New York State Department of Environmental Conservation
Division of Solid and Hazardous Materials
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December 20, 2006

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Ms. Suzanne Holt
Regulatory Agent for Mitsui Chemicals, Inc.
c/o Landis International, Inc.
P.O. Box 5126
Valdosta, Georgia 31603-5126

Dear Ms. Holt:

Re: Registration of the New Active Ingredient Dinotefuran Contained in the Pesticide Product Dinotefuran Technical (EPA Reg. No. 33657-10)

The New York State Department of Environmental Conservation (Department) has completed a technical review of the application (received August 8, 2005) and supplemental information submitted to date by Landis International, Inc., acting as authorized agent for Mitsui Chemicals, Inc., in support of registration of the referenced pesticide product. Dinotefuran Technical (EPA Reg. No. 33657-10) contains the new active ingredient dinotefuran (Chemical Code 044312).

Dinotefuran Technical (99.0% dinotefuran) is labeled for use only in the formulation of insecticide products used in the control of sucking, biting and chewing insects infesting cotton, leafy vegetables, fruiting vegetables, cucurbits, potatoes, grapes, head and stem brassica, turf and ornamentals, domestic outdoors (lawns, perimeters, and ornamentals), and certain public health pests.

The application package was deemed complete for purposes of technical review on May 8, 2006 following two notices of incompleteness (10/4/05 and 11/29/05). Pursuant to the review time frame specified in Environmental Conservation Law (ECL) §33-0704.2, a registration decision date of October 5, 2006 was established. By mutual agreement, the decision date was extended to December 4, 2006 in order to resolve remaining issues.

Toxicological, ecological and environmental fate risk assessments were conducted for Dinotefuran Technical. Dinotefuran water/soil methods were found to be technically sound and sufficient documentation was provided to demonstrate their effectiveness.

TOXOLOGICAL RISK ASSESSMENT: On an acute basis, Dinotefuran Technical was not very toxic by the oral, dermal or inhalation routes of exposure. This chemical was not very irritating to the eyes or skin (tested on rabbits), nor was it a skin sensitizer (tested on guinea pigs).

In a 28-day rat inhalation study, dinotefuran caused a decrease in body weight gain in males at exposures equivalent to 60 milligrams per kilogram body weight per day (mg/kg/day), which was the lowest dose tested. In a 90-day oral neurotoxicity study in rats, increased motor activity during week two of the study was reported at 327 mg/kg/day for males and 400 mg/kg/day for females. The respective no-observed-effect-levels (NOELs) were 33 and 40 mg/kg/day.

Dinotefuran caused some toxicity in chronic feeding studies in laboratory animals. In a one-year dog feeding study, a decrease in thymus weights in males occurred at the lowest dose tested, which was 20 mg/kg/day. In females, in addition to a decrease in thymus weights, a decrease in body weights and body weight gain were observed at 108 mg/kg/day; the NOEL was 22 mg/kg/day. In a chronic feeding/oncogenicity study in mice, dinotefuran caused a decrease in spleen weights in males and an increase in ovarian weights at the lowest doses tested, which were 3 and 4 mg/kg/day, respectively. In a chronic feeding/oncogenicity study in rats, kidney effects (pelvic mineralization and ulcerations) were observed in males at 991 mg/kg/day with a NOEL of 99.7 mg/kg/day. In females, an increase in ovarian weights and a decrease in body weights and body weight gain occurred at a dose of 1,332 mg/kg/day; the NOEL was 127.3 mg/kg/day. The United States Environmental Protection Agency (USEPA) Office of Pesticide Programs calculated an oral reference dose (RfD) for dinotefuran of 0.02 mg/kg/day based on the lowest-observed-effect level (LOEL) of 20 mg/kg/day in the one-year dog 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 using a LOEL instead of a NOEL). This RfD value has not yet been adopted by the USEPA Integrated Risk Information System (IRIS). While the use of NOEL from the mouse study could be used as an alternate basis for the derivation of an RfD, the USEPA chose not to use this value because the health effects in question did not follow a clear dose-response relationship, the standard deviations were large and there were no corroborative histopathological findings.

