicity

Species	% a.i.	NOAEC/LOAEC (ppm)	Endpoints Affected	MRID No. Author, Year	Study Classification
Fathead minnow (*Pimephales promelas*)	97.6	9.7/20	Length and dry weight	45422413 Drottar *et al.*, 2000	Supplemental

iii. Freshwater Invertebrates, Acute

A freshwater aquatic invertebrate toxicity test using the TGAI is required to establish the toxicity of clothianidin to aquatic invertebrates. The preferred test species is *Daphnia magna*. The data that was submitted that tested the parent compound showed that clothianidin is practically non-toxic to *Daphnia magna* with an acute 48-hour EC_{50} value of >119 ppm, but that it is very highly toxic to *Chironomus riparius* with an acute 48-hour EC_{50} value of 0.022 ppm. EFED will use the worst case value (EC_{50}= 0.022 ppm) for evaluating acute toxic exposure to freshwater invertebrates. Additional data (48-hour EC_{50}) on degradates (TZNG, MNG, and TMG) indicated a practically non-toxic to slightly toxic profile (EC_{50} = 64.0 to >115.2 ppm). The guideline requirements (72-2) for acute invertebrate toxicity are fulfilled (MRID #45422338; MRID #45422414).

Table B-11: Freshwater Invertebrate Acute Toxicity

Species	% a.i.	48-hour EC_{50} (ppm)	Toxicity category	MRID No. Author, Year	Study Classification
Waterflea (*Daphnia magna*)	99	>119	Practically non-toxic	45422338 Palmer, 2000	Core
Midge (*Chironomus riparius*)	97.6	0.022*	Very highly toxic	45422414 Mattock, 2001	Supplemental
Waterflea (*Daphnia magna*)	99.0 TZNG	64	Slightly toxic	45422401 Hendel, 2000	Core
Waterflea (*Daphnia magna*)	99.0 MNG	>100.8	Practically non-toxic	45422340 Hendel, 2000	Core
Waterflea (*Daphnia magna*)	95.1 TMG	>115.2	Practically non-toxic	45422339 Hendel, 2000	Supplemental

* The EC_{50} value for exposure to Clothianidin TI-435 was the most sensitive; EC_{50} values for TZMU, MU, and TZNG were >102 ppm, >83.6 ppm, and 0.386 ppm, respectively.

iv. Freshwater Invertebrate, Chronic

A freshwater aquatic invertebrate life-cycle test using the TGAI is required for clothianidin because the end-use product may be transported to water from the intended use site, and the following conditions are met: (1) the presence of clothianidin in water is likely to be continuous or recurrent and (2) aquatic acute LC_{50} or EC_{50} values are less than 1 ppm (i.e., 0.022 ppm), and (3) physicochemical properties indicate that clothianidin is persistent in the aquatic environment (e.g., half-life of 744 days aerobic soil metabolism).

The preferred test is a 21-day life cycle on *Daphnia magna*. The data that were submitted show that clothianidin has the potential for chronic toxicity to daphnids and possibly other freshwater invertebrates. Exposure to 0.12 ppm can result in reproductive effects, including the reduced number of juveniles produced per adult. The NOAEC of 0.042 ppm will be used in assessing risk. The guideline (72-4) is fulfilled (MRID #45422412).

Table B-12: Freshwater Aquatic Invertebrate Chronic Toxicity

Species	% a.i.	NOAEC/LOAEC (ppm)	Endpoints Affected	MRID No. Author, Year	Study Classification
Waterflea *(Daphnia magna)*	96	0.042/0.12	Reproduction	45422412 Noack *et al.*, 1998	Supplemental

vi. Freshwater Field Studies

No data submitted.

c. Toxicity to Estuarine and Marine Animals

i. Estuarine and Marine Fish, Acute

The preferred test species is sheepshead minnow. The data submitted showed that the LC_{50} = 93.6 ppm; therefore, clothianidin is categorized as slightly toxic to estuarine/marine fish on an acute basis. The guideline (72-3) is fulfilled (MRID #45422411).

Table B-13: Estuarine/Marine Fish Acute Toxicity

Species	% a.i.	96-hour LC_{50} (ppm)	Toxicity Category	MRID No. Author, Year	Study Classification
Sheepshead minnow *(Cyprinodon variegatus)*	97.6	>93.6	Slightly toxic	45422411 Scheerbaum, 1999	Supplemental

ii. Estuarine and Marine Fish, Chronic

No data submitted.

iii. Estuarine and Marine Invertebrates, Acute

Acute toxicity testing with estuarine/marine invertebrates using the TGAI is required for clothianidin because the end-use product is expected to reach this environment due to its use on crops with significant acreage in coastal counties (i.e., corn and canola). The preferred test species are mysid shrimp and eastern oyster. The data showed that clothianidin significantly reduced survival of mysid shrimp at 0.051 ppm, categorizing the compound as very highly toxic. Clothianidin was categorized as practically non-toxic to Eastern oyster because adverse effects did not occur for this species up to concentrations of 129.1 ppm. EFED will use the worst case value, LC_{50} = 0.051 ppm, for evaluating acute toxic exposure to estuarine/marine invertebrates. The data requirements (72-3b and 72-3c) are fulfilled (MRID # 45422404; MRID #45422403).

