New York State Department of Environmental Conservation
Division of Solid & Hazardous Materials
Bureau of Pesticides Management, 11th Floor
625 Broadway, Albany, New York 12233-7254
Phone: 518-402-8788 **FAX:** 518-402-9024
Website: http://www.dec.state.ny.us/website/dshm/pesticid/pesticid.htm
E-Mail: ppr@gw.dec.state.ny.us

February 7, 2007

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Jim Baxter
State Regulatory Manager
Dow AgroSciences, LLC
9330 Zionsville Road
Indianapolis, Indiana 46268-1054

Re: Withdrawal of Milestone Herbicide Application (EPA Reg. No. 62719-519) Containing the Active Ingredient Aminopyralid. Chemical Code: 005209.

Dear Mr. Baxter:

The New York State Department of Environmental Conservation (Department) has completed its technical review of the above-referenced new active ingredient (NAI) application. Dow AgroSciences submitted this application with additional information on September 29, 2005. The Department determined the initial submission to be incomplete on November 17, 2005. Dow AgroSciences provided the Department further information in support of this application on March 19, 2006. The information that was received for Milestone Herbicide, containing the new active ingredient aminopyralid, was determined to be complete for purposes of technical review per Department letter dated May 2, 2006. An initial registration decision date of September 29, 2006 was established. In an attempt to mitigate Department concerns about the environmental fate of aminopyralid, the registration decision date was waived until February 15, 2007.

Milestone Herbicide (EPA Reg. No. 62719-519) is labeled for control of susceptible broadleaf weeds, including invasive and noxious weeds in non-crop sites such as rangeland, permanent grass pastures, conservation reserve program (CRP) acres, non-cropland areas (such as roadsides), nonirrigation ditch banks, natural areas (such as wildlife management areas, wildlife openings, wildlife habitats, recreation areas, campgrounds, trailheads and trails), and grazed areas in and around these sites, without injury to most grasses. The label states that Milestone Herbicide may be applied foliarly with all types of spray equipment normally used for ground and aerial applications. The maximum single application rate for all sites is 7 fluid ounces of product per acre or 0.11 lb. acid equivalent (aminopyralid) per acre per season.

Milestone Herbicide contains 40.6% of the active ingredient aminopyralid, which acts as a systemic post-emergence herbicide. Aminopyralid belongs to the pyridine carboxylic acid class of herbicides including picloram and clopyralid. Aminopyralid's mode of action toward target weeds is not completely understood. However, the principle action of this group of compounds appears to effect cell wall plasticity and nucleic acid metabolism. Like clopyralid containing products, the Milestone Herbicide label warns the user of impacts to susceptible

broadleaf plants from use of aminopyralid treated compost or contact with manure or urine from animals that have grazed on treated areas.

The Department has conducted technical reviews with regard to the new active ingredient aminopyralid, as contained in Milestone Herbicide, for impacts to human health, nontarget organisms, and environmental fate. Review summaries are provided below:

Human Health Risk Assessment:

On an acute basis, the formulated product Milestone was not very toxic to laboratory animals by the oral, dermal or inhalation routes of exposure. This pesticide product was not very irritating to the eyes or skin (tested on rabbits) nor was it a skin sensitizer (tested on guinea pigs).

Because the active ingredient triisopropanolammonium salt of aminopyralid readily dissociates in an aqueous environment to aminopyralid, which is the herbicidally active component, toxicological studies conducted with aminopyralid (which are most of the studies discussed in this review) are relevant for the toxicological evaluation of this active ingredient salt. The acute toxicity studies on aminopyralid indicated that this active ingredient was not very toxic by the oral, dermal or inhalation exposure routes. This chemical was also neither a skin irritant nor a sensitizer. However, it was a severe eye irritant.

Aminopyralid caused some toxicity in chronic animal feeding studies. In a one-year dog feeding study, histopathological changes of the stomach characterized by slight diffuse hyperplasia and hypertrophy of the mucosal epithelium of the stomach, slight lymphoid hyperplasia of the gastric mucosa and slight mucosal inflammation were observed at doses of 967 milligrams per kilogram body weight per day (mg/kg/day) and 1,038 mg/kg/day for males and females, respectively. The respective no-observed-effect levels (NOELs) were 99.2 and 93.2 mg/kg/day. In a chronic mouse feeding study, no effects were reported at up to the highest dose tested, which was 1,000 mg/kg/day. In a chronic feeding study in rats, enlargement of the cecum portion of the large intestine and decreased body weights were observed at 500 mg/kg/day; the NOEL was 50 mg/kg/day. The USEPA Office of Pesticide Programs calculated an oral reference dose (RfD) for aminopyralid of 0.5 mg/kg/day, based on the NOEL of 50 mg/kg/day in the chronic feeding 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).

