Proposed Registration of Aminocyclopyrachlor on Non-Crop Areas, Sod Farms, Turf, and Residential Lawns

June 16, 2010

U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division

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Approved by: Lois Rossi

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Registration Division

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1. REGULATORY RATIONALE

The Agency is proposing to conditionally grant the first non-food use registrations of the active ingredient aminocyclopyrachlor, formulated as 2 technical products, 3 manufacturing-use products, and 15 end-use products. It is a selective herbicide providing pre- and post-emergent control of broadleaf weeds, woody species, vines, and grasses in non-crop areas [private, public, and military lands: uncultivated non-agricultural areas (such as airports, highway, railroad and utility rights-of-way, sewage disposal areas), uncultivated non-crop agricultural areas (such as farmyards, fuel storage areas, fence rows, non-irrigation ditchbanks, barrier strips), outdoor industrial sites (such as lumberyards, pipeline, and tank farms), natural areas (such as wildlife management areas, wildlife openings, wildlife habitats, recreation areas, campgrounds, trailheads, and trails)], turf/lawns (residential, industrial, and institutional), golf courses, parks, cemeteries, athletic fields, and sod farms.

Three forms of aminocyclopyrachlor are being proposed for registration: the parent acid (aminocyclopyrachlor), the methyl ester (aminocyclopyrachlor-methyl), and the potassium salt (aminocyclopyrachlor potassium salt). The parent acid, aminocyclopyrachlor, is considered the active ingredient.

Aminocyclopyrachlor may be applied in three different formulations: granular, water dispersible granular (dry flowable), and soluble liquid. Occupational application scenarios include: aerial (fixed wing or helicopter), ground boom, right-of-way sprayer, push-type spreader, push cyclone spreader, tractor drawn broadcast spreader, and lawn care operator (LOC) handgun. Broadcast applications may be performed by using either a single ground boom, a tractor type broadcast, or as a banded application for pre-plant, pre-emergence, or early post-emergence. Pre-plant applications can be made as either a single or split application that is either surface applied or incorporated. Residential application scenarios include low pressure hand wand, hose-end sprayer, and hand-held spreader (i.e. belly grinder). Proposed maximum annual application rates range from 0.05 – 0.324 lb acid equivalent (ae)/acre/year.

1.1. Chemical Information

Aminocyclopyrachlor is a systemic herbicide in the pyrimidine carboxylic acids class within the family of synthetic auxins, which disrupts gene expression resulting in undifferentiated cell division and elongation. It is biologically active in soil and is rapidly absorbed by roots and leaves. Effects to target weeds include downward bending of leaves, severe necrosis, stem thickening, growth stunting, leaf crinkling and cupping, calloused stems and leaf veins, and enlarged roots. Symptoms may begin from a few hours to a few days after application, and plant death may take weeks to several months.

1.1.1. Chemical Name: Aminocyclopyrachlor (parent acid)
6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylic acid

EPA PC Code: 288008
CAS Number: 858956-08-8
Mode of Action: Synthetic auxin-type herbicide causing disorganized plant growth (pyrimidine carboxylic acid)
Registrant: E.I. du Pont de Nemours and Company (EPA Company Number: 352)

Products:

EPA Reg. No.	Product Name	% a.i.
352-TIE (782)	DPX-MAT28 Technical Herbicide	89.3
352-TOA (796)	DPX-MAT28 10% Manufacturing Concentrate	10.0
352-TIT (787)	DPX-MAT28 50SG Herbicide	50.0
352-TOU (794)	DPX-MAT28 50SG Turf Herbicide	50.0
352-IRG (813)	DPX-MAT28 0.05G Turf Herbicide + Fertilizer	0.05
352-IRU (814)	DPX-MAT28 0.03G Turf Herbicide + Fertilizer	0.03
352-IRL (815)	DPX-MAT28 0.068G Lawn Herbicide + Fertilizer	0.068

1.1.2. Chemical Name: Aminocyclopyrachlor-methyl (methyl ester)
methyl 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylate

EPA PC Code: 288009
CAS Number: 858954-83-3
Mode of Action: Synthetic auxin-type herbicide causing disorganized plant growth (pyrimidine carboxylic acid)
Registrant: E.I. du Pont de Nemours and Company (EPA Company Number: 352)

Products:

EPA Reg. No.	Product Name	% a.i.
352-TIG (783)	DPX-KJM44 Technical Herbicide	95.6
352-TIU (784)	DPX-KJM44 80 MUP Herbicide	80.0
352-TOL (795)	DPX-KJM44 10% Manufacturing Concentrate	10.0
352-TIL (785)	DPX-KJM44 80XP Herbicide	80.0
352-TOE (792)	DPX-KJM44 80XP Turf Herbicide	80.0
352-TOT (797)	DPX-KJM44 0.064G Turf Herbicide + Fertilizer	0.064
352-INN (800)	DPX-KJM44 0.073G Lawn Herbicide + Fertilizer	0.073
352-ING (803)	DPX-KJM44 0.053G Lawn Herbicide + Fertilizer	0.053
352-INU (804)	DPX-KJM44 0.049G Lawn Herbicide + Fertilizer	0.049
352-INT (807)	DPX-KJM44 0.033G Lawn Herbicide + Fertilizer	0.033
352-IRR (811)	DPX-KJM44 0.02G Lawn Herbicide + Fertilizer	0.02

1.1.3. Chemical Name: Aminocyclopyrachlor potassium salt
potassium 6-amino-5-chloro-2-cyclopropyl-4-pyrimidinecarboxylate

EPA PC Code: 288010
CAS Number: 858956-35-1
Mode of Action: Synthetic auxin-type herbicide causing disorganized plant growth

(pyrimidine carboxylic acid)
Registrant: E.I. du Pont de Nemours and Company (EPA Company Number: 352)

Products:

EPA Reg. No.	Product Name	% a.i.
352-TIA (786)	DPX-MAT28 240SL Herbicide	25.0
352-TOG (793)	DPX-MAT28 240SL Turf Herbicide	25.0

1.2. Human Health Risk

A summary of the human health effects and risk of aminocyclopyrachlor as assessed in the Agency document titled "Aminocyclopyrachlor: Human Health Risk Assessment for Proposed Uses as an Herbicide" is provided below.