Dinotefuran did not cause developmental toxicity in the offspring of pregnant rabbits or rats administered this chemical during organogenesis at the highest doses tested, which were 300 and 1,000 mg/kg/day, respectively. However, maternal toxicity characterized by decreases in body weight gain and food consumption in both pregnant rabbits and pregnant rats occurred at 125 and 1,000 mg/kg/day, respectively; the respective NOELs were 52 and 300 mg/kg/day. In a rat multigeneration reproduction study, reproductive effects in males (slight increase in abnormal sperm morphology, slight decrease in testicular sperm count and motility) occurred at doses of 822 mg/kg/day, while effects in females (decrease in uterine weights, microscopic alterations of the uterus, decrease in primordial follicles, altered estrus cycle) occurred at 907 mg/kg/day. The respective NOELs were 241 and 268 mg/kg/day. A decrease in spleen weights also occurred in males and females at the same respective doses that caused the above-noted reproductive effects. Also observed in males was a decrease in body weight gain and food consumption at 822 mg/kg/day with a NOEL of 241 mg/kg/day.

Dinotefuron was not carcinogenic in either mice or rats. In addition, this chemical gave negative results in genotoxicity studies. Based on these data, the USEPA classified dinotefuran as "not likely to be a human carcinogen."

The New York State Department of Health (NYSDOH) briefly reviewed the environmental fate data on dinotefuran. These data indicate that this chemical and at least one of its degradates, MNG (1 methyl-2-nitroguanidine), may have the ability to leach through certain soil types and contaminate groundwater; the adsorption coefficients (K_{oc}), depending on soil type ranged from 23.3 to 33.6 for dinotefuran, and for its degradate MNG, the K_{oc} range was from

8 to 31. Accordingly, the Dinotefuran Technical label contains the environmental hazards statement, "The high water solubility of dinotefuran, and its degradate MNG, coupled with its very high mobility, and resistance to biodegradation indicates that this compound has a strong potential to leach to the subsurface under certain conditions as a result of label use. Use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in ground-water contamination."

There are no chemical specific federal or New York State drinking water/groundwater standards for dinotefuran or its degradate MNG. Based on their chemical structures, these compounds fall under the 50 microgram per liter (_g/L) New York State drinking water standard for "unspecified organic contaminants" (10 NYCRR Part 5, Public Water Systems). The New York State drinking water standard for the sum of "unspecified organic contaminants" and "principal organic contaminants" is 100 _g/L.

The available information on Dinotefuran Technical indicates that it was not very acutely toxic in laboratory animal studies. In addition, dinotefuran did not demonstrate developmental toxicity, genotoxicity or carcinogenicity. However, data from other studies have indicated that this chemical has the potential to cause some neurotoxic, immunotoxic and reproductive effects. Accordingly, the USEPA required the registrant to submit a developmental neurotoxicity study and a developmental immunotoxicity study, both to be conducted in rats. NYSDOH requested that the registrant be required to submit to the Department for NYSDOH review a copy of the USEPA Data Evaluation Record reports, or if unavailable a copy of the USEPA's detailed review of these two studies on dinotefuran when they become available. Finally, because dinotefuran and its MNG degradate appears to have the potential to leach through soil and contaminate groundwater/drinking water, the Department should consider whether mitigative measures (e.g., prohibiting its use in vulnerable areas) are necessary before registering any formulated products containing dinotefuran in New York State.

ECOLOGICAL RISK ASSESSMENT: The Department's Division of Fish, Wildlife & Marine Resources Bureau of Habitat had no objection to registration of Dinotefuran Technical as labeled. Any ecological issues will be addressed on a case-by-case basis as end-use product labels are submitted for consideration.

