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Denise M. Sheehan
Acting
Commissioner

November 16, 2005

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Ms. Karen Cain
State Regulatory Affairs Team Lead
Bayer CropScience
Research Triangle Park
P.O. Box 12014
Research Triangle Park, North Carolina 27709

Dear Ms. Cain:

Re: Withdrawal of Application for Registration of the New Product Poncho 600 (EPA Reg. No. 264-789-7501) Which Contains the New Active Ingredient Clothianidin

The New York State Department of Environmental Conservation (Department) acknowledges your request for **withdrawal** of your application for registration of one new pesticide product, Poncho 600 (EPA Reg. No. 264-789-7501), in New York State. The Department has reviewed your application, received April 27, 2004, and additional information, received September 30, 2004, February 23, 2005 and April 27, 2005, for registration of the new product. The product contains the new active ingredient **clothianidin** (chemical code 044309).

The application was deemed complete on June 13, 2005 and a registration decision was due by November 10, 2005.

Clothianidin is a new chloronicotinyl insecticide labeled as a seed treatment for use on canola, rapeseed and corn for the control of certain insect pests. The product is labeled for use in commercial liquid or slurry treaters by commercial treaters. The product is not for use in agricultural establishments in hopper-box, slurry-box, or similar on farm seed treatment applicators used at planting.

All seed treated with this product must be conspicuously colored at the time of treatment. An appropriate colorant must be added when this product is applied to seed to distinguish and prevent subsequent inadvertent use as a food for man or feed for animals. Regulations pertaining to coloration of treated seed enforced by 40 CFR § 153.155 must be strictly adhered to when using this product. Seed commercially treated with Poncho 600 must be labeled in compliance with the Federal Seed Act and as specified on the Poncho 600 label.

The Department has reviewed the information supplied to date in support of registration of the new product Poncho 600 (EPA Reg. No. 264-789-7501).

HUMAN HEALTH EFFECTS:

The New York State Department of Health (DOH) stated that neither the active ingredient, clothianidin, nor the formulated product, Poncho 600, was very acutely toxic to laboratory animals by the oral, dermal or inhalation routes of exposure. In addition, both the active ingredient and formulated product were not very irritating to the eyes or skin (tested on rabbits), nor were they skin sensitizers (tested on guinea pigs).

Clothianidin caused some toxicity in chronic animal feeding studies. In a one-year dog feeding study, signs of anemia (decreases in red blood cells, hematocrit and hemoglobin) were observed in females at a dose of 52.9 milligrams per kilogram body weight per day (mg/kg/day); the no-observed-effect level (NOEL) was 40.1 mg/kg/day. In males, no adverse effects were observed up to the highest dose tested which was 46.4 mg/kg/day. In a chronic feeding/oncogenicity study in mice, clothianidin caused decreased body weight and body weight gain in males at 254.1 and in females at 215.9 mg/kg/day; the respective NOELs were 171.4 and 65.1 mg/kg/day. In a chronic feeding/oncogenicity study in rats, histopathological liver effects, and decreases in body weights and food consumption were observed in males and females at doses of 156.5 and 97.8 mg/kg/day, respectively. Also, histopathological changes of the kidneys (males only) and ovaries were observed at these respective doses with corresponding NOELs of 82 and 32.5 mg/kg/day.

