

**New York State Department of Environmental Conservation
Division of Solid and Hazardous Materials**

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June 7, 2005

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Ms. Theresa K. Hass
State Registration Coordinator
Crompton Manufacturing Company, Inc.
74 Amity Road
Bethany, Connecticut 06524-3402

Dear Ms. Hass:

Re: Registration of the New Active Ingredient Novaluron Contained in the Pesticide Product Pedestal™ (EPA Reg. No. 66222-40-400)

The New York State Department of Environmental Conservation (Department) has completed a technical review of the subject application (received January 7, 2005) submitted by Crompton Manufacturing Company, Inc., and supporting documentation submitted by Makhteshim-Agan of North America, Inc. Pedestal™ is a subregistration of Makhteshim-Agan of North America's basic product, Rimon 10SC (EPA Reg. No. 66222-40). Pedestal™ (EPA Reg. No. 66222-40-400) contains the new active ingredient novaluron (Chemical Code 124002).

Pedestal™ (10% novaluron) is a suspension concentrate containing 0.83 pounds active ingredient per gallon. Product is labeled as a foliar applied insect growth regulator for control of certain insect pests on container grown ornamentals in greenhouses, shadehouses and outdoor nurseries. The Use Restrictions section of the label bears the statement, "Do not apply more than 52 fl. oz. of Pedestal™ per acre per year per crop." This is equivalent to a maximum of 0.34 pounds novaluron per acre per year per crop.

The Department hereby accepts Pedestal™ (EPA Reg. No. 66222-40-400) for registration in New York State. Enclosed for your files are the Certificate of Pesticide Registration and New York State stamped "ACCEPTED" label. A synopsis of the technical review and risk assessments follows.

The subject application package was deemed complete for purposes of technical review on February 23, 2005. Pursuant to the review time frame specified in Environmental Conservation Law (ECL) §33-0704.2, a registration decision date of July 22, 2005 was established.

Toxicological and environmental fate risk assessments were conducted for novaluron and the TM formulated product. An ecotoxicity risk assessment was not produced for this limited outdoor use pattern. Analytical methods for the determination of novaluron in water and soil by LC/MS are acceptable as submitted.

TOXICOLOGICAL RISK ASSESSMENT: Neither the active ingredient novaluron nor the formulated product PedestalTM was very acutely toxic to laboratory animals by the oral, dermal or inhalation routes of exposure. In addition, both the active ingredient and the formulated product were not very irritating to the skin (tested on rabbits), nor were they skin sensitizers (tested on guinea pigs). Whereas novaluron was not an eye irritant (tested on rabbits), PedestalTM was moderately irritating to the eyes.

The combined results of two subchronic feeding studies in rats indicate that novaluron caused a disruption in hematopoietic function of the spleen at a dose of 8.64 milligrams per kilogram body weight per day (mg/kg/day) in females and in males at 27.77 mg/kg/day. Additionally, decreases in red blood cell counts, hemoglobin and hematocrit were observed in females at 8.64 mg/kg/day. The no-observed-effect levels (NOELs) were 4.38 and 22.2 mg/kg/day for females and males, respectively. In a subchronic feeding study in mice, changes in red blood cell structure and an increase in absolute and relative spleen weights were observed in males and females at 135.9 and 135.6 mg/kg/day, respectively. The respective NOELs were 12.8 and 15.2 mg/kg/day.

Novaluron caused some toxicity in chronic animal feeding studies. In a one-year dog feeding study, hematological changes associated with histopathological changes in the spleen and liver were observed at a dose of 100 mg/kg/day; the NOEL was 10 mg/kg/day. In a chronic feeding/oncogenicity study in rats, red blood cell damage and turnover resulting in mild anemia were observed in males and females at 30.5 and 39.5 mg/kg/day, respectively. The respective NOELs were 1.1 and 1.4 mg/kg/day. In a chronic feeding/oncogenicity study in mice, red blood cell damage and turnover resulting in mild anemia occurred at doses of 53.4 mg/kg/day in males and 63.3 mg/kg/day in females. The respective NOELs were 3.6 and 4.3 mg/kg/day. The United States Environmental Protection Agency (USEPA) Office of Pesticide Programs calculated an oral reference dose (RfD) for novaluron of 0.011 mg/kg/day based on the NOEL of 1.1 mg/kg/day in the chronic feeding/oncogenicity study in rats and an uncertainty factor of 100. This RfD value has not yet been adopted by the USEPA Integrated Risk Information System (IRIS).