1.2.1. Toxicological Summary and Considerations

Pharmacokinetic oral studies indicate that both aminocyclopyrachlor and aminocyclopyrachlor-methyl are rapidly absorbed, with rapid metabolic conversion of aminocyclopyrachlor-methyl to aminocyclopyrachlor. Elimination is almost complete within 24 hours. Similar acute toxicities, subchronic dietary, reproductive toxicity, and gene mutation studies results for both chemicals, along with evidence from metabolism studies form a scientific justification for considering aminocyclopyrachlor and aminocyclopyrachlor-methyl toxicologically equivalent, thus allowing bridging of the toxicity database for aminocyclopyrachlor-methyl with studies using aminocyclopyrachlor.

The toxicology database for aminocyclopyrachlor is adequate for risk assessment for the proposed use patterns. Aminocyclopyrachlor has low acute toxicity by oral, dermal, and inhalation routes of exposure, and does not cause skin sensitization or irritation. However, it can cause mild eye irritation. Aminocyclopyrachlor and aminocyclopyrachlor-methyl have low subchronic toxicity via the oral route. The most sensitive species is the rat, with decreased body weight at the limit dose in subchronic dietary studies as the most sensitive endpoint of toxicity. The major effect observed across species for aminocyclopyrachlor was decreased body weight at the limit dose. No toxicity was observed in subchronic dietary studies in dogs at the highest dose of aminocyclopyrachlor tested, which was half the limit dose, but still higher than the dose at which no adverse effects occurred in the rat. No target organ of toxicity was identified. No sex differences in toxicity were observed for either aminocyclopyrachlor or aminocyclopyrachlor-methyl.

Aminocyclopyrachlor was not neurotoxic when administered acutely or subchronically via the oral route. Aminocyclopyrachlor-methyl showed no evidence of neurotoxicity or reproductive toxicity in an extended one generation reproductive toxicity study in rats. Aminocyclopyrachlor did not cause developmental toxicity in rats or rabbits. Therefore, there is low concern for reproductive, developmental, or neurotoxicity for aminocyclopyrachlor and aminocyclopyrachlor-methyl.

Aminocyclopyrachlor and aminocyclopyrachlor-methyl are considered to have low potential to cause chronic toxicity or carcinogenicity. No evidence of genotoxic effects was observed in mutagenicity studies *in vitro* for aminocyclopyrachlor and aminocyclopyrachlor-methyl or *in vivo* for aminocyclopyrachlor. No evidence of target organ toxicity was observed in oral subchronic studies for aminocyclopyrachlor and aminocyclopyrachlor-methyl at doses exceeding the limit dose.

Immunotoxicity was investigated via the oral route in two species (rats and mice) for aminocyclopyrachlor. There was no evidence of immunotoxicity.

1.2.1.1. Degradate of Concern

An environmental photodegradate of aminocyclopyrachlor present only in surface water was of possible concern for drinking water exposures. This photodegradate, cyclopropane carboxylic acid (IN-V0977), has a different mode of toxic action than aminocyclopyrachlor. Oral administration of cyclopropane carboxylic acid causes severe impairment of mitochondrial function by inhibiting the beta oxidation of fatty acids, resulting in microvesicular steatosis (accumulation of small fat droplets in cells). The liver is the most sensitive organ, and hepatocellular microvesicular steatosis is often accompanied by liver necrosis and inflammation, decreased hepatic glycogen, and decreased blood glucose levels. These effects have been observed with acute (one to three days) and longer (up to 14 days) exposure. The most sensitive species is the rabbit. Hepatic microvesicular steatosis in the rabbit follows a different dose-response than body weight decreases observed with aminocyclopyrachlor and aminocyclopyrachlor-methyl in rats, with a lowest observed adverse effect level (LOAEL) that is 100-fold lower. However, based on the proposed use pattern, the dietary exposure to IN-V0977 from drinking water is below the Agency's level of concern (LOC) (see Section 1.2.4).

1.2.2. Toxicological End Points and Doses

1.2.2.1. Acute Dietary

For aminocyclopyrachlor, no acute reference dose (aRfD) or acute population adjusted dose (aPAD) was established because no toxicity was observed at the limit dose in the acute oral toxicity studies.

For the degradate IN-V0977, the Agency has established an aRfD of 0.0026 mg/kg (body wt)/day, based on the LOAEL of 2.55 mg/kg/day from a rabbit study in which hepatic steatosis was observed and an uncertainty factor of 1000X. The 1000X uncertainty factor takes into account interspecies and intraspecies variability (10X for each) as well as the uncertainty associated with extrapolation of a no observed adverse effect level (NOAEL) from a LOAEL (10X).