Clothianidin caused some developmental toxicity in the offspring of pregnant rabbits, but not pregnant rats, administered this chemical during organogenesis at doses that also caused maternal toxicity. In rabbits, an increased incidence of a missing lobe of the lung and a decreased incidence of ossified sternal centra were reported at a maternal dose of 75 mg/kg/day; the NOEL was 25 mg/kg/day. Maternal toxicity (decreased food consumption and body weight gain, early delivery) was reported at 75 mg/kg/day with a NOEL of 25 mg/kg/day. In rats, no developmental toxicity was reported at the highest dose tested (125 mg/kg/day). Maternal animals showed a decrease in body weight gain and food consumption at 40 mg/kg/day; the NOEL was 10 mg/kg/day. In a rat multi-generation reproduction study, a decrease in absolute thymus weight in both males and females and a delay in sexual maturation (males only) were reported at doses of 31.2 (males) and 36.8 mg/kg/day (females). The respective NOELs were 9.8 and 11.5 mg/kg/day. Also observed in males were a decrease in sperm motility and an increased number of sperm with detached heads at a dose of 163.4 mg/kg/day, with a NOEL of 31.2 mg/kg/day. Parental toxicity, characterized by a decrease in body weight, body weight gain and absolute and relative thymus weights occurred in males and females at doses of 163.4 and 188.8 mg/kg/day, respectively, with respective NOELs of 31.2 and 36.8 mg/kg/day. The United States Environmental Protection Agency (USEPA) Office of Pesticide Programs calculated an oral reference dose (RfD) for clothianidin of 0.0098 mg/kg/day based on the NOEL of 9.8 mg/kg/day in the rat multi-generation reproduction study and an uncertainty factor of 1,000 (10x to account for intraspecies differences, 10x to account for interspecies differences and an additional 10x to account for a lack of a developmental immunotoxicity study). This RfD value has not yet been adopted by the USEPA Integrated Risk Information System.

The USEPA determined that clothianidin did not cause a statistically significant increase in tumors in either mice or rats. In addition, this chemical generally gave negative results in genotoxicity studies. Based on the lack of evidence for carcinogenicity in rats and mice, the USEPA classified clothianidin as "not likely to be a human carcinogen."

The USEPA established tolerances for clothianidin residues in or on corn (sweet, kernel plus cob with husk removed) at 0.01 parts per million (ppm) and canola seed (0.01 ppm). The chronic population adjusted dose (cPAD) for clothianidin is 0.0098 mg/kg/day and has the same basis as the RfD. The USEPA estimated that chronic dietary exposure to clothianidin would be 5.9 percent of the cPAD for the general U.S. population, 9.8 percent for infants less than one year old, 18 percent for children one to two years old and 13 percent for children three to five years old. This chronic exposure analysis is based on the conservative assumptions of 100 percent crop-treatment and tolerance level residues of clothianidin.

The USEPA conducted a risk assessment for dermal and inhalation exposures of workers to clothianidin. For loaders/applicators, a margin of exposure (MOE) was estimated to be 380 for combined dermal and inhalation exposures and was based on a worker treating 250,000 pounds of seeds per day using 0.4 pounds of clothianidin per 100 pounds of seeds (the maximum labeled application rate). For this MOE estimate, it was assumed that workers wore a single layer of clothing and gloves (the Poncho 600 label requires long-sleeved shirt, long pants, shoes plus socks and chemical-resistant gloves). The USEPA used a dermal absorption factor of one percent (based on study data in monkeys) and assumed 100 percent absorption for inhalation exposure. The NOEL used for estimating the MOE was 9.8 mg/kg/day from the rat multi-generation reproduction study. Generally, the USEPA considers MOEs of 100-fold or greater to provide adequate worker protection. For post-application exposures (handling and planting of treated seeds) of workers, the MOEs ranged from 15,000 to 26,000.

There are no chemical specific federal or New York State drinking water/groundwater standards for clothianidin. Based on its chemical structure, clothianidin falls under the 50 microgram per liter New York State drinking water standard for "unspecified organic contaminants" (10 NYCRR Part 5, Public Water Systems).

The available information on clothianidin and Poncho 600 indicates that neither the active ingredient nor the formulated product is very acutely toxic in laboratory animal studies. Furthermore, clothianidin was not carcinogenic in rats or mice. Although data from chronic and developmental/reproductive studies showed that this chemical has the potential to cause some toxicity, the estimated risks to workers from use of the Poncho 600 product are within the range that is generally considered acceptable by the USEPA. In addition, dietary exposure of the general public to clothianidin from the labeled crops is not expected to pose significant health risks.