Table B-14: Estuarine/Marine Invertebrate Acute Toxicity

Species	% a.i..	96-hour acute toxicity LC_{50}/EC_{50} (ppm)	Toxicity Category	MRID No. Author, Year	Study Classification
Eastern oyster (*Crassostrea virginica*)	97.6	EC_{50} >129.1	Practically non-toxic	45422404 Scheerbaum, 1999	Core
Mysid *(Mysidopsis bahia)*	97.6	LC_{50} = 0.051	Very highly toxic	45422403 Drottar *et al.*, 2000	Core

iv. Estuarine and Marine Invertebrate, Chronic

An estuarine/marine invertebrate life-cycle toxicity test using the TGAI is required for clothianidin because the end-use product is expected to transport to an estuarine/marine environment from the intended use site (i.e., corn and canola), and the following conditions are met: (1) the pesticide is intended for use such that its presence in water is likely to be continuous or recurrent regardless of toxicity, (2) an aquatic acute LC_{50} or EC_{50} is less than 1 ppm (e.g., mysid LC_{50} = 0.051 ppm), and (3) studies of other organisms indicate that the reproductive physiology of fish and/or invertebrates may be affected, physicochemical properties indicate cumulative effects, or the pesticide is persistent in water (e.g., half-life of 744 days aerobic soil metabolism).

The preferred test species is mysid shrimp. The data submitted indicate that clothianidin reduced the number of young per reproductive day at 9.7 ppb. The NOAEC of 5.1 ppb will be used in assessing risk. The guidelines (72-4c) have been fulfilled (MRID #45422405).

Table B-15: Estuarine/Marine Invertebrate Life-Cycle Toxicity

Species	% a.i.	39-day NOAEC/LOAEC (ppb)	Endpoints Affected	MRID No. Author, Year	Study Classification
Mysid *(Mysidopsis bahia)*	97.6	5.1/9.7	Reproduction	45422405 Drottar *et al.*, 2000	Core

v. Estuarine and Marine Field Studies

No data submitted.

d. Toxicity to Aquatic and Terrestrial Plants

i. Aquatic Plants

Several aquatic plant toxicity studies using the TGAI are required to establish the toxicity of clothianidin to non-target aquatic plants. The recommendation is for testing on five species: freshwater green alga *(Selenastrum capricornutum)*, duckweed *(Lemna gibba)*, marine diatom *(Skeletonema costatum)*, blue-green algae *(Anabaena flos-aquae)*, and a freshwater diatom. Studies submitted for two of the five recommended species showed that exposure to clothianidin at levels greater than or equal to 3.5 ppm reduced biomass of aquatic non-vascular plants and increased the incidence of necrotic fronds in aquatic vascular plants. Studies on degradates (TMG, MNG and TZNG) showed reductions in green algal cell density when exposed to levels >1.46 ppm. The EC_{50} of 64 ppm will used for evaluating acute toxic exposure to non-target aquatic plants. The guideline requirements (122-2 and 123-2) are fulfilled (MRID #45422503; MRID #45422504) for two of the five required species.

Table B-16: Non-target Aquatic Plant Toxicity

Species [Study Type]	% a.i.	EC_{50}/NOAEC (ppm)	Endpoints Affected	MRID No. Author, Year	Study Classification
Duckweed (*Lemna gibba*) [Tier 2]	97.6	>121/59	Necrotic fronds	45422503 Palmer *et al.*, 2000	Core
Green Algae (*Selenastrum capricornutum*) [Tier 2]	97.6	64/3.5	Biomass	45422504 Sutherland *et al.*, 2000	Core
Green Algae (*Selenastrum capricornutum*) [Tier 2]	95.1 TMG	10/1.46	Cell density	45422505 Dorgerloh, 2000	Core
Green Algae (*Selenastrum capricornutum*) [Tier 1]	99.0 MNG	>100.6/100.6	None	45422506 Dorgerloh, 2000	Core
Green Algae (*Selenastrum capricornutum*) [Tier 1]	99.0 TZNG	>103/<103	Cell density	45422507 Dorgerloh, 2000	Core

ii. Terrestrial Plants

Terrestrial Tier II studies are required for all low dose pesticides (those with the maximum use rate of 0.5 lbs a.i./A or less) and for any pesticide showing a negative response equal to or greater than 25% in Tier I studies.

Two Tier I terrestrial plant toxicity studies were conducted to establish the toxicity of clothianidin to non-target terrestrial plants. The recommendations for seedling emergence and vegetative vigor studies are for testing of (1) six species of at least four dicotyledonous families, one species of which is soybean (*Glycine max*) and the second of which is a root crop, and (2) four species of at least two monocotyledonous families, one of which is corn (*Zea mays*). The studies that were submitted tested formulated products of clothianidin (49.3% TI-435 50% WDG). The results of these studies showed that exposure to 214-218 ppm elicited no effect on non-target terrestrial plants, so Tier II tests were not necessary. The EC_{25} of >214 ppm will used for evaluating toxic exposure to non-target terrestrial plants. The guidelines (122-1a and 122-1b) are fulfilled (MRID #45422501; MRID #45422502).

Table B-17: Non-target Terrestrial Plant Toxicity

Species [Study Type]	% a.i.	EC_{25}/ NOAEC (ppm)	Endpoints Affected	MRID No. Author, Year	Study Classification
Dicots: Soybean (*Glycine max*), Pinto bean (*Phaseolus vulgaris*), Radish (*Raphanus sativus*), Cabbage (*Brassica oleracea*), Lettuce (*Lactuca sativa*), Tomato (*Lycopersicon esculentum*) Monocots: Corn (*Zea mays*), Wheat (*Triticum aestivum*), Ryegrass (*Lolium perenne*), Onion (*Allium cepa*) [Tier I Seedling Emergence]	49.3 TI-435 50% WDG	>214/214	None	45422501 Brignole *et al.*, 2000	Core
Dicots: Soybean (*Glycine max*), Pinto bean (*Phaseolus vulgaris*), Radish (*Raphanus sativus*), Cabbage (*Brassica oleracea*), Lettuce (*Lactuca sativa*), Tomato (*Lycopersicon esculentum*) Monocots: Corn (*Zea mays*), Wheat (*Triticum aestivum*), Ryegrass (*Lolium perenne*), Onion (*Allium cepa*) [Tier 1 Vegetative Vigor]	49.3	>218/218	None	45400502 Brignole *et al.*, 2000	Core

APPENDIX C: Calculations for Seed Treatment

Acute RQ calculations for Clothianidin-treated seeds.