1.2.2.2. Chronic Dietary

For aminocyclopyrachlor, the Agency has established a chronic reference dose (cRfD) and a chronic population adjusted dose (cPAD) of 0.35 mg/kg/day, based on the NOAEL of 350

mg/kg/day from the 90-day oral toxicity study in rats and an uncertainty factor of 1000X. In this study, decreased body weights, body weight gains, food consumption, and food efficiency in both sexes were observed at the LOAEL of 1044.6/1424.9 mg/kg/day. The 1000X uncertainty factor takes into account interspecies and intraspecies variability (10X for each) as well as the uncertainty associated with using an endpoint from a subchronic study to assess chronic exposure (10X).

For the degradate IN-V0977, the Agency has established a cRfD of 0.00087 mg/kg/day, based on the LOAEL of 2.55 mg/kg/day from a rabbit study in which hepatic steatosis was observed and an uncertainty factor of 3000X. The 3000X uncertainty factor takes into account interspecies and intraspecies variability (10X for each), uncertainty associated with extrapolation of a NOAEL from a LOAEL (10X), and uncertainty arising from using a short-term study to assess long-term risk (3X).

1.2.2.3. Short- and Intermediate-Term Incidental Oral and Inhalation

The Agency has established a LOC of 3.5 mg/kg/day for the margin of exposure (MOE) of 100, based on the NOAEL of 350 mg/kg/day from the chronic 90-day oral toxicity study in rats and an uncertainty factor of 100X (10X interspecies x 10X intraspecies). In this study, decreased body weights, body weight gains, food consumption, and food efficiency in both sexes were observed at the limit dose LOAEL of 1044.6/1424.9 mg/kg/day. Long-term incidental oral exposures are not anticipated based on the proposed use pattern.

1.2.2.4. Short- and Intermediate-Term Dermal

No dermal endpoint was established because no toxicity was observed at the limit dose in the 28-day dermal toxicity study. The 90-day dermal toxicity study was waived because the 28-day dermal toxicity study is considered suitable for long-term exposures and all endpoints of concern were assessed.

1.2.2.5. Cancer

The Agency has classified aminocyclopyrachlor as “Not likely to be Carcinogenic to Humans” based on the lack of evidence of genotoxic effects in the *in vitro* and *in vivo* mutagenicity studies. Aminocyclopyrachlor is considered to have low potential to cause chronic toxicity or carcinogenicity. No evidence of target organ toxicity was observed in oral subchronic studies at doses exceeding the limit dose. Therefore, cancer risk was not assessed.

1.2.3. Consideration of Toxicity to Children

Food Quality Protection Act (FQPA) considerations do not apply to aminocyclopyrachlor for the non-food use patterns described in this risk assessment. However, the Agency has reviewed the toxicity database and has determined that the young will not be particularly sensitive to the effects of aminocyclopyrachlor when used in residential settings based on the following:

- The toxicity database is considered complete and includes acceptable developmental

toxicity studies in rats and rabbits, a two-generation reproductive toxicity study in rats, and an extended one-generation reproductive toxicity study in rats that included a modified functional observational battery.

- No evidence of neurotoxicity was observed in the acute or subchronic neurotoxicity studies in rodents at the limit dose after exposure to aminocyclopyrachlor. Also, no evidence of neurotoxicity was observed in an extended one-generation reproduction study in rats with aminocyclopyrachlor-methyl that included a modified functional observational battery.
- No evidence of developmental toxicity was observed when aminocyclopyrachlor was administered in the diet of rats or orally by gavage to rabbits at the limit dose.
- No evidence of adverse effects of aminocyclopyrachlor or aminocyclopyrachlor-methyl on reproduction or fertility parameters was observed in dietary studies with rats.
- No evidence of prenatal toxicity was observed following maternal exposure to aminocyclopyrachlor. There is no evidence of increased susceptibility following *in utero* exposure to aminocyclopyrachlor in rats or rabbits in developmental toxicity studies, which showed no adverse effects in offspring at the limit dose. An increase in abortions in maternal rabbits was observed at the limit dose, but this was considered secondary to decreases in body weight. There was also no evidence of increased susceptibility of offspring to aminocyclopyrachlor in reproduction and fertility studies in rats, for which adverse effects were limited to decreased body weights in both maternal animals and offspring at the limit dose. Therefore, the young are *not* considered more susceptible than adults to adverse effects from aminocyclopyrachlor or aminocyclopyrachlor-methyl.
- There are no residual uncertainties identified in the exposure databases. EPA made conservative (protective) assumptions in the ground and surface water modeling used to assess exposure to aminocyclopyrachlor in drinking water. EPA used similarly conservative assumptions to assess post-application exposure of children including incidental oral exposure of toddlers. These assessments will not underestimate the exposure and risks posed by aminocyclopyrachlor.

1.2.4. Dietary Risk

Dietary risk assessment addresses exposure that individuals receive through food consumption and drinking water. Since there are no proposed food uses for aminocyclopyrachlor, only dietary exposure to aminocyclopyrachlor and its environmental degradates from drinking water were considered.

For aminocyclopyrachlor, no acute dietary risk assessment was performed since no acute toxicity endpoint was identified. Cancer risks from dietary exposure to aminocyclopyrachlor and the degradate IN-V0977 in drinking water were not assessed since no cancer dietary endpoint was identified. Risks for chronic dietary exposures to aminocyclopyrachlor from drinking water were considered, and the risk estimates for the general U.S. population and all other regulated population subgroups are below the Agency's LOC of greater than 100% of the cRfD. Chronic exposure to aminocyclopyrachlor from drinking water will occupy <1% of the cRfD for infants less than 1 year old, the population subgroup with the highest estimated exposure.

