New York State Department of Environmental Conservation
Division of Solid and Hazardous Materials
Bureau of Pesticides Management, 11th Floor
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October 3, 2005

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Ms. Judy Fersch
State Registration Specialist
BASF Corporation
P.O. Box 13528/ 26 Davis Drive
Research Triangle Park, North Carolina 27009-3528

Dear Ms. Fersch:

Re: Registration of the Pesticide Product Pylon Miticide-Insecticide (EPA Reg. No. 241-374) Which Represents a Major Change in Labeling for the Active Ingredient Chlorfenapyr (chemical code 129093)

The New York State Department of Environmental Conservation (Department) has reviewed your application, received September 24, 2004, from BASF Corporation to register the Major Change in Labeling for Pylon Miticide-Insecticide in New York State. The product contains the active ingredient **chlorfenapyr.**

The application was deemed complete for purposes of review on November 10, 2004 and a registration decision, after several extensions, is due by **October 15, 2005.**

Pylon Miticide-Insecticide contains the active ingredient chlorfenapyr ((4-bromo-2-(4-chlorophenyl)-1-(ethoxymethyl-5-(trifluoromethyl)-1H-pyrrole-3-carbonitrile)) and is labeled for use on ornamental crops and fruiting vegetable crops grown in commercial greenhouses. Pylon Miticide-Insecticide is currently registered in New York State for the control of mites, caterpillars, fungus gnats and thrips on ornamental crops grown in commercial greenhouses. The proposed use of Pylon Miticide-Insecticide on food crops represents a major change in labeling for the active ingredient chlorfenapyr in New York State.

Human Health Review:

The New York State Department of Health (DOH) stated in their previous review (December 2001) of Pylon Miticide-Insecticide, that the available information indicated neither this product nor the active ingredient chlorfenapyr is very acutely toxic or irritating in laboratory

animal studies. Chlorfenapyr caused liver toxicity and changes in brain morphology in subchronic and chronic feeding studies in rodents. Chlorfenapyr caused some post-implantation loss in rabbits at maternally toxic doses, but no developmental or reproductive effects were reported in rats. The United States Environmental Protection Agency (USEPA) Office of Pesticide Programs established a Reference Dose (RfD) of 0.003 mg/kg/day based on a NOEL of 2.6 mg/kg/day from a one-year dietary neurotoxicity study and an uncertainty factor of 1,000. The 1,000-fold uncertainty factor was used to account for intra- and inter-species differences and for the absence of a developmental neurotoxicity study. This RfD has not yet been adopted by the USEPA's Integrated Risk Information System (IRIS). A current search of the toxicological literature did not find any additional information on chlorfenapyr.

Chlorfenapyr caused increased liver, histiocytic and testicular tumors in rats as measured by trend analysis, but no increase in tumors by pair-wise comparisons between dose groups. No increase in tumors was noted in mice and the compound was negative in a number of genotoxicity studies. The USEPA Cancer Peer Review Committee initially described the carcinogenic potential of chlorfenapyr as "cannot be determined, suggestive." More recently, the USEPA reworded their classification of chlorfenapyr to "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential."

The USEPA established a tolerance for chlorfenapyr in or on fruiting vegetables at 1.0 part per million. The USEPA estimated that chronic dietary exposure to these residues would be 24% of the chronic population adjusted dose (cPAD) of 0.003 mg/kg/day for the general U.S. population, ten percent of the cPAD for all infants less than one-year old, and 47% of the cPAD for all children one- to two-years old. This chronic exposure analysis is based on the assumption that 100% of crops are treated and contain tolerance level residues. Actual residues and resulting exposure levels are expected to be less than this assessment estimates.