1) Dose for Bobwhite quail exposure to Canola seed treatment

0.0046 lbs ai/lbs seed
0.0046 lbs ai/0.45 kg seed
0.01 lbs ai/kg seed
4545 mg ai/kg seed

Dose = $(FI)(C)(T)/M_{bird}$

FI = food ingestion rate (kg/day) for Bobwhite quail = 0.0148 kg/day
C = ai concentration on seed (mg/kg)
T = time for food consumption (assume 1 day)
M_{bird} = mass (weight) of bird (kg)

$$\text{Dose} = \frac{(0.0148\ \text{kg/day})\ (4545\ \text{mg/kg seed})\ (1\text{day})}{0.178\ \text{kg}} = 378\ \text{mg/kg}$$

2) Acute dose for Bobwhite quail (0.178 kg) on Corn seed

1,200 seeds/lb
1.25 mg ai/kernel
or
1,500 mg ai/lb seed (given: 1kg = 2.2lbs)
3,300 mg ai/ 2.2 lbs seed
3,300 mg ai/ 1 kg seed

$$\text{Dose} = \frac{(0.0148\ \text{kg/day})\ (3000\ \text{mg/kg seed})\ (1\text{day})}{0.178\ \text{kg}} = 274.3\ \text{mg/kg}$$

3) Acute dose for small mammal (0.015 kg) on canola seed

$$\text{Dose} = \frac{(0.0022\ \text{kg/day})\ (454\ \text{mg/kg seed})\ (1\text{day})}{0.015\ \text{kg}} = 66.6\ \text{mg/kg}$$

4) Acute dose for small mammal (0.015 kg) on corn seed

$$\text{Dose} = \frac{(0.0022\ \text{kg/day})\ (3300\ \text{mg/kg seed})\ (1\text{day})}{0.015\ \text{kg}} = 484\ \text{mg/kg}$$

5) Number of corn seeds that will kill a Bobwhite quail (acute effects)

Label states that there is 1.25 mg ai / seed

$$\text{Seed/bird} = \frac{\text{(LD50 mg/kg) Bird weight kg)}}{\text{mg ai/ seed}}$$

$$\frac{(2000 \text{ mg/kg}) (0.178 \text{ kg})}{1.25 \text{ mg ai/ seed}} = 285 \text{ corn seeds/bird}$$

6) Number of canola seeds that will kill a Bobwhite quail (acute effects)

Label states that there is 0.6 kg ai/100 kg seed
or 600,000 mg ai / 100 kg seed. Given that 345 canola seed[1] = 1 g or 34 x 10^6 seeds / 100kg.
Therefore 600,000 mg ai / 34 x 10^6 seeds = 0.017 mg ai/seed

$$\text{Seed/bird} = \frac{\text{(LD50 mg/kg) Bird weight kg)}}{\text{mg ai/ seed}}$$

$$\frac{(2000 \text{ mg/kg}) (0.178 \text{ kg})}{0.017 \text{mg ai/ seed}} = 20{,}941 \text{ canola seeds/bird}$$

Calculations for estimating acute and chronic risk to mammals from ingestion of treated corn seed

1) $$\text{Seed/mammal} = \frac{\text{(Effect)(Mammal wt)}}{\text{(mg ai /seed)}}$$

Chronic	**Acute**
$\frac{(75 \text{ mg/kg/day})(0.015 \text{ kg})}{1.25 \text{ mg ai/seed}} = 0.9$ seeds/day	$\frac{(389 \text{ mg/kg/day})(0.015 \text{ kg})}{1.25 \text{ mg ai/seed}} = 4.7$ seeds/day
$\frac{(75 \text{ mg/kg/day}) (0.035 \text{ kg})}{1.25 \text{ mg ai/seed}} = 2.1$ seeds/day	$\frac{(75 \text{ mg/kg/day}) (0.035 \text{ kg})}{1.25 \text{ mg ai/seed}} = 10$ seeds/day

---

[1]Seed weight was obtained from the code of Federal Regulations, Section 7, Part 201, Federal Seed Act Regulation (2002)

$$\frac{(75\ mg/kg/day)\ (1.0\ kg)}{1.25\ mg\ ai/seed} = 60\ seeds/day$$

Calculations for estimating chronic risk to birds from ingestion of treated corn seed

1) Seed/bird = $\frac{(LOAEL)(Bird\ wt)}{(mg\ ai\ /seed)}$ =

Bobwhite quail $\frac{(525\ mg/kg/day)(0.178\ kg)}{1.25\ mg\ ai/seed} = 75\ seeds/day$

passerines $\frac{(525\ mg/kg/day)\ (0.020\ to\ 0.1\ kg)}{1.25\ mg\ ai/seed} = 8 - 42\ seeds/day$

Calculations for estimating chronic risk to mammals from ingestion of treated canola seed

1) Seed/bird = $\frac{(LOAEL)(Mammal\ wt)}{(mg\ ai\ /seed)}$ =

$$\frac{(75\ mg/kg/day)(0.015\ kg)}{0.017\ mg\ ai/seed} = 66\ seeds/day$$

$$\frac{(75\ mg/kg/day)\ (0.035\ kg)}{0.017\ mg\ ai/seed} = 154\ seeds/day$$

$$\frac{(75\ mg/kg/day)\ (1.0\ kg)}{0.017\ mg\ ai/seed} = 4{,}412\ seeds/day$$

Calculations for estimating chronic risk to birds from ingestion of treated canola seed