ECOLOGICAL EFFECTS:

The USEPA review data indicates the following:

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

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

Clothianidin is practically non-toxic to the blue-gill sunfish, 96-hour LC_{50} = 117 ppm, and practically non-toxic to the rainbow trout, 96-hour LC_{50} = 105 ppm. It ranges from very highly toxic to *Chronomus riparius*, 48-hour EC_{50} = 0.022 ppm, to practically non-toxic to *Daphnia magna*, 48-hour EC_{50} = 110 ppm. It does not appear to present a risk to terrestrial plants, aquatic vascular plants or aquatic nonvascular plants. There is concern for the persistence of clothianidin in aquatic sediments, and uncertainty about effects on benthic organisms. As a condition of registration, a sediment toxicity test on the midge, *Chronomus riparius*, is required.

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

Clothianidin is categorized as highly toxic to bees on an acute oral and contact basis. In the Honey Bee Acute Contact and Oral Toxicity test, the LD_{50} value for the oral test was 0.0037 µg a.i./bee with a NOEL of 0.0009 µg a.i./bee. The Office of Pesticide Programs does not have a categorization scheme for acute oral toxicity to honey bees. However, according to the acute oral toxicity categorization scheme based on ICBB (1985), an LD_{50} less than 1.0 µg a.i./bee is considered highly toxic. The results of the contact test was an LD_{50} value of 0.044 µg a.i./bee with a NOEL of 0.0095 µg a.i./bee. According to toxicity category descriptions for honey bee acute contact toxicity, an LD_{50} less than 2 µg a.i./bee is considered highly toxic.

Other neonicotinoid compounds have resulted in incidents to honey bees. The National Union of French Beekeepers had concerns regarding imidacloprid seed treatments 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 confirmed imidacloprid toxic residue levels in the sunflower nectar. This 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.

The use of clothianidin as a seed treatment reduces the possibility of acute toxic risk to birds and mammals. However, this use pattern has the potential for chronic toxic risk to birds (≤0.178 kg) and mammals (0.035 - 0.15 kg) through seed ingestion during foraging in treated fields, as well as acute toxic risk to aquatic invertebrates from runoff.

There is also uncertainty regarding 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 that are exposed in utero. Mammalian data shows that ingestion of clothianidin treated seeds can result in developmental effects and the data also suggests that chronic toxicity in mammals can be manifested as systemic effects. 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.

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 site there was so little decline in clothianidin residues over 25 months that a dissipation half-life could not be calculated). Photolysis appears to be much more rapid than other avenues of degradation/dissipation of clothianidin in the laboratory studies, however, the very slow rate of dissipation observed in field studies suggests photolysis probably is not significant under most actual-use conditions.

Available data indicate that clothianidin on corn and canola should result in minimal acute toxic risk to birds. However, assessments show that exposure to treated seeds through ingestion may result in chronic toxic risk to non-endangered and endangered small birds (e.g., songbirds) and acute/chronic toxicity risk to non-endangered and endangered mammals. Clothianidin, when used as a seed treatment, has the potential for toxic chronic exposure to honey bees, as well as other nontarget pollinators, through the translocation of clothianidin residues in nectar and pollen. Clothianidin should not present a direct acute or chronic risk to freshwater and estuarine/marine fish, or a risk to terrestrial or aquatic vascular and nonvascular plants. The fate and disposition of clothianidin in the environment suggest a compound that is a systemic insecticide that is persistent and mobile, stable to hydrolysis, and has potential to leach to ground water, as well as runoff to surface waters.

Based on the high toxicity of clothianidin and the potential long-term chronic effects to honey bees, environmental persistence, possible role as an endocrine disrupter, chronic toxic risk to non-endangered and endangered small birds, and acute/chronic toxicity to non-endangered and endangered mammals, Poncho 600 should not be accepted for registration in New York State.

ENVIRONMENTAL FATE AND GROUNDWATER IMPACTS:

The Department's groundwater staff stated that the maximum labeled application rate on corn is 1.25 mg ai/kernel, or 5.64 fl oz per 80,000 unit of seed. Corn is seeded at 26,000 to 35,000 kernels per acre. According to the USEPA, at the 35,000 per acre rate, the maximum application rate is 0.1 lb ai/a/yr. The maximum application rate for canola and rapeseed is 0.024 lb ai/a/year. The inerts do not appear to be solvent carriers.