Novaluron caused neither developmental nor maternal toxic effects in rats or rabbits orally administered this chemical during organogenesis at the highest dose level tested, which was 1,000 mg/kg/day. In a rat multigeneration reproduction study, a decrease in sperm count was observed at 297.5 mg/kg/day; the NOEL was 74.2 mg/kg/day. No adverse reproductive effects were observed in females at up to and including the highest dose tested which was 1,009.8 mg/kg/day. Parental toxicity, characterized by an increase in absolute and relative spleen weights occurred at the lowest doses tested, which were 74.2 and 84 mg/kg/day for males and females, respectively.

Novaluron did not cause oncogenic effects in either rat or mouse chronic feeding studies. Except for one genotoxicity study which gave equivocal results, all other genotoxicity studies on novaluron gave negative results. Based on the lack of evidence for carcinogenicity in rats and mice, the USEPA classified novaluron as “not likely to be carcinogenic to humans.”

To address worker risks, the registrant submitted a USEPA risk assessment for intermediate-term combined dermal and inhalation exposures of workers to novaluron. Although this risk assessment was not specifically conducted for the labeled use of this active ingredient on container grown ornamentals in greenhouses, shadehouses and outdoor nurseries, it contains information that is applicable to this use. Using the USEPA’s dermal and inhalation absorption factors of 10% and 100%, respectively, and a NOEL of 4.38 mg/kg/day for females in the 90-day rat feeding studies on novaluron, we calculated a margin of exposure (MOE) of 245 for combined dermal and inhalation exposures to this active ingredient, as used in the Pedestal product. For these exposures, we assumed that workers (mixer/loader/applicators) wore a single layer of clothing and gloves (the PedestalTM label requires long-sleeved shirt, long pants, shoes plus socks and chemical-resistant gloves). From the USEPA Pesticide Handler Exposure Database (PHED), we obtained dermal and inhalation exposures to novaluron of 2.50 and 0.12 mg per pound of this active ingredient applied. The labeled application rate for novaluron is up to 0.34 pounds per acre per season. We further assumed that a greenhouse/outdoor nursery worker would treat 10 acres a day, which is a probably an overestimate of use. Consequently, the MOEs for workers could be greater than 245. The USEPA generally considers MOEs of 100-fold or greater to provide adequate worker protection.

There are no chemical-specific federal or New York State drinking/groundwater standards for novaluron. Based on its chemical structure, novaluron 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 novaluron and PedestalTM indicates that neither the active ingredient nor the formulated product is very acutely toxic in laboratory animal studies. Furthermore, novaluron did not demonstrate developmental toxicity properties, nor was it carcinogenic in mice and rats. Although this chemical can cause adverse hematological effects at relatively low doses, the estimated risks to workers from the use of PedestalTM are within the range that is generally considered acceptable. While the PedestalTM product causes some eye irritation, the label contains the precautionary statement, “Causes moderate eye irritation. Avoid contact with skin, eyes or clothing.” which is compatible with the USEPA Label Review Manual guidance. Air impacts in greenhouses from PedestalTM use are not expected to be a concern as the active ingredient has a low vapor pressure (1.2×10^{-7} mm Hg at 22 degrees Celsius) and the product does not contain significant amounts of volatile organic solvents.

ECOTOXICITY REVIEW: The Department’s Bureau of Habitat reviewed the use of PedestalTM insecticide on container grown ornamentals plants and had no objection to its registration. A risk assessment was not produced for this review.

ENVIRONMENTAL FATE RISK ASSESSMENT: PedestalTM is an insect growth regulator for control of certain insect pests on container grown ornamentals in greenhouse, shadehouses and outdoor nurseries. The product contains 10% by weight active ingredient (or 0.83 lb ai/gallon) and is packaged as a suspension concentrate. The maximum application rate is

6 to 8 fluid ounces of product (or 0.39 to 0.052 lb ai) per application. The maximum labeled application rate is 52 fluid ounces of product or 0.34 lb ai/a/yr/crop. It may be applied only once every 30 days and only once per generation of insect. The product is applied foliarly by compressed air, hydraulic or handheld sprayers. The primary mode of action is by disrupting cuticle formation and deposition occurring when insects molt, resulting in their death. The technical review follows:

Solubility: The solubility of the novaluron is 3 &g/L at 25°C.

Hydrolysis: In a study that USEPA found acceptable, novaluron is stable to hydrolysis at pHs 5 and 7. At pH 9, reviewer-calculated extrapolated half-lives were 87.7 and 113.6 days on two different ring-labeled studies. Further tests at higher temperatures suggested that novaluron hydrolysis is temperature dependent, with half-lives of 1.2 days and 8.5 hours at 50°C and 70°C, respectively.