The weight of evidence from developmental toxicity studies conducted on pregnant rats and rabbits indicates that aminopyralid caused limited toxicity to the offspring of rabbits but not rats. In rats, neither developmental nor maternal toxicity was reported at doses up to 1,000 mg/kg/day, the highest dose tested. In rabbits, one developmental toxicity study showed no developmental effects at the highest dose of aminopyralid tested, which was 500 mg/kg/day. Maternal toxicity, characterized by a decrease in body weight and food consumption as well as the appearance of ulcers/erosions in the glandular mucosa of the stomach, was reported at a maternal dose of 500 mg/kg/day; the NOEL was 250 mg/kg/day. In a second developmental toxicity study conducted on rabbits, a decrease in fetal body weight occurred at a dose of 520 mg/kg/day with a NOEL of 260 mg/kg/day. Maternal toxicity (decreased body weight, food consumption, mild incoordinated gait) was reported at a dose of 260 mg/kg/day; the NOEL was 104 mg/kg/day. In a rat multigeneration reproduction study, neither reproductive toxicity nor parental toxicity was observed up to the highest dose tested, which was 1,000 mg/kg/day.

Aminopyralid did not cause oncogenic effects either in rat or mouse chronic feeding/oncogenicity studies. This chemical gave negative results in several genotoxicity studies. Based on the lack of evidence for carcinogenicity in rats and mice, the USEPA classified aminopyralid as “not likely to be a carcinogen.”

The USEPA established tolerances for aminopyralid residues in or on wheat grain at 0.04 parts per million (ppm) and wheat bran at 0.1 ppm. The chronic population adjusted dose (cPAD) for aminopyralid is 0.5 mg/kg/day and has the same basis as the RfD. The USEPA estimated that the chronic dietary exposure to aminopyralid would be less than 1% of the cPAD for each of the following population subgroups: general U.S. population; infants less than one year old; children one to two years old; children six to twelve years old. This chronic exposure analysis is based on the conservative assumptions that 100% of the crops would be treated with aminopyralid and that all treated crops would have aminopyralid residues at the respective tolerance levels.

The USEPA conducted an occupational risk assessment for exposure of pesticide handlers to aminopyralid as used in the Milestone product according to this product's label directions. For these workers, only exposure to the active ingredient through the inhalation route was assessed. The USEPA noted that no dermal toxicity endpoint was selected since no systemic toxicity from this exposure route was observed in a 28-day dermal toxicity study conducted on rats at the limit dose of aminopyralid, which was 1,000 mg/kg/day. For short- and intermediate-term inhalation exposures to these workers, the estimated margins of exposure (MOEs) ranged from 40,000 to 700,000. For these estimates, a 100% absorption from inhalation exposure was assumed. The NOEL used for estimating these MOEs was 104 mg/kg/day obtained from a rabbit developmental toxicity study on aminopyralid. Since no dermal toxicity endpoints were selected, the USEPA did not require an occupational risk assessment from potential post-application exposures of workers to aminopyralid. The USEPA, however, did conduct a post-application exposure assessment of children who could play in areas (e.g., recreational areas) that were treated with the Milestone product. The USEPA's estimated MOEs for children from hand-to-mouth transfer of aminopyralid residues, as well as from ingestion of pesticide-treated turfgrass and soil, were 61,000, 250,000 and 19,000,000, respectively. Generally, the USEPA considers MOEs of 100-fold or greater to provide adequate protection.

There are no chemical specific federal or New York State drinking water/groundwater standards for the triisopropanolammonium salt of aminopyralid, triisopropanolammonium itself or aminopyralid. 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 aminopyralid and Milestone indicates that neither the active ingredient nor the formulated product was overall very acutely toxic in laboratory animal studies. Furthermore, aminopyralid was not carcinogenic in rats or mice, nor was it genotoxic. Although data from some chronic and developmental toxicity studies showed that this chemical has the potential to cause some toxicity at relatively high doses, the estimated risks to workers and the general public from use of the Milestone product are within the range that is generally considered acceptable. In addition, dietary exposure of the general public to aminopyralid is not expected to pose significant health risks.