Groundwater staff stated the following:

Solubility: Clothianidin has a solubility of 327 mg/L.

Hydrolysis: The USEPA found this study acceptable. Clothianidin is stable to hydrolysis at pH's 5 and 7. At pH 9, the half life was 3.7 days at 62°C and 0.7 days at 74°C. Two major degrades were formed at pH 9. At 62°C, 2-chlorothiazol-5-ylmethylamine (ACT) reached 53.6%, and *N*-(2-chlorothiazol-5-ylmethyl)-*N*'-methylurea (TZMU) reached 14.7% of applied at 7 days post treatment. At 74°C, ACT and TZMU reached 59.2% and 22.6% respectively at 1.9 days post treatment.

Aqueous Photolysis: EPA found this study acceptable. Nitroimino- and thiazolyl- [^{14}C] clothianidin degraded rapidly in sterile, pH 7 buffer solution at 25°C under continuous irradiation; the half-lives were 3.4 and 3.1 hours respectively. Four major degradates were found in the Nitroimino-^{14}C study. Methylguanidine (MG), TZMU, 4-hydroxy-2-methylamino-2-imidazolin-5-one (HMIO) and methylurea (MU) were found with maximum concentrations of

34.7% (432 hours), 29.3% (24 hours), 26.6% (24 hours) and 11% (432 hours) of the applied, respectively. In the thiazolyl-^{14}C study, 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.

The USEPA found this study supplemental. In non-sterile river water pH 7 to 9.6, nitroimino- and thiazolyl- [^{14}C] clothianidin degraded with half-lives of 25.1 and 27.7 hours, respectively. The temperature range was 21.5 to 31.3°C. In the nitroimino-^{14}C study, clothianidin degraded to MG, HMIO and MU with concentrations of 46.5% (696 hours), 28.0% (120 hours) and 12.0% (432 hours) of the applied, respectively. In the thiazolyl-^{14}C study, clothianidin degraded mainly to CO_2 at 28.5% (696 hours), Urea, *N*-(2-clorothiazol-5-ylmethyl)-*N*'-methylguanidine (TMG), 3-methylamino-1H-imidazop1,5-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.

Soil Photolysis: EPA found this study acceptable. Clothianidin degraded with a half-life of 8.2 days in a sandy loam soil at 20°C. No major degradates occurred.

Aerobic Soil Metabolism:

Soil Type	% OC	Soil pH	Aerobic Half-life	Soil Type	% OC	Soil pH	Aerobic Half-life
silt loam[S]	2.66	7.8	148	silt loam[A]	1.37	6.74	578
silt loam[S]	0.86	8.1	239	silt loam[S]	3.27	6.66	693
loamy sand[A]	2.5	6.0	495	sandy loam[A]	1.12	6.7	990
loamy sand[S]	0.4	6.8	533	loam[S]	1.41	6.67	1155
sand[S]	0.73	6.22	533	loamy sand[S]	0.35	6.67	6932

A- EPA found this study acceptable.
S - EPA found this study supplemental.

The half-life of MNG was 65-116 days and the USEPA found the study to be supplemental. The half-life of TZNG was 53-122 days and the USEPA found the study to be supplemental. Neither was a major degradate, however, the USEPA felt that the maximum concentrations of MNG and TZNG in the soils were probably limited by the relatively rapid rate of degradation of these two compounds compared to the slower rate of degradation of clothianidin. They did not state what these two degradates degraded to.

Adsorption/Desorption:

Soil Type	% OC	Soil pH	Ads/Des Koc Parent[A]	Ads/Des Koc MNG[S]	Ads/Des Koc TZMU[S]	Ads/Des Koc TZNG[S]	Ads/Des Koc TMG[S]
loamy sand	2.5	6.0	119/170	5.2/	46.4/68.5	204.5/270.8	641.6/782.3
loamy sand	0.4	6.8		21.4/	53.3/63	261.4/346.2	6159.4/9013

sand	0.73	6.8	129/154				
silt loam	1.37	6.74		16.5/13	56/71.2	242.6/276.2	1349.5/1585
clay loam			123/139				
sandy loam			84/95	25.3/34.9	57.5/76.8	236/280.6	525/602.5
sandy loam			345/382	34.3/44	95.8/122.8	432.5/527.2	3620/4991.7

A- EPA found this study acceptable.
S - EPA found this study supplemental.