1) Seed/bird = $\frac{(LOAEL)(Bird\ wt)}{(mg\ ai\ /seed)}$ =

Bobwhite quail $\frac{(525\ mg/kg/day)(0.178\ kg)}{0.017\ mg\ ai/seed} = 5{,}497\ seeds/day$

passerines $\frac{(525\ mg/kg/day)\ (0.020\ to\ 0.1\ kg)}{0.017\ mg\ ai/seed} = 617 - 3{,}088\ seeds/day$

Appendix D: Data Requirement Table

Date: January 2003
Chemical No: 044309

CLOTHIANIDIN
DATA REQUIREMENTS FOR THE
ENVIRONMENTAL FATE AND EFFECTS DIVISION

Data Requirements	Composition[1]	Use Pattern[2]	Bibliographic Citation	Study Classification	Additional Data Required Under FIFRA
§158.290 ENVIRONMENTAL FATE					
Degradation Studies-Lab:					
161-1 Hydrolysis	PAIRA	1 and 2	45422317	Core	No
161-2 Photolysis in Water	PAIRA	1 and 2	45422318, 45422320, 45422322 45422319, 45422321	Core Supplemental	No, but related special studies are requested.
161-3 Photolysis on Soil	PAIRA	1 and 2	45422323	Core	No
Metabolism Studies-Lab:					
162-1 Aerobic Soil Metabolism	PAIRA	1 and 2	4.54223254542e+31	Core Core Supplemental Supplemental	No
162-2 Anaerobic Soil Metabolism		1 and 2			No
162-3 Anaerobic Aquatic Metabolism	PAIRA	1 and 2	45422330	Core	No
162-4 Aerobic Aquatic Metabolism	PAIRA	1 and 2	4542232445422329	Unacceptable Unacceptable	Yes
Mobility Studies:					
163-1 Mobility (unaged)	PAIRA	1 and 2	4.54223114542e+39	Core Supplemental Supplemental Supplemental Supplemental	No
163-1 Mobility (aged)		1 and 2	45422312	Supplemental	No
163-2 Laboratory volatility		1 and 2			No
163-3 Field volatility		1 and 2			No

CLOTHIANIDIN
DATA REQUIREMENTS FOR THE
ENVIRONMENTAL FATE AND EFFECTS DIVISION

Data Requirements	Composition[1]	Use Pattern[2]	Bibliographic Citation	Study Classification	Additional Data Required Under FIFRA
Dissipation Studies-Field:					
164-1 Terrestrial field dissipation	TEP	1 and 2	45422331 45422508 45422332 45422333 45422334 45422335 45422336 45422601, 45422605 45422602, 45422603 45422604 45422612 45422337	Supplemental Supplemental Core Core Core Core Core Supplemental Supplemental Supplemental Supplemental Supplemental	No
Accumulation Studies:					
165-4 Fish bioaccumulation		1 and 2			No
Ground Water Monitoring Studies:					
166-1 Small scale prospective groundwater study.	TEP	1 and 2			Reserved
§158.440 SPRAY DRIFT					
201-1 Droplet Size Spectrum					
202-1 Drift Field Evaluation					

1. Composition: PAIRA=Technical grade of the active ingredient; PAIRA=Pure active ingredient, radiolabeled; TEP=Typical end-use product

2. Use Patterns: 1=Terrestrial/Food; 2=Terrestrial/Feed; 3=Terrestrial Non-Food; 4=Aquatic Food; 5=Aquatic Non-Food (Outdoor); 6=Aquatic Non-Food (Industrial); 7=Aquatic Non-Food (Residential); 8=Greenhouse Food; 9=Greenhouse Non-Food; 10=Forestry; 11=Residential Outdoor; 12=Indoor Food; 13=Indoor Non-Food; 14=Indoor Medical; 15=Indoor Residential

Data Requirements	Composition[1]	Use Pattern[2]	Bibliographic Citation	Study Classification	Additional Data Required Under FIFRA

§158.490 WILDLIFE AND AQUATIC ORGANISMS

Avian and Mammal Studies:

Data Requirements	Composition[1]	Use Pattern[2]	Bibliographic Citation	Study Classification	Additional Data Required Under FIFRA
71-1(a) Acute Avian Oral, Quail	TGAI	1 and 2	45422417 45422418	Core Supplemental	No
71-1(b) Acute Avian Oral, Quail/Duck	(TEP)	1 and 2	Not applicable		No
71-2(a) Acute Avian Diet, Quail	TGAI	1 and 2	45422419	Core	No
71-2(b) Acute Avian Diet, Duck	TGAI	1 and 2	45422420	Core	No
71-3 Wild Mammal Toxicity		1 and 2	Not applicable		No
71-4(a) Avian Reproduction, Quail	TGAI	1 and 2	45422421	Core	No
71-4(b) Avian Reproduction, Duck	TGAI	1 and 2	45422422	Supplemental	No
71-5(a) Simulated Terrestrial Field Study					
71-5(b) Actual Terrestrial Field Study					
Non-guideline Avian Acute Dietary, Quail/Pigeon	TGAI	1 and 2	45422515 45422516 45422517	Supplemental Supplemental Supplemental	No
Freshwater Fish Studies:					
72-1(a) Acute Fish Toxicity, Bluegill	TGAI	1 and 2	45422407	Core	No
72-1(c) Acute Fish Toxicity, Rainbow Trout	TGAI	1 and 2	45422406	Supplemental	No
72-1(d) Acute Fish Toxicity, Rainbow Trout	DEG	1 and 2	45422408 45422409 45422410	Supplemental Supplemental Supplemental	No