The USEPA reported the results of a risk assessment for short- and intermediate-term combined dermal and inhalation exposures of greenhouse workers to chlorfenapyr. For mixer/loader/applicators of high-pressure handwand applications, a margin of exposure (MOE) of 550 was estimated based on a worker applying 1,000 gallons of diluted Pylon Miticide-Insecticide per day and wearing personal protective equipment (long-sleeved shirt and long pants, shoes plus socks, and chemical-resistant gloves) as per label requirements. For post-application activities (hand harvesting, pruning, staking, thinning, training, tying, scouting and weeding), an MOE was estimated to be 1,500 based on the assumptions that 20% of the applied chlorfenapyr was available as dislodgeable residue, a five percent dermal absorption rate, and a restricted entry interval of 12 hours. The NOEL used in estimating these MOEs was 3.9 mg/kg/day from the 90-day oral study in the dog. Generally, MOEs of 100-fold or greater are considered adequate by USEPA for worker exposure.

Based on its chemical structure, chlorfenapyr falls under the 50 microgram per liter (_g/L) general New York State drinking water standard for "unspecified organic contaminants" (10 NYCRR Part 5, Public Water Systems). Using the USEPA's RfD of 0.003 mg/kg/day and procedures for deriving ambient water standards and guidelines based on non-oncogenic effects (6 NYCRR Part 702.5), a value of 21 _g/L can be calculated for chlorfenapyr.

The available information on chlorfenapyr and the formulated product Pylon Miticide-Insecticide indicates that they were not very acutely toxic in laboratory animal studies. Chlorfenapyr also did not cause developmental or reproductive effects in rats, and only caused developmental effects in rabbits at maternally toxic doses. Chlorfenapyr caused some effects following chronic exposure and this chemical has some carcinogenic potential. While the expected exposure from the labeled use of Pylon Miticide-Insecticide should not pose significant risks to workers or the general public, we still have generic concerns for registering pesticide products with carcinogenic potential unless either the needs are significant or they replace products that pose greater risks. The information in the original registration package did not provide an adequate basis for determining the need for nor the comparative risks of this product in New York State when used on fruiting vegetable crops grown in commercial greenhouses. The Department requested that the registrant submit additional information indicating that there is a need for the Pylon product and that it poses lesser risks than the alternatives.

In response to these concerns, BASF Corporation submitted a comprehensive weight-of-evidence analysis to argue that the USEPA classification of chlorfenapyr as "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential" should be modified to "not likely to be a human carcinogen." When we compared the registrant's weight-of-evidence analysis with the carcinogenicity study data reviewed by the USEPA's Cancer Peer Review Committee (Memorandum, January 9, 1997: Carcinogenicity Peer Review of Chlorfenapyr), we found that overall the registrant's argument is not sufficiently persuasive that chlorfenapyr should be classified as "not likely to be a human carcinogen." The main thrust of the registrant's argument is that overall there is no increase in liver adenomas/carcinomas, malignant histiocytic sarcomas, testicular interstitial cell tumors and uterine endometrial stromal polyps by pair-wise comparisons between groups of rats fed different doses of chlorfenapyr. The registrant further argues that the positive trends in tumor incidence resulting from oral exposure to increasing doses of chlorfenapyr are not significant when compared to the tumor incidence in historical controls. To support their argument, the registrant cites only maximum percent control tumor incidence values instead of the mean values and ranges which would better illustrate background tumor incidence. Furthermore, the registrant dismisses the experimental control values obtained from the rat carcinogenicity study on chlorfenapyr, by stating that these values are "…uniquely and abnormally low." While we acknowledge that the registrant makes some valid points in their analysis, we believe that the USEPA's classification of the carcinogenic potential of chlorfenapyr as "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential" is appropriate and should not be reclassified to "not likely to be a human carcinogen." In addition, the registrant's focus on specific carcinogenicity issues to the exclusion of the other issues raised in our initial review (i.e., the comparative risks posed by this product and the need for use on fruiting vegetables) does not address the overall concerns for registering this product.