ENVIRONMENTAL FATE RISK ASSESSMENT: Dinotefuran is a systemic nicotinoid insecticide, and belongs to the nitroguanidine sub-class, along with clothianidin, imidacloprid and thiamethoxam.

Dinotefuran Technical (99% dinotefuran) is labeled for use only in the formulation of end-use insecticide products.

Transformation products:

UF	M1; 1-methyl-3-(tetrahydro-3-furylmethyl)urea
unidentified	M3
guanidine	M9
MU N-methylurea	M11
MG hydrogen chloride	M13; 1-methylguanidinium chloride
DN-2-OH + DN-3-OH	M14
BCDN succinate.	M15; 3-(methylamino-0-oxa-2-aza-4-azoniabicyclo[4.3.0]non-3-ene hydrogen succinate

MNG	1, methyl-2-nitroguanidine
DN	1-methyl-3-(tetrahydro-3-furylmethyl)guanidinium
NG	Nitroguanidine
MG	1-methylguanidine

Solubility: The solubility of dinotefuran is 39,830 ppm.

Solubility of MNG: The solubility of degradate MNG is 11,480 ppm.

Hydrolysis: In a study that USEPA found supplemental (MRID 45640101), dinotefuran had half-lives of 7,701; 3,465; 1,155 days in pH 4, 7 and 9 buffer solutions, respectively. In a study that USEPA found acceptable (MRID 45640102), dinotefuran was stable at in pH 4, 7 and 9 buffer solutions at 25^{o}C.

Hydrolysis of DN: In a study that USEPA found supplemental (MRID 45640104), no significant degradation occurred during the five-day study.

Hydrolysis of MNG: In a study that USEPA found supplemental (MRID 45640103), MNG was stable at pHs 4, 7 and 9 at 51^{o}C.

Aqueous Photolysis: In a study that USEPA felt provided useful information but needed to be upgraded (MRID 45640105), the phototransformation half-life was 1.8 days. The environmental phototransformation half-life, determined by the study author, was 2.3 to 2.4 days at 30 to 50^{o} N latitude. Major transformation products including M1, M13, M14 and M15.

In a study that USEPA found unacceptable (MRID 45640106), the phototransformation half-lives in river water was 2.3 hours and in purified water was 2.5 hours. The environmental half-life is expected to be 2.4 hours.

Aqueous Photolysis of DN: In a study that USEPA found supplemental (MRID 45640108), the phototransformation half-life at pH 5 was 26.7 days with one major degradate: MG at 10.8%. At pH 7, the half-life was 266.6 days. At pH 9, DN was stable.

Aqueous Photolysis of MNG: In a study that USEPA found supplemental (MRID 45640107), the phototransformation half-life at pH 7 was 1.2 days with major degradates M3, M9, and M11.

Soil Photolysis: In a study that USEPA found unacceptable (MRID 45640109) for many reasons, in a loamy sand soil the half-life in the irradiated soil was 46.2 days.

Anaerobic Aquatic Metabolism: In a study that USEPA found supplemental (MRID 45891616), in a demineralized water-silt loam soil, the half-life in the entire system was 65 days, in the water was 51 days and in the soil was 62 days. DN was the only major degradate found.

Anaerobic Soil Metabolism: A copy of California's review indicates that the study requirements have not been satisfied for this active ingredient.

Aerobic Aquatic Metabolism: In a study that USEPA found supplemental (MRID 45640117), in a river water/sandy loam sediment, the half-life in the entire system was 79.3 days, in the water was 73.2 days and in the sediment was 108.5 days. DN phosphate was the only major degradate found. In a

pond water/loam system, in the entire system the half-life was 76 days, in the water was 52.6 days and in the sediment was 131.2 days. DN was the only major degradate found.