Data Requirements	Composition[1]	Use Pattern[2]	Bibliographic Citation	Study Classification	Additional Data Required Under FIFRA
Freshwater Invertebrate Studies:					
72-2(a) Acute Aquatic Invertebrate Toxicity	TGAI	1 and 2	45422338	Core	No
72-2(b) Acute Aquatic Invertebrate Toxicity	DEG	1 and 2	45422414 45422401 45422340 45422339	Supplemental Core Core Supplemental	No
72-2 Acute Aquatic Invertebrate Toxicity	LEA	1 and 2	45422402 45422415 45422416	Invalid Invalid Invalid	Yes
OPPTS 850.1790 Chronic Freshwater Invertebrate Sediment Toxicity	TGAI	1 and 2	45422509	Invalid	Yes
OPPTS 850.1790 Chronic Freshwater Invertebrate Sediment Toxicity	DEG	1 and 2	45422510	Invalid	Yes
Freshwater/Estuarine/Marine Fish Studies:					
72-3(a) Acute Estu/Mari Tox Fish	TGAI	1 and 2	45422411	Supplemental	No
72-3(b) Acute Estu/Mari Tox Mollusk	TGAI	1 and 2	45422404	Core	No
72-3(c) Acute Estu/Mari Tox Shrimp	TGAI	1 and 2	45422403	Core	No
72-3(d) Acute Estu/Mari Tox Fish	(TEP)	1 and 2	Not applicable		No[3]
72-3(e) Acute Estu/Mari Tox Mollusk	(TEP)	1 and 2	Not applicable		No[3]
72-3(f) Acute Estu/Mari Tox Shrimp	(TEP)	1 and 2	Not applicable		No[3]
72-4(a) Early Life-Stage Fish	TGAI	1 and 2	45422413	Supplemental	No
72-4(b) Life Cycle Aquatic Invertebrate	TGAI	1 and 2	45422412 45422405	Supplemental Core	No

Data Requirements	Composition[1]	Use Pattern[2]	Bibliographic Citation	Study Classification	Additional Data Required Under FIFRA
72-5 Life Cycle Fish (Freshwater Fish)	TGAI	1 and 2			No[3]
72-6 Aquatic Org. Accumulation	TGAI	1 and 2	Not applicable		No
72-7(a) Simulated Aquatic Field Study		1 and 2	Not applicable		No
72-7(b) Actual Aquatic Field Study		1 and 2	Not applicable		No
§158.540 PLANT PROTECTION					
Terrestrial and Aquatic Plant Studies:					
122-1(a) Seed Germ./Seedling Emerg.-Tier I	DEG	1 and 2	45422501	Core	No
122-1(b) Vegetative Vigor-Tier I	DEG	1 and 2	45422502	Core	No
122-2 Aquatic Plant Growth-Tier I	DEG	1 and 2	45422506 45422507	Core Core	No
123-1(a) Seed Germ./Seedling Emerg.-Tier II	(TEP)	1 and 2			No
123-1(b) Vegetative Vigor-Tier II	(TEP)	1 and 2			No
123-2 Aquatic Plant Growth-Tier II	TGAI	1 and 2	45422503 45422504 45422505	Core Core Core	Yes[4]
124-1 Terrestrial Field Study		1 and 2	Not applicable		No
124-2 Aquatic Field Study		1 and 2	Not applicable		No
§158.490 INSECT TESTING					
Terrestrial Insect Studies:					
141-1 Honey Bee Acute Contact	TGAI	1 and 2			No

Data Requirements	Composition[1]	Use Pattern[2]	Bibliographic Citation	Study Classification	Additional Data Required Under FIFRA
141-1 Honey Bee Acute Contact	DEG	1 and 2	45422426 45422427 45422428 45422429 45422430	Core Core Core Core Core	No
141-2 Honey Bee Residue on Foliage	(TEP)	1 and 2	Not applicable		No

Data Requirements	Composition[1]	Use Pattern[2]	Bibliographic Citation	Study Classification	Additional Data Required Under FIFRA
141-5 Field Test for Pollinators	TGAI	1 and 2	45422431 45422432 45422433 45422434 45422435 45422436 45422437 45422438 45422439 45422440	Supplemental Supplemental Invalid Invalid Supplemental Supplemental Supplemental Invalid Invalid Supplemental	No
70.1 Special Study : Evaluate effects in bee hive		1 and 2			Yes
Terrestrial Invertebrate Studies:					
OPPTS 850.6200 Subchronic Invertebrate, Earthworm	TGAI	1 and 2	45422511	Supplemental	No
OPPTS 850.6200 Subchronic Invertebrate, Earthworm	DEG	1 and 2	45422512 45422513	Supplemental Supplemental	No
Non-guideline Chronic Invertebrate Reproduction Toxicity, Earthworm	TGAI	1 and 2	45422525	Supplemental	No
Non-guideline Field Invertebrate Population Toxicity, Earthworm	TGAI	1 and 2	45422526	Supplemental	No

1. Composition: PAIRA=Technical grade of the active ingredient; PAIRA=Pure active ingredient, radiolabeled; TEP=Typical end-use product

2. Use Patterns: 1=Terrestrial/Food; 2=Terrestrial/Feed; 3=Terrestrial Non-Food; 4=Aquatic Food; 5=Aquatic Non-Food (Outdoor); 6=Aquatic Non-Food (Industrial); 7=Aquatic Non-Food (Residential); 8=Greenhouse Food; 9=Greenhouse Non-Food; 10=Forestry; 11=Residential Outdoor; 12=Indoor Food; 13=Indoor Non-Food; 14=Indoor Medical; 15=Indoor Residential

3. May be required in the future.

APPENDIX E: Aquatic Exposure: Sci-Grow, GENEEC, and First Water Quality Modeling Results

Clothianidin: GENEEC Results

With GENEEC2, the modeling results were exactly the same for corn and canola (even though the application rate for corn is about twice the rate for canola, the deeper incorporation for treated corn seed reduced the amount available for runoff by about one half compared to canola).