Justification for registering the proposed use of Pylon Miticide-Insecticide on food crops in New York State could be based on the registrant's claim that the control of Lepidopterans, mites and thrip insects has become less effective by these pests having "…developed resistance to many of the currently registered products as documented by government, university and industry organizations." By comparison, "Chlorfenapyr, the active ingredient (a.i.) in Pylon, belongs to the Pyrrole class of insecticides/miticides and has demonstrated excellent activity against resistant pests." To substantiate this claim, the Department requested that the registrant provide some

examples from agriculture authorities supporting the need for a product such as Pylon Miticide-Insecticide. In response to this issue, the registrant recently (June 29, 2005) submitted two summaries on insect resistance and mode-of-action for insecticides. These materials do not provide an adequate basis for determining the need for the Pylon product, nor do they address the issue of comparative risks with other products that can be used on fruiting vegetables.

To address the comparative risks and need for this product, several responses were received from Cornell University staff. Currently horticultural soaps and oils, ddvp and malathion are used on greenhouse fruiting vegetables to control mites. DDVP and malathion are organophospate pesticides currently undergoing registration review by the USEPA, and therefore, Pylon is a potential organophospate replacement. Additionally, the manufacturer of malathion appears to be removing greenhouse uses of malathion. For spider mite control Floramite is used almost exclusively. The addition of Pylon as a rotational product would be helpful for insect resistance management. Cornell University staff also stated the use of Pylon would be unique and very desirable for problems with broad or cyclamen mite as well as tomato russet mite.

Bureau of Habitat (BOH) Review:

Note: All use, chemical, toxicity, and environmental fate information contained herein was taken from the data package submitted by BASF corporation.

Use Profile: Pylon is labeled for control of mites, caterpillars, gnats, and thrips on ornamental crops grown in commercial greenhouses. Applications are made at rates of 2.6 to 20 fluid ounces, 0.04 to 0.32 pounds active ingredient (a.i.), in 100 gallons of water. The label instructs the user to "use sufficient spray volume to ensure thorough coverage." The only indication of how much mixture should be applied per unit of area is given in footnote 2 regarding mite treatments. It states "May require two (2) applications on a 5-7 day spray schedule at the 5.2 fl oz/100gal. (0.08 lb ai/A) under high mite pressure." The A in "0.08 lb ai/A" term is assumed to mean acre.

To manage resistance development, the label states: 1) Do not apply Pylon more than two times consecutively or a total of three times during a growing cycle, 2) Do not apply Pylon to consecutive crops in a greenhouse structure, or 3) Pylon should be applied in combination with other effective miticides/insecticides with a different mode of action when used in a subsequent crop in the same greenhouse structure.

Chemical Description: Pylon is 21.4% chlorfenapyr(4-bromo-2-(4-chlorphenyl)-1-(ethoxymethyl)-5-(trifluoromethyl)-1H-pyrrole-3-carbonitrile) which belongs to a new chemical class, the pyrroles. Chlorfenapyr is a pro-insecticide, it is converted in vivo via mixed function oxidases to the compound CL303268. CL303268 then uncouples oxidative phosphorylation in the mitochondria, resulting in disruption of ATP production, cellular death, and organism mortality.

Technical chlorfenapyr has a water solubility of 0.14 mg/L at pH 7. It has a low vapor pressure, 1.0X10-7 mmHg, volatilization will not contribute significantly to dissipation. Its octanol/water partition coefficient, K_{OW}, is 67,670 at 25^{O} C. A Bluegill sunfish accumulation study yielded bioconcentration factors for edible and nonedible tissues of 830x and 3400x, respectively. Its depuration half-life, T1/2, was approximately four days. Roughly 97% of the accumulated residues had depurated within 21 days of exposure cessation.

Toxicity And Environmental Fate: Chlorfenapyr is slightly to highly toxic to mammals. It is highly to very highly toxic to birds, and is very highly toxic to all aquatic organisms for which data was submitted. The January 10, 1997 USEPA Environmental Fate and Effects Review of chlorfenapyr use on cotton states that chlorfenapyr is one of the most chronically toxic pesticides to avian species that they had evaluated.

Chlorfenapyr degrades slowly by both biotic and abiotic pathways with the exception of aqueous photolysis, and is likely to remain in the environment as the parent compound for extended periods. It is stable to hydrolysis. Its aqueous photolysis T1/2 is seven to eight days at pH 7. Soil surface photolytic T1/2 is 75 (+/- 21) days. Microbial metabolism is slow, aerobic and anaerobic soil metabolism T1/2s are 3.8 years and roughly two years, respectively.