Aerobic Soil Metabolism: Two studies were done that USEPA found supplemental (MRID 45640111 and 45640112). California's concurrent review (dated September 18, 2003), indicated that the studies were acceptable. USEPA documentation indicated that the deficiencies in the aerobic metabolism studies had not been explained to their satisfaction. In the August 9, 2005 USEPA memorandum from José Luis Meléndez to Rita Kumar, USEPA stated: "The registrant did not provide sufficient information to upgrade the aerobic soil metabolism study MRID# 45640111. The study is still considered supplemental." "At this time the EFED does not have sufficient information to do a comprehensive evaluation of the aerobic soil metabolism study of dinotefuran (MRID# 4560112[1]). The study remains supplemental."

Soil	% OM	pH	t _ in days	Degradates
Madison Farm Loamy sand	1.2	7.2	38	MNG 14.6%
Findak Garden Loam	5.5	7.5	17	MNG 15%
Van Ess Loam	2.2	7.3	78	
Misich Loam	4.9	5.3	89	
R. Myron N Loamy sand	5.6	7.1	20	MNG 23.96% NG 14.33%
Loamy sand[1]	1.1	6.9	100	MNG 13.7%

Aerobic Soil Metabolism of MNG: According to the USEPA memorandum dated August 9, 2005, in Table 2 under MRID 45640112, the USEPA stated "Furthermore, the above mentioned study gives sufficient data on the dissipation of MNG, the major transformation product of dinotefuran. The registrant reported a DT50 = 87.7 days and the DT90 = 291 days at 20^{o}C." USEPA still found this study supplemental.

USEPA went on in that same memorandum to discuss a separate study (RCC Study No. 844180) and reported that half-lives in a silt loam, sandy loam and clay loam (no parameters provided) were 45.4, 173 and 64.3 days, respectively. However, the study itself was not submitted to USEPA, only the results.

Adsorption/Desorption: Two studies were conducted for the parent compound, one found supplemental (MRID 45640115)[l] and one found acceptable (MRID 45640114)[2].

Soil Type	Adsorption K_{oc}	Desorption K_{oc}	% Organic Carbon	pH
clay loam [1]	23.3	NP	2.6	6.7
loam [1]	31.4	NP	1.21	7.5
clay [1]	33.6		3.33	7.0
loamy sand [1]	25.3		1.5	5.9
loamy sand [2]	6	66	2.17	5.7
silt loam [2]	22	178	1.0	5.8
loam [2]	42	397	2.4	6.2
sandy loam [2]	45	213	1.6	5.8
clay loam [2]	42	299	2.9	5.7

For degradate MNG (MRID 45640116), USEPA found this study supplemental:

Soil Type	Adsorption K_{oc}	Desorption K_{oc}	% Organic Carbon	pH
loamy sand	8	12	2.17	5.7
silt loam	16	ND	1.0	5.8
loam	31	25	2.4	6.2
sandy loam	8	ND	1.6	5.8
clay loam	24	28	2.9	5.7

For degradate DN (MRID 45640113), USEPA found this study supplemental:

Soil Type	Adsorption K_{oc}	Desorption K_{oc}	% Organic Carbon	pH
clay	270	335	2.63	7.0
sandy loam	413	516	0.71	6.5
loam	87	128	2.4	5.5
sandy loam	58	84	3.6	5.1
clay loam	2502	3130	2.9	5.7

Terrestrial Field Dissipation: In a study that USEPA found acceptable (MRID 45640118):

Soil Type	% Organic Carbon	pH	T _	% Degradate
California sandy loam	0.27	8.8	65.4 days	MNG 31.5%
Georgia sandy loam	0.43	6.5	19.4 days	MNG 5.3%
New York sandy loam	3.91	6.6	55.9	MNG 6.6%

Label Statements: The following paragraph is found under Environmental Hazards on this label:

> "Dinotefuran and its degradate, MNG, have the properties and characteristics associated with chemicals detected in ground water. The high water solubility of dinotefuran, and its degradate, MNG, coupled with its very high mobility and resistance to biodegradation indicates that this compound has a strong potential to leach to the subsurface under certain conditions as a result of label use. Use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in groundwater contamination. Periodic monitoring of shallow groundwater in the use area is recommended."