Ecological Risk Assessment:

Aminopyralid exhibits low toxicity to virtually all test organisms for which data were submitted. With the exception of vascular plants, it is classified as practically nontoxic on an acute basis to all terrestrial and aquatic organisms used in the standard suite of pesticide toxicity testing. As with nearly any substance, chronic effects can be produced with extended exposure to high levels of aminopyralid. Eight mammalian genotoxicity and/or mutagenicity studies were submitted, seven of which produced negative results. The eighth showed induced chromosomal aberrations but only at concentrations toxic to the cells themselves.

Aerobic microbial metabolism and runoff and/or leaching will be the primary routes of aminopyralid dissipation from application sites. Many of the submitted fate studies were

classified supplemental for a variety of reasons during USEPA review. The general conclusion based on the uncertainty in the fate and transport assessment, is that aminopyralid will be moderately persistent and mobile.

Aminopyralid is stable to hydrolysis and anaerobic metabolism. It degraded rapidly in laboratory aquatic photolysis studies with a half-life, $T_{1/2}$, of 0.6 days, it will likely do the same in shallow clear natural waters. Its soil surface photolysis $T_{1/2}$ is 72 days. The single aerobic soil metabolism study submitted yielded useable results for only one of the five soils studied. In the soil yielding useable data, a silt loam, aminopyralid had a nonlinear $T_{1/2}$ of 42 days. The observed time to 50% dissipation or DT_{50} was 50 to 60 days. The single submitted aerobic aquatic study, a water/sediment system study design, was classified supplemental because the sediment compartment became anaerobic shortly after study initiation. $T_{1/2}$s in the water layers ranged from 126 to 433 days. Aminopyralid is stable to anaerobic microbial metabolism. Terrestrial field dissipation $T_{1/2}$s for the entire sampled soil profile were 26 and 34 days at the California and Mississippi sites, respectively. DT_{90} for the same sites were 85 and 114 days. No degradation products were detected in either study.

EXPOSURE MODELING: Conservative screening assessments were conducted to estimate potential terrestrial and aquatic nontarget organism aminopyralid exposures. Avian and mammalian terrestrial food item aminopyralid residues were estimated for six different food groups following use of Milestone at the highest label rate. Aminopyralid water concentrations were estimated from direct inadvertent aerial application of Milestone to surface waters and from a runoff event immediately following application. Aminopyralid toxicity values, basic chemical characteristics, and environmental fate $T_{1/2}$s derived in various studies were used as direct inputs in the Department's computer models. Comparisons of terrestrial food item residues and water concentrations to test organism toxicity thresholds were determined using AVTOX, MAMTOX, DIRECT APPLICATION, and PONDTOX (the runoff simulation) computer models.

RISK ASSESSMENT: As determined by the modeling results, no nontarget organism toxicity thresholds were exceeded in the highly conservative scenarios simulated by the Department's computer modeling programs. There is the potential for secondary effects through habitat modification or damage with Milestone but the label includes extensive use precautions and warnings which, if followed, should prevent such effects.

Environmental Fate Risk Assessment:

Solubility: Aminopyralid acid has a solubility of 2,480 mg/L.

Hydrolysis: (MRID 46235726) In a study that USEPA found acceptable, aminopyralid was stable at pHs 5, 7, and 9.

Aqueous Photolysis: (MRID 46235727) In a study that USEPA found supplemental, the predicted environmental half-life is 0.6 days. Major transformation products include oxamic acid, malonamic acid, and four or more unidentified acid amides.

Soil Photolysis: (MRID 46235728) In a study that USEPA found supplemental, the predicted half-life is 72.2 days.

Anaerobic Aquatic Metabolism: (MRID 46235730) In a study that USEPA found acceptable, aminopyralid was stable in a sediment/pond water system in North Dakota, and in a flooded soil system in England.

Aerobic Aquatic Metabolism: (MRID 46235731) In a study that USEPA found supplemental, in a French water-sand sediment system, the half-life in water was 126 days and 866 days in the entire system. In an Italian water-silt loam sediment system, the half-life in water was 239 days and 462 days in the entire system. In a U.S. water-sandy loam sediment system, the half-life in

water was 433 days and 990 days in the entire system. No major transformation products were found.

Aerobic Soil Metabolism: (MRID 46235729) In a study that USEPA found supplemental, no major transformation products were found. In the Notice of Registration dated August 10, 2005, the USEPA required that this study be repeated in its entirety based on problems with the testing and the wide range of values found for half-lives.