The only information of much value in the terrestrial field dissipation study results, contained in a USEPA Data Evaluation Record (DER) covering five studies, are the "minimum ranges of *dissipation* half-lives" calculated by the reviewer. None of the field studies addressed chlorfenapyr field degradation. The estimated dissipation T1/2 times ranged from roughly five months to over two years.

Risk Assessment: Fish and wildlife exposures from the Pylon labeled greenhouse uses should be minimal to nonexistent. The label contains extensive warnings in the ENVIRONMENTAL HAZARDS section regarding contamination of surface waters which should prevent exposure via drainage. Properly contained use should not adversely affect fish and wildlife resources. To minimize the potential for misuse of this highly toxic, widely toxic, very persistent product, only certified applicators or those under their direct supervision should be allowed to use it. Given the characteristics of chlorfenapyr, a Restricted Use NY registration is warranted.

Groundwater/ Drinking Water Review:

Staff first reviewed this active ingredient in 2001 for use as a foliar spray in greenhouses to control spider mites, fungus gnats, thrips, and certain caterpillars on greenhouse ornamentals. It was again reviewed in 2002 for use as a subterranean termiticide product.

BASF is applying to add fruiting vegetables in commercial greenhouses to the label. This is the first food use for chlorfenapyr. Pylon contains 21.4% active ingredient by weight, or 2 lb ai/gallon. Chlorfenapyr is liquid that is mixed with water and foliarly applied. It contains 21.4% by weight active ingredient. The maximum application rate to ornamentals is three applications not to exceed 41 oz product or 0.64 lb ai per crop growing cycle. According to the label, each “crop” can get the maximum of 41 oz product or 0.64 lb ai. A greenhouse generally has three “crops” per year; spring bedding plants, fall mums and kale crops, and winter pointsettias. The inerts do not appear to be solvent carriers.

The groundwater staff does not object to the registration of this product as labeled, however, should the registrant apply for other than greenhouse uses in the future, the application should be carefully reviewed because this active ingredient is persistent and accumulates in soil when used on a yearly basis.

Technical Review:

Most of the information was gathered from the 8/31/98 EFED memorandum. Frequently, the information presented in the memorandum contradicted the information presented in the DERs. Because the date on the memorandum supercedes the DERs, the memorandum information was used to make the environmental fate determination.

Hydrolysis: Chlorfenapyr is stable at pHs 5, 7 and 9.

Aqueous Photolysis: Chlorfenapyr has half-lives of 5.1 to 5.4, 6.9 to 8.1 and 4.8 to 4.9 days in sterile aqueous solutions of pH 5, 7 and 9, respectively. One degradate was found, CL357806, ranging from 55% to 73% of applied based on pH. However, aqueous photolysis is not a major degradation route because this is a foliar spray for greenhouse use.

Soil Photolysis: Chlorfenapyr has a half-life in a sandy loam soil of approximately 75 $\pm$ 21 days (MRID42770242). According to the 8/31/98 memorandum, the half-life is approximately 0.4 years (146 days).

Aerobic Soil Metabolism: Chlorfenapyr has a half-life in sandy loam of 3.8 years (MRID42770243); however, USEPA felt this data was anomalous. In the 8/31/98 EFED memorandum, USEPA indicated that the half-life is 1.4 years based on five soils (MRID44452621–not presented with application).

Aerobic Aquatic Metabolism: Chlorfenapyr has a half-life of 0.8 years in the aqueous portion and 1.1 years in the soil portion, according to the 8/31/98 EFED memorandum.

Anaerobic Soil Metabolism: Chlorfenapyr has an estimated half-life of two years according to the 8/31/98 EFED memorandum.