Ecological risk was assessed with photolysis (from soil surface) Half-Life of 34 days (Used in place of the aqueous photolysis half-life of 1.10 days because there was much greater stability in water in aquatic toxicity studies as well as field studies where clothianidin was applied to the soil surface), the results were:

GENERIC EECs (IN MICROGRAMS/LITER (PPB)) Version 2.0 Aug 1, 2001
Aqueous Half-life = 34 days

PEAK GEEC	MAX 4 DAY AVG GEEC	MAX 21 DAY AVG GEEC	MAX 60 DAY AVG GEEC	MAX 90 DAY AVG GEEC
2.44	2.44	2.42	2.39	2.37

Note that this represents a deviation from the usual use of the aqueous photolysis study (half-life of 1.10 days):

GENERIC EECs (IN MICROGRAMS/LITER (PPB)) Version 2.0 Aug 1, 2001
Aqueous Half-life = 1.10 days

PEAK GEEC	MAX 4 DAY AVG GEEC	MAX 21 DAY AVG GEEC	MAX 60 DAY AVG GEEC	MAX 90 DAY AVG GEEC
2.44	2.43	2.36	2.21	2.11

Table E-1. Input parameters for GENEEC2 - Use of Clothianidin as a seed treatment October, 2002 - Using model version dated 08/05/01 and input selection guidance dated 02/28/02. These are the input values used in the ecological risk assessment.

Input	Value	Source	Comments
Run #	3 (corn) 5 (canola)		Reviewer's choice
Output File name	GENEEC_CLOTHI3.TXT		Reviewer's choice
Chemical name	Clothianidin		Also known as TI-435.
Crop name	Corn	Proposed label	Seed treatment

	Canola		
Application rate (lb ai/acre)	0.1	Proposed label treatment rate of 1.25 mg ai/ individual corn seed	Based on seeding density of 90,000 seeds per hectare (MRID 45422423 - field toxicity effects on birds) - converts to 36,400 seeds per acre
	0.05	Proposed label maximum treatment rate of 0.6 kg ai/ 100 kg canola seed	Based on seeding rate of approximately 8 kg seed per hectare (MRID 45422424 - field toxicity effects on birds)
Maximum number of applications/year	1	Proposed label	Seed treatment only
Koc	84	MRID 45422311	Lowest non-sand value; Lächer Höf silt loam
Soil aerobic metabolic half-life (days)	744	MRIDs 45422325 & 45422326	Calculated per guidance for n = 9. Fugay soil not included in calculation because too little degradation occurred to accurately calculate half-life.
Pesticide wetted in? (Yes/no)	No		Seed treatment
Method of application	Granular		Seed treatment use is treated as granular for purposes of GENEEC
Incorporation depth (inches)	2	corn	Based on planting depth of 4-5 cm (MRID 45422423 - field toxicity effects on birds)
	0.5	canola	Based on planting depth of 1 cm (MRID 45422519 - laboratory toxicity effects on spiders)
Solubility (ppm)	300	MRID 45422317	Solubility stated as 300 mg/L
Aquatic metabolic half-life (days)	1488	MRID 45422324	2x aerobic soil half-life used since there was no acceptable aerobic aquatic study.

Aquatic photolysis half-life (days)	1.1 to 34	MRID 45422323 (soil); 45422318, 45422320, & 45422322, 45422319, 45422321 (water)	Longest half-life of 34 days used instead of aqueous photolysis half-life because of demonstrated persistence in water and on soil surface exposed to sunlight. Lower value of 1.1 days used from natural water photolysis study.

RUN No. 3 FOR Clothianidin (TI-435) ON **Corn** * INPUT VALUES *

Using 2x aerobic half-life for aquatic metabolism, 34-day aqueous photolysis half-life.

RATE (#/AC) ONE(MULT)	No.APPS & INTERVAL	SOIL Koc	SOLUBIL (PPM)	APPL TYPE (%DRIFT)	NO-SPRAY (FT)	INCORP (IN)
.100(.100)	1 1	84.0	300.0	GRANUL(.0)	.0	2.0

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (POND)	PHOTOLYSIS (POND-EFF)	METABOLIC (POND)	COMBINED (POND)
744.00	2	N/A	34.00- 4216.00	******	1099.83

GENERIC EECs (IN MICROGRAMS/LITER (PPB)) Version 2.0 Aug 1, 2001

PEAK GEEC	MAX 4 DAY AVG GEEC	MAX 21 DAY AVG GEEC	MAX 60 DAY AVG GEEC	MAX 90 DAY AVG GEEC
2.44	2.44	2.42	2.39	2.37

RUN No. 4 FOR Clothianidin (TI-435) ON **Corn** * INPUT VALUES *

Using 2x aerobic half-life for aquatic metabolism, 1.10-day aqueous photolysis half-life.

RATE (#/AC) ONE(MULT)	No.APPS & INTERVAL	SOIL Koc	SOLUBIL (PPM)	APPL TYPE (%DRIFT)	NO-SPRAY (FT)	INCORP (IN)
.100(.100)	1 1	84.0	300.0	GRANUL(.0)	.0	2.0

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (POND)	PHOTOLYSIS (POND-EFF)	METABOLIC (POND)	COMBINED (POND)
744.00	2	N/A	1.10- 136.40	******	124.95

GENERIC EECs (IN MICROGRAMS/LITER (PPB)) Version 2.0 Aug 1, 2001

PEAK GEEC	MAX 4 DAY AVG GEEC	MAX 21 DAY AVG GEEC	MAX 60 DAY AVG GEEC	MAX 90 DAY AVG GEEC
2.44	2.43	2.36	2.21	2.11

RUN No. 5 FOR Clothianidin (TI-435) ON **Canola** * INPUT VALUES *
Using 2x aerobic half-life for aquatic metabolism, 34-day aqueous photolysis half-life.