The major route of environmental degradation of aminocyclopyrachlor is aqueous photolysis, which produces five degradates. Of these, one environmental degradate, IN-V0977 (cyclopropane carboxylic acid), was of concern. Dietary assessments of acute and chronic dietary exposures of cyclopropane carboxylic acid from drinking water were performed, and are below the Agency's LOC of greater than 100% of the aRfD/cRfD. Acute exposure to the degradate IN-V0977 from drinking water will occupy 13% of the aRfD and 9.9% of the cRfD for infants less than 1 year old, the population subgroup with the highest estimated exposure.

1.2.5. Residential Risk

Residential risk assessment addresses exposures that individuals receive through their use of consumer products and exposures that individuals receive from frequenting areas that have been previously treated with aminocyclopyrachlor.

1.2.5.1. Residential Handler Risk

Residential handler exposure to aminocyclopyrachlor may occur dermally and by inhalation. No dermal risk was assessed because no toxicity was observed at the limit dose in the subchronic dermal toxicity study. Inhalation risk was assessed by analysis of short-term and intermediate-term exposures using the lawn/turf products with the highest application rates (0.07 - 0.10 lb ae/A) and hazards identified in subchronic oral toxicity studies.

The Agency has identified the following residential exposure scenarios from applications to lawns/turf:

Mixing/Loading/Applying

- Low Pressure Handwand (dry flowable and soluble liquid)
- Hose-End Sprayer (dry flowable and soluble liquid)
- Hand-Held Spreader/Belly Grinder (granular)

The margins of exposure (MOEs) for the three inhalation exposure scenarios range from 7,300,000 to 41,200,000. Since the Agency's LOC is for MOEs less than 100, residential handler exposures are not of concern.

1.2.5.2. Residential Post-Application Risk

Residential post-application exposure to aminocyclopyrachlor may occur dermally and orally for a variety of populations. No dermal risk was assessed because no toxicity was observed at the limit dose in the subchronic dermal toxicity study. Oral risk in toddlers was assessed by analysis of short-term and intermediate-term post-application exposures using the lawn/turf product with the highest application rate (0.10 lb ae/A).

The Agency has identified the following residential post-application exposure scenarios from applications to lawns/turf:

Toddlers

- Hand-to-Mouth Activity on Lawn/Turf
- Object-to-Mouth Activity on Lawn/Turf
- Soil Ingestion

The single and combined MOEs for short-term and intermediate-term oral exposures range from 234,000 to 70,000,000. Since the Agency's LOC is for MOEs less than 100, residential post-application exposures are not of concern for any population, including toddlers.

1.2.6. Aggregate Risk

Aggregate risk assessment addresses combined exposures that individuals receive from dietary and residential exposures to aminocyclopyrachlor. Quantitative, aggregate exposure and risk assessments for aminocyclopyrachlor are not required for the proposed non-food use patterns because Food Quality Protection Act (FQPA) considerations do not apply. However, the potential for significant aggregate exposures to aminocyclopyrachlor from dietary (drinking water) and residential uses relative to non-aggregate exposures was considered. The highest estimated residential exposure (0.000048 mg/kg/day via inhalation during mixing, loading, and applying a granular formulation with a belly grinder) was combined with the highest estimated dietary exposure (0.002778 mg/kg/day for all infants < 1 year old). This combined value of 0.003 mg/kg/day was over 1000- fold lower than the point of departure of 3.5 mg/kg/day, based on the most conservative LOC for MOE (350 mg/kg/day with MOE =100). This estimate indicates that aggregate exposures to aminocyclopyrachlor will not result in significantly increased risk relative to non-aggregate exposure.

1.2.7. Occupational Risk

Occupational risk assessment addresses risks to individuals who are exposed to aminocyclopyrachlor as part of their employment, via contact while using commercial products (handler) or by being in areas that have been previously treated (post-application).

1.2.7.1. Occupational Handler Risk

Occupational handler exposure to aminocyclopyrachlor may occur dermally and by inhalation. No dermal risk was assessed because no toxicity was observed at the limit dose in the subchronic dermal toxicity study. Inhalation risk was assessed by analysis of short-term and intermediate-term exposures using the products with the highest application rates (0.07 - 0.28 lb ae/A) and hazards identified in subchronic oral toxicity studies.

The Agency has identified the following occupational exposure scenarios from applications to private, public and military lands including un-cultivated non-agricultural (non-crop) areas such as airports, highways, railroads, golf courses, lumber yards, wild life habitats, multi family residential complexes, recreation areas, sod farms, utility rights of way, and residential lawns:

Mixing/Loading

- Groundboom (dry flowable and soluble liquid) to non-crop areas, golf courses, sod farms, and lawn/turf

- Aerial (fixed and non-fixed wing) (dry flowable) to non-crop areas
- LCO handgun (dry flowable and soluble liquid) to non-crop areas, golf courses, sod farms, and lawn/turf
- Right-of-way sprayer (dry flowable and soluble liquid) to non-crop areas, golf courses, sod farms, and lawn/turf
- Push-type spreader (granular) to golf courses, sod farms, and lawn/turf
- Tractor drawn broadcast spreader (granular) to golf courses, sod farms, and lawn/turf
- Push cyclone spreader (granular) to golf courses, sod farms, and lawn/turf

Applying

- Groundboom (dry flowable and soluble liquid) to non-crop areas, golf courses, sod farms, and lawn/turf
- Aerial (fixed and non-fixed wing) (dry flowable) to non-crop areas
- LCO handgun (dry flowable and soluble liquid) to non-crop areas, golf courses, sod farms, and lawn/turf
- Right-of-way sprayer (dry flowable and soluble liquid) to non-crop areas, golf courses, sod farms, and lawn/turf
- Tractor drawn broadcast spreader (granular) to golf courses, sod farms, and lawn/turf

Flagging

- Aerial (fixed and non-fixed wing) (dry flowable) to non-crop areas

The MOEs for the identified inhalation exposure scenarios range from 190,000 to 50,000,000. Since the Agency's LOC is for MOEs less than 100, occupational handler exposures are not of concern.