Adsorption/Desorption: This study was found to be upgradable and partially satisfied the data requirements; however, USEPA felt that despite the shortcomings of the study, chlorfenapyr was strongly bound to all test soils and would not be expected to be mobile. The K_{oc}s for the parent are 13214 in loamy sand, 14117 in sandy loam, 12321 in loam and 18095 in silt loam. In the 8/31/98 memorandum, USEPA indicated that chlorfenapyr has a relatively high K_{oc} of about 12000 and, as such, leaching would not be significant in soil dissipation studies.

The study for the degradate (in the same soils as the parent) was acceptable and found the K_{oc}s for the degradate are 5000 in loamy sand, 2352 in sandy loam, 2774 in loam and 2095 in silt loam.

Field Dissipation: Five studies were done, and all were upgradable, and further information was needed. The studies did not investigate or attempt to identify degradates, so the routes of dissipation cannot be established. USEPA stated in the DER that, "However, it is clear from these studies that parent pesticide AC303,630 is indeed persistent, as defined below, and does not leach." Minimum field dissipation half-lives were stated to be 0.4 to 0.6 years in loamy sand, 0.4 to 0.8 years in sandy loam, 0.6 to 0.9 years in silt loam, 0.6 to 1.4 years in clay loam, and 0.8 to 2.1 years in sand.

A May 6, 1997 letter to the USEPA presented data indicating that the registrant went back and did degradate work and found an average field dissipation half-life of the parent of 273 days (175 to 418 days). They indicated that CL312,094 was found at a maximum of 30% and two minor (<10%) degradates, CL303268 and CL322118 were found. These degradates further degraded to form CL303267, CL325195 and CL322250. However, there is nothing in the application from USEPA indicating that they found this supplemental data acceptable.

In the 8/31/98 memorandum, USEPA indicated that two supplemental multiyear soil dissipation studies demonstrated the trend toward increasing concentrations over time. Soil concentrations ranged from 0.1 ppm in the first year to 0.3 and 0.4 ppm in the fourth year of the study.

In the 8/31/98 memorandum, USEPA indicated that the half-life was 1.3 years based on five small-plot cotton studies in four cotton states (MRID43492850).

Computer Modeling: Computer modeling was not performed because of the extremely high K_{oc}s.

Given the very high K_{oc}s for chlorfenapyr, there is very little probability that this product, when used as directed in greenhouses, will cause any impact to groundwater. However, should the registrant apply for other than greenhouse uses in the future, the application should be carefully reviewed because this active ingredient is very persistent and accumulates in soil when used on a yearly basis.

Summary:

The Department concludes that Pylon Miticide-Insecticide should not have an adverse effect on the health of workers or the general public, the fish and wildlife resources, or the ground and surface water of New York State when used as labeled. However, the Department has determined that the Pylon Miticide/Insecticide product should be registered as "**Restricted Use**" based on the concerns raised in the nontarget organism and environmental fate reviews. Use restrictions will limit the use of the Pylon product to only certified applicators or those working directly with a certified applicator. The "Restricted Use" status will provide a higher level of assurance that the product will be applied according to label directions. Any new applications containing this active ingredient which demonstrate a labeled use outside the controlled environment of a commercial greenhouse, will be reviewed with a high degree of caution toward the protection of aquatic and avian resources.

Please note that the Pylon Miticide/Insecticide product is to be classified as "restricted use" under rules and regulations 6 NYCRR 326.2(g). As such, this product is restricted in its purchase, distribution, sale, use and possession in New York State.

According to New York State Department of Environmental Conservation Regulations 6 NYCRR 326.3(a): **"It shall be unlawful for any person to distribute, sell, offer for sale, purchase for the purpose of resale, or possess for the purpose of resale, any restricted pesticide unless said person shall have applied for, and been issued a commercial permit."**

Enclosed for your record is a copy of the New York State stamped "ACCEPTED" label for Pylon Miticide/Insecticide (EPA Reg. No. 241-374).

BASF Corporation is reminded that if New York State registration is requested for this product or for any other product which contains chlorfenapyr with an increased application rate and/or expanded use sites, the product will be considered **a Major Change in Labeling and the Department will require an extensive review.**

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

Sincerely,

Maureen P Serafini

Maureen P. Serafini
Director
Bureau of Pesticides Management

Enclosure

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