RATE (#/AC) ONE(MULT)	No.APPS & INTERVAL	SOIL Koc	SOLUBIL (PPM)	APPL TYPE (%DRIFT)	NO-SPRAY (FT)	INCORP (IN)
.050(.050)	1 1	84.0	300.0	GRANUL(.0)	.0	1.0

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (POND)	PHOTOLYSIS (POND-EFF)	METABOLIC (POND)	COMBINED (POND)
744.00	2	N/A	34.00- 4216.00	******	1099.83

GENERIC EECs (IN MICROGRAMS/LITER (PPB)) Version 2.0 Aug 1, 2001

PEAK GEEC	MAX 4 DAY AVG GEEC	MAX 21 DAY AVG GEEC	MAX 60 DAY AVG GEEC	MAX 90 DAY AVG GEEC
2.44	2.44	2.42	2.39	2.37

RUN No. 6 FOR Clothianidin (TI ON **Canola** * INPUT VALUES *
Using 2x aerobic half-life for aquatic metabolism, 1.10-day aqueous photolysis half-life.

RATE (#/AC) ONE(MULT)	No.APPS & INTERVAL	SOIL Koc	SOLUBIL (PPM)	APPL TYPE (%DRIFT)	NO-SPRAY (FT)	INCORP (IN)
.050(.050)	1 1	84.0	300.0	GRANUL(.0)	.0	1.0

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (POND)	PHOTOLYSIS (POND-EFF)	METABOLIC (POND)	COMBINED (POND)
744.00	2	N/A	.14- 17.36	******	17.16

GENERIC EECs (IN MICROGRAMS/LITER (PPB)) Version 2.0 Aug 1, 2001

PEAK GEEC	MAX 4 DAY AVG GEEC	MAX 21 DAY AVG GEEC	MAX 60 DAY AVG GEEC	MAX 90 DAY AVG GEEC

2.44	2.43	2.36	2.21	2.11

FIRST Modeling Inputs and Results

Note: Inputs were the same as for GENEEC2 (see Table E-1).

RUN No. 1 FOR Clothianidin ON Corn * INPUT VALUES *

Using 34-day photolysis half-life, 1488-day aerobic aquatic half-life.

RATE (#/AC) ONE(MULT)	No.APPS & INTERVAL	SOIL Koc	SOLUBIL (PPM)	APPL TYPE (%DRIFT)	%CROPPED AREA	INCORP (IN)
.100(.100)	1 1	84.0	300.0	GRANUL(.0)	46.0	2.0

FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (RESERVOIR)	PHOTOLYSIS (RES.-EFF)	METABOLIC (RESER.)	COMBINED (RESER.)
744.00	2	N/A	-34.00--4216.00	******	1488.00

UNTREATED WATER CONC (MICROGRAMS/LITER (PPB)) Ver 1.0 AUG 1, 2001

PEAK DAY (ACUTE) CONCENTRATION	ANNUAL AVERAGE (CHRONIC) CONCENTRATION
2.099	1.164

RUN No. 2 FOR Clothianidin ON Canola * INPUT VALUES *

Using 34-day photolysis half-life, 1488-day aerobic aquatic half-life.

RATE (#/AC) ONE(MULT)	No.APPS & INTERVAL	SOIL Koc	SOLUBIL (PPM)	APPL TYPE (%DRIFT)	%CROPPED AREA	INCORP (IN)
.050(.050)	1 1	84.0	300.0	GRANUL(.0)	87.0	1.0

FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (RESERVOIR)	PHOTOLYSIS (RES.-EFF)	METABOLIC (RESER.)	COMBINED (RESER.)
744.00	2	N/A	34.00- 4216.00	******	1099.83

UNTREATED WATER CONC (MICROGRAMS/LITER (PPB)) Ver 1.0 AUG 1, 2001

PEAK DAY (ACUTE) CONCENTRATION	ANNUAL AVERAGE (CHRONIC) CONCENTRATION

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--------------------------------------------------------------------
          3.969                          2.140


     RUN No.   4 FOR Clothianidin     ON    Canola          * INPUT VALUES *
Using 1.10 day photolysis half-life, 1488-day aerobic aquatic half-life.
 --------------------------------------------------------------------
   RATE (#/AC)    No.APPS &    SOIL  SOLUBIL  APPL TYPE  %CROPPED INCORP
    ONE(MULT)     INTERVAL     Koc   (PPM )   (%DRIFT)     AREA    (IN)
 --------------------------------------------------------------------
 .050(   .050)    1   1       84.0  300.0   GRANUL(  .0)  87.0    1.0

 FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)
 --------------------------------------------------------------------
 METABOLIC  DAYS UNTIL  HYDROLYSIS   PHOTOLYSIS   METABOLIC  COMBINED
  (FIELD)  RAIN/RUNOFF  (RESERVOIR)  (RES.-EFF)   (RESER.)   (RESER.)
 --------------------------------------------------------------------
  744.00        2           N/A       .14-    17.36   ******      17.16