Environmental Fate Requirements of Conditional Registration issued September 17, 2004:

1. A confirmatory photodegradation in soil study to evaluate photodegradation as a major degradation pathway. This study was due September 14, 2005.
2. Either an upgraded aerobic soil metabolism study, or a complete new study, addressing the fate of the major transformation products. This study was due September 14, 2005.
3. A new anaerobic aquatic/soil metabolism study.
4. An aerobic aquatic metabolism study to assess future aquatic uses may be needed.

END-USE PRODUCTS: In conjunction with the review of the subject technical product, the Department has conducted risk assessments for the following products containing dinotefuran:

Safari 20 SG Insecticide (EPA Reg. No. 33657-16-59639) - labeled for foliar and systemic insect control in ornamental plants grown in commercial, industrial and residential areas, indoor and outdoor nursery and greenhouse ornamental production.
Venom 20 SG Insecticide (EPA Reg. No. 33657-17-59639) - labeled for control of sucking and chewing insects infesting leafy vegetables (except Brassica).
Venom Insecticide (EPA Reg. No. 59639-135) - labeled for control of sucking and chewing insects infesting cotton, cucurbits, fruiting vegetables, grapes, head and stem Brassica, leafy vegetables and potatoes.

Review of these end-use products with outdoor uses has identified the potential for adverse impacts to nontarget organisms and groundwater/drinking water. Excerpts from ecological effects and groundwater risk assessments follow. The full text of the review is available in the technical issues letter, dated October 6, 2006, at Cornell's Pesticide Management Education Program website: http://pmep.cce.cornell.edu/profiles/index.html.

The uses proposed by these products currently present an unacceptable risk to honey bees and other organisms dependant on plant pollen and nectar. Product labels should instruct the user to not make any dinotefuran applications until after the target plants are through blooming and pollen and nectar are no longer present. Label statements claiming that these products will have minimal impacts to non-target beneficial arthropods are not supported by the data submitted with the applications. The submitted data demonstrate that the opposite is in fact the case.

The high water solubility of dinotefuran and its degradate MNG together with their very high mobility and resistance to biodegradation indicate that these compounds have a strong potential to leach to the subsurface. Based on the environmental fate data, the groundwater advisory statement and LEACHP simulations, the potential for dinotefuran and its degradate MNG to impact groundwater/drinking water resources in New York State cannot be discounted.

REGISTRATION ACTION: Dinotefuran Technical, is labeled only for formulation into insecticide end-use products. When used as labeled, the subject technical product should not cause unreasonable adverse effects to humans or the environment. **The Department hereby accepts Dinotefuran Technical (EPA Reg. No. 33657-10) for registration in New York State.** Enclosed for your files are the Certificate of Pesticide Registration and New York State stamped "ACCEPTED" label.

The FIFRA sec. 3(c)(7)(A) conditional registration of Dinotefuran Technical (EPA Reg. No. 33657-10) required the registrant to submit developmental neurotoxicity and developmental immunotoxicity studies, both to be conducted in rats, within two years from the date of registration (9/17/04). When available, Mitsui Chemicals must submit to this Department the USEPA Data Evaluation Record (DER) reports for these studies.

Please note that a proposal by Mitsui Chemicals, Inc., or any other registrant to register a product containing dinotefuran, whose labeled uses are likely to increase the potential for significant exposure to humans, non-target organisms or the environment, would constitute a major change in labeled (MCL) use pattern. Such an application must contain the above mentioned DER reports, meet the requirements specified in 6 NYCRR Part 326.17., and be accompanied by a new application fee.

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

Sincerely,

Maureen P Serafini

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
cc: w/o enc. - L. Garcia, Valent U.S.A. Corporation