1.2.7.2. Occupational Post-Application Risk

Occupational post-application exposure to aminocyclopyrachlor may occur dermally and by inhalation. No dermal risk was assessed because no toxicity was observed at the limit dose in the subchronic dermal toxicity study. A quantitative post-application inhalation risk assessment was not deemed necessary, based on the high occupational handler MOE values. Post-application exposures would be lower than those for handlers due to aminocyclopyrachlor's low vapor pressure and dilution in outdoor air. Therefore, occupational post-application exposures are not of concern.

1.3. Environmental Risk

A summary of the environmental fate and ecological effects and risks of aminocyclopyrachlor as assessed in the Agency document titled "Ecological Risk Assessment for the Section 3 New Chemical Registration of Aminocyclopyrachlor on Non-crop Areas and Turf" is provided below.

1.3.1. Environmental Summary and Considerations

A dissociation constant study indicated that the potassium salt form of aminocyclopyrachlor rapidly dissociates to the acid when it is mixed with water prior to application. This similarity in behavior once the potassium salt is dissociated in water allows bridging of the environmental fate and toxicity database for aminocyclopyrachlor potassium salt with studies using aminocyclopyrachlor.

Laboratory and field dissipation studies indicated that aminocyclopyrachlor-methyl rapidly hydrolyzes to aminocyclopyrachlor in alkaline aquatic environments, moist soils, and soil/water slurries. Degradation under environmentally-relevant pH conditions is primarily microbe mediated. Therefore, aminocyclopyrachlor-methyl applications may result in short-term exposures to the methyl ester form prior to hydrolysis to the acid. Aquatic studies on freshwater fish and invertebrates for aminocyclopyrachlor-methyl showed higher toxicity than aminocyclopyrachlor. As a result, with the exception of acute aquatic toxicity data, acute/chronic terrestrial and chronic aquatic toxicity data may be bridged for aminocyclopyrachlor-methyl with studies using aminocyclopyrachlor.

1.3.1.1. Degradates of Concern

Model estimates suggest that degradates IN-LXT69 and IN-YY905 may be more toxic than aminocyclopyrachlor to daphnids on a chronic basis. Based on human health effects evaluation of degradates (see Sections 1.2.1.1 and 1.2.4), the degradate IN-V0977 may be more toxic than aminocyclopyrachlor to birds and mammals. However, by comparing the concentrations expected in the environment to the effects thresholds, IN-V0977 would have to be more than two orders of magnitude more toxic than aminocyclopyrachlor to exceed the Agency's LOC. Also, since aqueous photolysis is the only significant rapid degradation pathway of aminocyclopyrachlor, aquatic exposure to the three degradates of concern would not result in any additional risks over those presented from exposure to aminocyclopyrachlor unless the degradates were considerably more toxic.

1.3.2. Environmental Fate

Aminocyclopyrachlor is non-volatile, highly soluble in water, and highly mobile to mobile in soils. Dissipation in the environment is expected to occur predominantly via aqueous photolysis, runoff, and leaching. Terrestrial field dissipation occurred with half-lives ranging from 22 to 126 days. Aminocyclopyrachlor was detected at soil depths of 70 – 90 cm at 365 days, indicating that leaching of residues into groundwater may occur.

Aminocyclopyrachlor is environmentally persistent in diverse environments. It persists in aerobic aquatic environments with a dissipation time of greater than 100 days and in aerobic terrestrial environments with a half-life of 373 days. It is also stable in anaerobic aquatic environments with a half life of 1733 days and in anaerobic terrestrial environments with a half-life of 6932 days. It has a low tendency for bioaccumulation.

The major route of degradation of aminocyclopyrachlor is abiotic via aqueous photolysis with a half-life of l.2 days in shallow, clear, and well-lit natural (pH 6.2) water bodies and 7.8 days in pH 4 buffer solution. However, it is slowly photolyzed on soil, with a half-life of 129 days. Aminocyclopyrachlor is stable to hydrolysis at pH 4, 7, and 9.

To address concerns with the potential leaching of aminocyclopyrachlor that may result from the persistence and mobility described above, end-use product labels will be required to include surface and ground water advisories that stress the potential of runoff after treatment and descriptions of conditions that may promote leaching to groundwater (see Section 2.2.1).

1.3.3. Ecological Risk

Ecological risk assessment addresses exposures that non-target aquatic and terrestrial organisms and plants receive through the use of aminocyclopyrachlor.

A screening-level risk assessment based on proposed uses suggests that aminocyclopyrachlor presents potential risk to terrestrial and semi-aquatic plants and to organisms that depend on the plants for habitat and forage.

To better characterize and confirm chronic risks to birds and freshwater invertebrates, additional data will be required as a condition of registration (see Section 2.1.2). To mitigate potential risk to non-target terrestrial and semi-aquatic plants, end-use product labels will be required to include language that is intended to keep the pesticide on the treatment area (see Section 2.2.4).

1.3.3.1. Aquatic Risk

The highest surface water estimated environmental concentration (EEC) values resulted from proposed aerial non-crop applications at 0.284 lb ae/A. This conservative approach of using an EEC of 0.284 lb ae/A will also cover turf applications, which resulted in lower EECs. EECs were compared to toxicity endpoints to derive risk quotients (RQs), which is then compared to the Agency's LOC.