Soil type	pH	% OC	First order half-life in days, linear regression	First order half-life in days, nonlinear regression	First order half-life in days, linear regression[1]	First order half-life, nonlinear regression[1]
Silt Loam[2]	4.6	1.5	73	38.7	103.5[3]	58.2
Loam	7.5	3.4	62.4	17.0	63.7	30.4
Sandy loam	7.3	1.2	31.9	19.4	55.9	25.8
Clay loam	4.8	3.6	330.1	330.1	533.2	533.2
Clay	7.5	3.4	9.4	6.1	31.5	17.9

[1]Half-lives treating nonextractable residues as parent.
[2] This was the only acceptable portion of the aerobic metabolism study.
[3]This was the value used by the USEPA in their modeling.

Adsorption/Desorption: (MRID 46235732) USEPA found this study supplemental.

Soil type	pH	% OC	Average Adsorption Koc	Average Desorption Koc
Silt Loam	7.8	1.0	4.49	598.44
Clay	7.5	3.2	1.05	NA
Silty clay loam	7.8	3.9	7.39	92.16
Sand	6.6	1.6	4.59	162.27
Soil type	pH	% OC	Average Adsorption Koc	Average Desorption Koc
Loam	6.1	1.0	7.54	1914.50
Clay	6.9	1.5	2.33	NA
Clay loam	4.8	3.6	10.05	105.66
Loamy sand	4.5	0.6	24.30	362.78

Field Dissipation: (MRID 46235734) In a study that USEPA found supplemental, the half-life in a silty loam in the surface soil was 32.1 days, and 34 days in the total soil profile. In a sandy loam, the half-life in the surface soil was 20.0 days, and 26 days in the total soil profile. No major transformation products were found.

Computer Modeling: Running LEACHM on Riverhead soil using an adsorption K_{oc} of 24.3, a half-life of 103.5 days (the only one found acceptable by the USEPA) and an application rate of 0.11 lb ai/acre/year, the model projected breakthrough in year 2, and cyclic peaks ranging from 0 to about 14 ppb. Changing to the desorption K_{oc} of 362.78, the model projected accumulation, reaching a high of about 0.038 ppb.

Staff also ran the modeling using the average of the sandy loam half-lives, or 33.2 days. Using the adsorption K_{oc} of 24.3, and an application rate of 0.11 lb ai/acre/year, the model projected breakthrough in year 2, and cyclic peaks ranging from 0 to about 4 ppb. Changing to the desorption K_{oc} of 362.78, the model projected cyclic peaks, reaching a high of about 0.0002 ppb.
Groundwater Modeling Summary:

Only one of the half-life values was accepted by the USEPA. There were concerns regarding the wide variability in the other listed half-life values. Therefore, staff ran the

LEACHM modeling program using the accepted 103.5 day half-life. This half-life, together with the variation between the adsorption and desorption K_{oc}s for the loamy sand soil, made it difficult to achieve a clear understanding of the actual environmental behavior of aminopyralid when used as labeled. Also as printed in the Notice of Registration dated August 10, 2005 for Milestone, the USEPA directed Dow AgroSciences, LLC, to repeat the entire aerobic metabolism study.

A supplemental groundwater impact review was conducted by the Department using additional information submitted by Dow AgroSciences on December 21, 2006. The document was entitled "Aminopyralid NYSDEC Leaching Assessment Response" dated December 20, 2006. While the response submitted by Dow AgroSciences, LLC, was informative, the Department could not ignore the inadequacy of the original aerobic metabolism study. Therefore the Department could not ensure that the labeled use of aminopyralid would not negatively impact groundwater resources in sensitive areas of New York State.

Summary:

The Department accepts Dow AgroSciences decision to **withdraw** their application of Milestone Herbicide (EPA Reg. No. 62719-519) which contains the new active ingredient aminopyralid.

The Department will also close registration review on two new product applications, also containing aminopyralid, that were on hold pending registration of Milestone Herbicide:

Milestone VM (EPA Reg. No. 62719-537)
ForeFront R & P (EPA Reg. No. 62719-524)

Please note that Dow AgroSciences will be required to submit new application forms and fees upon re-submission of Milestone Herbicide or any product containing aminopyralid. The Department recognizes that Milestone Herbicide is an important new tool for controlling invasive and noxious weeds and that it is classified as "Reduced Risk" by the United States Environmental Protection Agency (USEPA) for its limited impacts to human health and nontarget organisms. However, the Department does not consider products which have the potential to impact groundwater resources as "Reduced Risk" without acceptable environmental fate data. Since there appears to be no unreasonable risk to human health or non-target organisms, the Department will conduct a limited technical review of the environmental fate of aminopyralid upon submission of the new aerobic soil metabolism study required by USEPA.

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

Please contact 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

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