Anaerobic Aquatic Metabolism: The USEPA found this study to be acceptable. Clothianidin degraded with half-lives ranging from 14 days in the water phase, 37 days in the sediment phase, and 27 days overall. No major degradates were found.

Aerobic Aquatic Metabolism: The USEPA found this study to be unacceptable. It was prepared in response to Canadian guidelines and does not fulfill Subdivision N Guidelines.

Terrestrial Field Dissipation: The USEPA found these studies acceptable. Clothianidin degraded in a sand soil with a half-life of 277 days, in a clay loam soil with a half-life of 1386 days, in a silt loam (Canada) of 365 days, and in a silt loam of 315 days. No major degradates were found. Clothianidin was generally not detected below the 45 cm depth, and degradates were generally only detected in the 0-15 cm soil layer.

In a lysimeter study in sandy loam, no parent was found in the leachate. Approximately 60% of applied was found in the soil. One minor degradate was found in the soil. The USEPA found this study acceptable. In a second lysimeter study, no parent was found in the leachate, only minor degradates. Approximately 46% of applied was found in the soil. The USEPA found this study acceptable.

Modeling: Staff modeled clothianidin using middle of the road parameters; a K_{oc} of 170, a half-life of 495 days and the maximum application rate of 0.1 lb ai/a/yr. The model projected breakthrough in 4 months, and a consistent level of between 5 and 6 ppb.

Seed Leaching Study: Staff reviewed the seed leaching study submitted on April 8, 2005. The study appears to be typical of a column leaching study, however, it does not support the registration of this product in New York State. The study submitted was performed using loam soil containing much more organic matter and a higher pH than the vulnerable soils of New York State. Typical soils of Long Island consist of sandy loam with about 1% organic matter and a pH of 5.5 or less. Review of this study does not alleviate staff's concerns that use of this product could have a significant negative impact on groundwater quality.

Summary: This active ingredient is persistent and mobile. Modeling corn with middle of the road parameters, not worst case parameters, indicates a significant negative impact to groundwater when used as labeled. This product appears to have a significant potential to cause a negative groundwater impact just from use of treated seed.

Due to the above-mentioned concerns of the Department, Bayer CropScience has requested the withdrawal of the Poncho 600 (EPA Reg. No. 264-789-7501) application for registration until such time as additional pertinent data is available.

Bayer CropScience understands that the application fee is forfeited, and that any subsequent application for registration of this product will require a complete application and fee, including any additional information regarding potential long-term chronic effects to honey bees, possible role of clothianidin as an endocrine disrupter, chronic toxic risk to non-endangered and endangered small birds, and acute/chronic toxicity to non-endangered and endangered mammals. Any available information or discussions regarding field dissipation, persistence and seed leaching should also be submitted.

Please be reminded that any unregistered pesticide product may not be sold, offered for sale, distributed, or used in New York State.

The Department is aware that there is no regulatory prohibition from shipping previously treated seed into this State. However, the technical concerns identified in this letter exist for the sale and use of seed treated with clothianidin regardless of the location of treatment.

Also, please be aware that any subsequent application for registration of any clothianidin containing product will, most likely, raise the same technical concerns. Therefore, applications will require the above-mentioned additional information in order to address the Department's concerns.

Please note that pesticide active ingredient information, which includes the Department's registration decision letters, are available on the Cornell University Pesticide Management Education Program (PMEP) website (http://pmep.cce.cornell.edu/profiles/).

If you have any questions, please contact Samuel Jackling, Chief of our Pesticide Product Registration Section, at (518) 402-8768.

Sincerely,

Maureen P. Serafini
Director
Bureau of Pesticides Management

cc: N. Kim/D. Luttinger - NYS Dept. of Health
R. Zimmerman/ R. Mungari - NYS Dept. of Ag. & Markets
W. Smith - Cornell University, PMEP