1.3.3.1.1. Fish Risk

Aminocyclopyrachlor is practically non-toxic to freshwater and estuarine/marine fish on an acute basis. Acute risk was not quantified since no toxicity was observed at the highest concentration tested; therefore, RQs are not expected to exceed LOCs. Aminocyclopyrachlor-methyl is slightly toxic to freshwater fish on an acute basis; however, the RQ of <0.01 does not exceed the LOC. Chronic risk to freshwater fish resulted in a RQ of <0.01 and does not exceed the LOC.

1.3.3.1.2. Aquatic Invertebrate Risk

Aminocyclopyrachlor and aminocyclopyrachlor-methyl are slightly toxic to freshwater invertebrates on an acute basis; however, RQs of <0.01 do not exceed LOCs. Aminocyclopyrachlor is practically non-toxic to estuarine/marine invertebrates on an acute basis;

where the RQ <0.01 does not exceed the LOC.

In the chronic freshwater invertebrate (daphnid) study, non dose-response mortalities were observed at the three lowest treatment levels. Therefore, the resulting toxicity values could not be used quantitatively to assess chronic risk to aquatic invertebrates. Despite the lack of valid data, chronic risk to freshwater invertebrates is not expected to exceed the Agency's LOC. Environmental concentrations of aminocyclopyrachlor in surface waters from applications at the proposed maximum rates are expected to be in the parts per billion (ppb) range; whereas all aquatic toxicity studies were conducted at concentrations in the parts per million (ppm) range. Based on the results of chronic studies in freshwater fish, where the no observed adverse effect concentration (NOAEC) is 11 ppm, EPA also expects the freshwater invertebrate NOAEC to be in the ppm range, well above the expected environmental concentrations. A repeated Freshwater Invertebrate Life Cycle Toxicity Test (Guideline 850.1300) is expected to be confirmatory and will be required as a condition of registration (see Section 2.1.2).

1.3.3.1.3. Aquatic Plant Risk

Risks to aquatic vascular and non-vascular plants resulted in RQs <0.01, which do not exceed the Agency's LOC.

1.3.3.2. Terrestrial Risk

Terrestrial wildlife EECs are estimated emphasizing a dietary exposure route for uptake of pesticide residues on vegetative matter and insects. Birds are used as surrogates for terrestrial-phase amphibians and reptiles. Honey bee is used as a surrogate for terrestrial invertebrates.

1.3.3.2.1. Avian Risk

Aminocyclopyrachlor and aminocyclopyrachlor-methyl are practically non-toxic to birds (also terrestrial-phase amphibians and reptiles) on an acute basis. Acute risk was not quantified since no toxicity was observed; therefore, RQs are not expected to exceed LOCs.

The submitted avian reproduction studies were invalid due to improper husbandry practices (small cage sizes) that may have caused incidental mortalities in quails and reduced egg production in mallards. Despite the improper husbandry conditions, there was no evidence in either study of adverse treatment-related effects, including overt toxicity, mortality, effects on feed consumption and body weight, macroscopic findings, or reproductive effects. A repeated Avian Reproduction Toxicity Test (Guideline 850.2300) is expected to be confirmatory and will be required as a condition of registration (see Section 2.1.2).

1.3.3.2.2. Mammalian Risk

Aminocyclopyrachlor and aminocyclopyrachlor-methyl are practically non-toxic to mammals on an acute basis. Acute risk was not quantified since no toxicity was observed; therefore, RQs are not expected to exceed LOCs. Chronic risks to mammals resulted in RQs of <0.1 and do not exceed the LOC.

1.3.3.2.3. Terrestrial Invertebrate Risk

Aminocyclopyrachlor is practically non-toxic to terrestrial invertebrates, due to lack of mortality and sublethal effects in the honey bee study for aminocyclopyrachlor. An acute earthworm toxicity study for aminocyclopyrachlor-methyl also showed no mortalities or behavioral abnormalities, but the study is classified as supplemental since the Agency does not currently have an OPPTS guideline for earthworms. The Agency does not routinely quantify risks to terrestrial invertebrates.

1.3.3.2.4. Terrestrial Plant Risk

As expected for herbicides, terrestrial and semi-aquatic plants are sensitive to aminocyclopyrachlor, where RQs exceeded the LOC. Non-target terrestrial and semi-aquatic plants may be exposed to aminocyclopyrachlor via runoff and spray drift, with dicots being more susceptible than monocots. To mitigate potential risk to non-target terrestrial and semi-aquatic plants, end-use product labels will be required to include language that is intended to keep the pesticide on the treatment area (see Section 2.2.4).

1.4. Public Interest

Aminocyclopyrachlor poses very low risk to humans, including workers and the general population, due to its low toxicity and low volatility. Similarly, because of its low toxicity to terrestrial and aquatic non-target organisms other than plants, aminocyclopyrachlor poses low environmental risks.