Aqueous Photolysis: In a study that the USEPA found scientifically valid, but did not need to be repeated, the half-lives were found to be 173.3 and 119.5 days in two ring-labeled studies with one major transformation product: 2,6-difluorobenzamine (Product 4).

Soil Photolysis: In a study that the USEPA found scientifically valid, but did not need to be repeated, the half-lives were found to be 231.1 and 288.87 in two ring-labeled studies in a sandy loam soil with no major transformation products.

Aerobic Soil Metabolism: In a study that the USEPA found acceptable, novaluron had a half-life of 10-12 days in clay loam (pH 8.8, 1.7% OC) and sandy loam (pH 5.8, 0.8% OC) and 5 days in a silt loam soil (pH 7.0, 3.7% OC) all at 20°C.

Anaerobic Soil Metabolism: In a supplemental study, the half-life in a water/sandy loam soil was 65.8 days in the soil, <3 days in the water and 53.7 days in the total system with one major transformation product: 1-[3-Chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea. In a second ring-labeled study, the half-life was 42.2 days in the soil, <3 days in the water and 44.7 days in the total system with two major transformation products: 2,6-difluorobenzoic acid and CO₂.

In an acceptable study, the half-life in a water/loam soil was 63 days in the soil, <1 days in the water and 50.6 days in the total system with one major transformation product: 1-[3-Chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea. In a second ring-labeled study, the half-life was <91 days, the first sampling time with two major transformation products: 2,6-difluorobenzoic acid and CO₂.

Aerobic Aquatic/Soil Metabolism: In a supplemental study, the half-life in a ditch water/loamy sand soil was 9.06 days in the soil, <0.87 days in the water and 9.72 days in the total system with one major transformation product: 1-[3-Chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)

phenyl]urea. In a second ring-labeled study, the half-life was 10.3 days in the soil, <1.4 days in the water and 9.06 days in the total system with one major transformation product: CO₂.

In a supplemental study, the half-life in a pond water/clay loam soil was 17.1 days in the soil, 1.08 days in the water and 5.7 days in the total system with one major transformation product: 1-[3-Chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy) phenyl]urea. In a second ring-labeled study, the half-life was 30.4 days in the soil, <1.31 days in the water and 23.7 days in the total system with one major transformation product: CO₂.

Adsorption/Desorption: USEPA found this scientifically valid and could be used to fulfill the USEPA data requirements:

Soil Type	Adsorption K _{oc}	Desorption K _{oc}	% OM	pH
Sandy loam	1950	2811	1.8	5.8
Sandy loam	2088	2913	0.8	5.8
Silty clay loam	2563	3475	2.4	6.0
Silt loam	2505	3379	1.9	7.1

Soil Column Leaching: In a study that USEPA found scientifically valid and could be used to fulfill the Subdivision N guidelines, novaluron was slightly mobile in columns of clay loam (1.5% OC), sandy loam (0.8% OC), silty loam (3.7% OC), and sandy loam (1.8% OC).

Field Dissipation: In a study the USEPA found acceptable, the half-lives of novaluron in a California sandy loam soil was 14-30 days. The dissipation routes could not be determined. In a New York sand-loamy sand, the half-life was 170 days with one major transformation product: chlorophenyl urea (CPU). This half-life was considered to be highly uncertain. In a Louisiana silt loam, a Washington loamy sand-sandy loam and a Nova Scotia sandy loam, the half-lives could not be determined.

Computer Modeling: Computer modeling was run using Riverhead profile, a K_{oc} of 2913, a half-life of 12 days, and an application rate of 0.62 lb novaluron/acre. The model projected no active ingredient in leachate due to the high K_{oc} and short half-life of novaluron.

REGISTRATION ACTION: The Department hereby accepts Pedestal™ (EPA Reg. No. 66222-40-400) for registration in New York State. Enclosed for your files are the Certificate of Pesticide Registration and New York State stamped “ACCEPTED” label (coded 002/061802).

Please note that a proposal by Crompton Manufacturing Company, Inc., or any other registrant to register a product containing novaluron, whose labeled uses are likely to increase the potential for significant exposure to humans or impact to the environment, would constitute a major change in labeled (MCL) use pattern. Such an application must be accompanied by a new application fee and meet the requirements specified in 6 NYCRR Part 326.17.

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

Sincerely,

Ms. Theresa K. Hass 6 .

Maureen P. Serafini
Director
Bureau of Pesticides Management

Enclosures

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