 UNTREATED WATER CONC (MICROGRAMS/LITER (PPB))     Ver 1.0 AUG 1, 2001
 --------------------------------------------------------------------
      PEAK DAY  (ACUTE)        ANNUAL AVERAGE (CHRONIC)
       CONCENTRATION                 CONCENTRATION
 --------------------------------------------------------------------
        3.969                          1.058
```

SCI-GROW Modeling Inputs and Results

Table E-2. Environmental fate input parameters for clothianidin in SCI-GROW.

Using model version dated 08/01/01 and input selection guidance dated 02/28/02.		
Parameter	**Clothianidin**	**Source**
Application rate (lb ai/acre)	0.1	Proposed label treatment rate of 1.25 mg ai/ individual corn seed or kernal
Organic Carbon Partition Coefficient (Koc)	84	MRID 45422311. Minimum value calculated per guidance for pesticides with widely varying Kocs.
Aerobic Soil Metabolism Half-Life (days)	33	MRIDs 45422325 & 45422326. Median value calculated per guidance for pesticides with aerobic metabolism studies in more than 4 soils.

SCI-GROW Model Output:

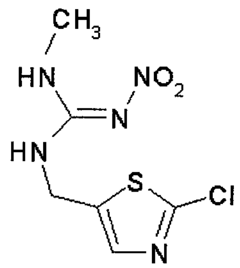
```
               VERSION 2.2: NOVEMBER 1, 2001

RUN No.    1 FOR Clothianidin        ** INPUT VALUES **
--------------------------------------------------------
 APP RATE    APPS/   TOTAL/     SOIL   AEROBIC SOIL METAB
 (LBS/AC)    YEAR    SEASON     KOC     HALFLIFE (DAYS)
--------------------------------------------------------
    .100       1       .100      84.0      533.00

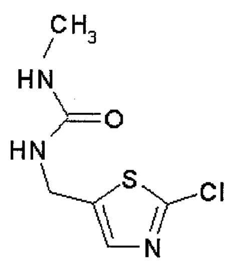

GROUND-WATER SCREENING CONCENTRATION (IN UG/L - PPB)
--------------------------------------------------------
                        1.455433
--------------------------------------------------------
```

Appendix I: Structures of Clothianidin and its Degradates

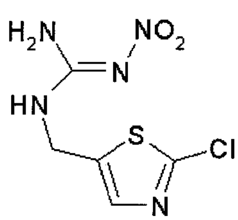
Parent TI-435
Clothianidin



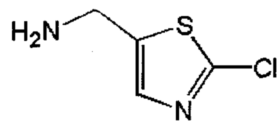
Degradate 1
TZMU
N-(2-chloro-5-thiazolyl-methyl)-N'-methylurea
(aka TI-435 urea)



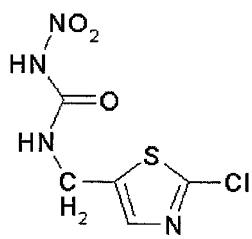
Degradate 2
TZNG
N-(2-chloro-5-thiazolyl methyl)- *N'*-nitroguanidine (aka desmethyl TI435)



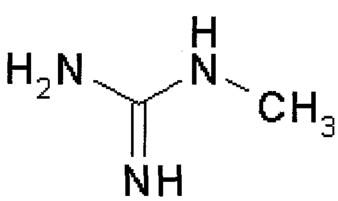
Degradate 3
ACT
2-chlorothiazol-5-yl
methylamine



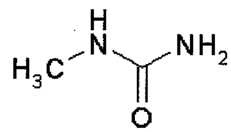
Degradate 4
CTNU
N-(2-chlorothiazol-5-ylmethyl)-*N'*-nitrourea



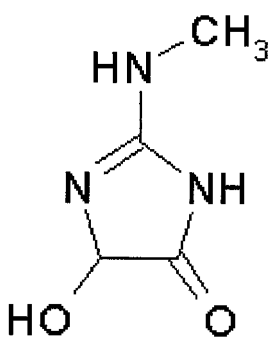
Degradate 5
MG
Methylguanidine



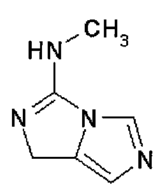
Degradate 6
MU
Methylurea



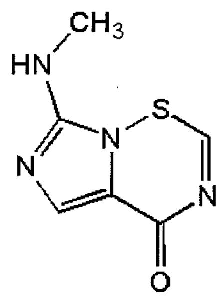
Degradate 7
HMIO
4-Hydroxy-2-methylamino-2-imidazolin-5-one



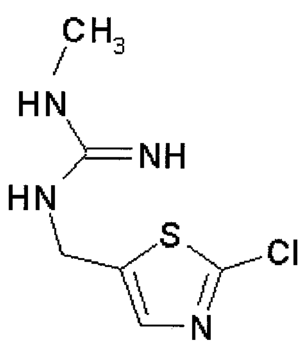
Degradate 8
MAI
3-Methylamino-1*H*-imidazo [1,5-c]-imidazole



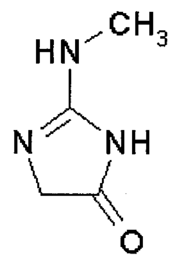
Degradate 9
MIT
7-Methylamino-4H-imidazo[5,1-b][1,2,5]thiadiazin-4-one



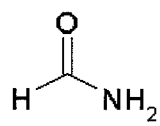
Degradate 10
TMG
N-(2-chlorothiazol-5-ylmethyl)- *N'*-methyl guanidine



Degradate 11
MIO
2-Methylamino-2-imidazolin-5-one



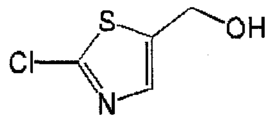
Degradate 12
FA
Formamide



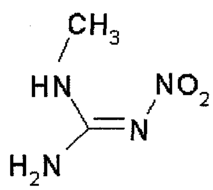
Degradate 13
Urea

Degradate 14
CTCA
2-Chlorothiazole-5-carboxylic acid

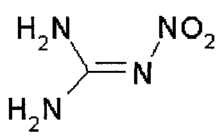
Degradate 15
TZOH
2-Chlorothiazol-5-yl
methanol



Degradate 16
MNG
N-methyl-N'-
nitroguanidine



Degradate 17
NG (NTG)
Nitroguanidine



Degradate 18
TZU
N-(2 chloro-5-thiazolylmethyl) urea