The benefits afforded by registration of aminocyclopyrachlor may be substantial. Along with other herbicides in the same chemical family, this herbicide will be an important component in integrated pest management programs for both non-crop and turf areas. Aminocyclopyrachlor controls a broad spectrum of weeds, including difficult to manage invasive and noxious brush and herbicide-resistant species. In particular, aminocyclopyrachlor demonstrates very good long-term control of Leafy Spurge, considered one of the most difficult to control invasive weeds in the western United States. Leafy Spurge is listed as a noxious weed in 22 states, making control mandatory by legal statute in those areas. Very few alternative chemicals provide effective long-term control of Leafy Spurge, which reproduces aggressively, actively destroying native biodiversity and rendering pastures and rangelands unfit for cattle and horses grazing due to its unpalatability and toxicity. A single application of aminocyclopyrachlor will provide long-lasting control, obviating the need for multiple applications of the current alternatives and thereby reducing the pesticide load in the environment. Aminocyclopyrachlor will also provide the commercial turf industry with an important tool. Because of its low volatility, it can be used in turf applications around valuable ornamental plants with less risk of damage than the current staples of the industry, 2,4-D and dicamba.

Based on these considerations, the Agency believes that the registration of aminocyclopyrachlor is in the public's interest.

2. PROPOSED REGULATORY DECISION

The Agency is proposing to grant the first registrations of the active ingredient aminocyclopyrachlor, formulated as 2 technical products, 3 manufacturing-use products, and 15 end-use products. It is a selective herbicide providing pre-emergence and post-emergence control of broadleaf weeds, woody species, vines, and grasses in non-crop areas [private, public, and military lands: uncultivated non-agricultural areas (airports, highway, railroad and utility rights-of-way, sewage disposal areas), uncultivated non-crop agricultural areas (farmyards, fuel storage areas, fence rows, non-irrigation ditchbanks, barrier strips), outdoor industrial sites (lumberyards, pipeline, and tank farms), natural areas (wildlife management areas, wildlife openings, wildlife habitats, recreation areas, campgrounds, trailheads, and trails)], turf/lawns (residential, industrial, and institutional), golf courses, parks, cemeteries, athletic fields, and sod farms.

In the Federal Register of January 27, 2010 (75 FR 4384), EPA issued a notice pursuant to section 3(c)(4) of FIFRA entitled "Pesticide Products; Registration Applications" in the docket EPA-HQ-OPP-2009-0789 announcing receipt of applications to register pesticide products containing the new active ingredient, aminocyclopyrachlor, by E.I. du Pont de Nemours and Company. There were no comments received in response to the notice of receipt.

2.1. Data Requirements

The Agency has determined that additional data are required in order to better characterize risk. The studies identified below will be required as a condition of the registration of aminocyclopyrachlor.

2.1.1. Human Health Data Requirements

The human health risk assessment concluded that the following study is required in support of the proposed uses:

- ***A repeated-dose study in a sensitive species is required to address the hazard of subchronic/chronic exposure to the environmental degradate cyclopropane carboxylic acid (IN-V0977):*** *To account for the lack of this study, EPA applied an additional 3X uncertainty factor (UF) to the point of departure (POD) used in the chronic exposure assessment for drinking water. Even with the additional UF and the conservative assumptions of the drinking water models used to estimate concentrations of aminocyclopyrachlor in drinking water, estimated chronic risk is well below the LOC (<10% of the cPAD for all population groups).*

2.1.2. Environmental Data Requirements

The ecological risk assessment concluded that the following studies are required in support of the proposed uses:

- ***Avian Reproduction Toxicity Test (850.2300)****:*
  Data are required for both an upland game and waterfowl species for the proposed use patterns. The submitted studies were invalid due to improper husbandry practices that may have caused incidental mortalities in quails and reduced egg production in mallards. Despite the improper husbandry conditions, there was no evidence in either study of adverse treatment-related effects, including overt toxicity, mortality, effects on feed consumption and body weight, macroscopic findings, or reproductive effects. Therefore, submission of a repeat-study performed under proper husbandry conditions is expected to be confirmatory and will better characterize chronic risk to birds.

- ***Freshwater Invertebrate Life-Cycle Toxicity Test (850.1300)****:*
  Non dose-response mortalities were observed in the three lowest treatment levels for the submitted freshwater daphnid study. Therefore, the resulting toxicity values could not be used quantitatively to assess chronic risk to aquatic invertebrates. Despite the lack of valid data, chronic risk to freshwater invertebrates is not expected to exceed the Agency's LOC. Environmental concentrations of aminocyclopyrachlor in surface waters from applications at the proposed maximum rates are expected to be in the parts per billion (ppb) range; whereas all aquatic toxicity studies were conducted at concentrations in the parts per million (ppm) range. Based on the results of chronic studies in freshwater fish, where the NOAEC is 11 ppm, EPA also expects the freshwater invertebrate NOAEC to be in the ppm range, well above the expected environmental concentrations. Therefore, submission of a repeat-study is expected to be confirmatory and will better characterize chronic risk to freshwater invertebrates.

2.2. Label Requirements

2.2.1. Environmental Hazards

Based on potential leaching and runoff that may result from the persistence and mobility of aminocyclopyrachlor, the following surface and ground water advisories must be placed on all aminocyclopyrachlor end-use product labels.

Surface Water Advisory

Products Primarily Intended for Commercial Use on Non-Crop Areas, Sod Farms, and Turf/Lawns
"This Product may impact surface water quality due to spray drift and runoff of rain water. This is especially true for poorly draining soils and soils with shallow ground water. This product is classified as having high potential for reaching surface water via runoff for several months after application. A level, well-maintained vegetative buffer strip between areas to which this product is applied and surface water features such as ponds, streams, and springs will reduce the potential loading of aminocyclopyrachlor from runoff water and sediment. Runoff of this product will be reduced by avoiding applications when rainfall is forecasted to occur within 48

hours. See manual at the following Internet address: http://www.wsi.nrcs.usda.gov/products/W2Q/pest/core4.html"

Products Primarily Intended for Consumer Use on Residential Lawns
"This Product may impact surface water quality due to spray drift and runoff of rain water. This is especially true for poorly draining soils and soils with shallow ground water. This product is classified as having high potential for reaching surface water via runoff for several months after application. Avoid accidental or intentional application of this product to ditches, swales, drainage ways or impervious surfaces such as driveways. Runoff of this product to surface water will be reduced by avoiding applications when rainfall is forecasted to occur within 48 hours."

Ground Water Advisory

All End-Use Products
"This chemical has properties and characteristics associated with chemicals detected in ground water. This chemical may leach into ground water if used in areas where soils are permeable, particularly where the water table is shallow."

2.2.2. Plant Residue

Although no incidents have been reported for aminocyclopyrachlor, a pyrimidine carboxylic acid, because it is a new chemical; several incidents have been reported for a similar class of chemicals, the pyridine carboxylic acids, which includes herbicides such as aminopyralid, clopyralid, and picloram. Incidents were reported where treated plant residues or manure from animals which were fed treated residues were used in compost, which caused desirable crop or lawn damage. Some states as well as the United Kingdom were prompted to take regulatory action due to these incidents. Since aminocyclopyrachlor also shares the persistent and systemic nature in soil and the high seedling emergence toxicity with these similar chemicals, similar incidents could occur following application of aminocyclopyrachlor. Therefore, the Agency is requiring that the following language be placed on all aminocyclopyrachlor end-use product labels:

Plant Residue Restrictions

Products Primarily Intended for Commercial Use on Non-Crop Areas
"Do not use plant material treated with this product for mulch or compost."

Products Primarily Intended for Commercial Use on Sod Farms and Turf/Lawns
"Do not send grass clippings from treated areas to a composting facility or use grass clippings from treated areas for mulch or compost. Applicators must give notice to property owner/property manager/residents to not use grass clippings from treated turf for mulch or compost."

Products Primarily Intended for Consumer Use on Residential Lawns

"Do not use grass clippings from treated areas for mulch or compost. Grass clippings must either be left on the treated lawn or if allowed by local yard waste regulations, disposed of in the trash"

2.2.3. Livestock

Aminocyclopyrachlor can be applied in uncultivated agricultural areas and other areas with potential exposure to livestock via feeding or grazing. Since aminocyclopyrachlor is proposed for non-food use and no tolerances have been established on livestock commodities, the following restriction is required on all end-use labels to protect feeding exposure to livestock.

Livestock Restriction

Products for Use on Non-Crop Areas
"Do not graze or feed forage, hay, or straw from treated areas to livestock."

2.2.4. Spray Drift

As expected for an herbicide, aminocyclopyrachlor presents potential risk to terrestrial plants, particularly through spray drift (see Section 1.3.3.2.4). In order to mitigate risk to non-target plants and keep the pesticide on the intended treatment area, the following spray drift language must be placed on all aminocyclopyrachlor end-use product labels:

Spray Drift Management
The phrase "(>150 – 200 microns)" must be removed from the current spray drift management statement so that it reads *"The most effective way to reduce spray drift potential is to apply large droplets. The best drift management strategy is to apply the largest droplets that provide sufficient coverage and control."*

Products Primarily Intended for Commercial Use on Non-Crop Areas

Aerial Application Restriction
"When applying by air, maintain a 50-foot buffer around non-target aquatic areas and between the point of direct application and the closest downwind edge of non-target terrestrial areas. Apply only using nozzles which will deliver coarse or greater (VMD >350 microns) droplets as defined by ASABE S572 standard. Do not release spray at a height greater than 10 feet above the ground or crop canopy unless a greater height is required for aircraft safety. Do not apply when wind speed is greater than 10 mph. Do not apply during a temperature inversion."

Ground Application Restriction
"When applying by ground, maintain a 50-foot buffer around non-target aquatic areas and between the point of direct application and the closest downwind edge of non-target terrestrial areas. Apply only using nozzles which will deliver coarse or greater (VMD >350 microns) droplets as defined by ASABE S572 standard. Do not apply with a nozzle height greater than 4 feet above the ground or crop canopy. Do not apply when wind speed is greater than 10 mph. Do not apply during a temperature inversion."

Products Primarily Intended for Commercial Use on Sod Farms and Turf/Lawns (Ground Applications Only)

Application Restriction
"Maintain a 25-foot buffer around non-target aquatic areas and between the point of direct application and the closest downwind edge of non-target terrestrial areas. Apply only using nozzles which will deliver coarse or greater (VMD >350 microns) droplets as defined by ASABE S572 standard. Do not apply with a nozzle height greater than 4 feet above the ground or crop canopy. Do not apply when wind speed is greater than 10 mph. Do not apply during a temperature inversion."

2.2.5. Restricted-Entry Interval (REI)

The REI must be changed to 12 hours from the proposed REI of 4 hours. The minimum standard REI for agricultural pesticides is 12 hours. EPA allows a reduced REI of 4 hours for certain minimum-risk pesticides that meet low-toxicity standards and that have not been reported to cause illness or injury due to post-application exposure. Since aminocyclopyrachlor is a new pesticide with no history of actual use, incident information (illness or injury reports) is not available for this chemical. Therefore, EPA believes the minimum standard REI of 12 hours is appropriate for aminocyclopyrachlor.

2.3. Proposed Registration Decision

In accordance with FIFRA Section 3(c)(7)(C), the Agency believes that the conditional registration of aminocyclopyrachlor will not cause any unreasonable adverse effects to human health or to the environment and that the use of the pesticide is in the public's interest; and is therefore proposing to grant the conditional registration.