

4-AMINOPYRIDINE

Task 2: Topical Discussions

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4-AMINOPYRIDINE

TASK 2

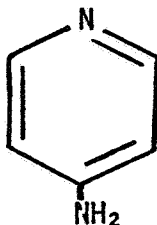
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4-AMINOPYRIDINE

TASK 2

AVITROL 200



4-Aminopyridine

Data requirements for the manufacturing-use formulation consist of hydrolysis and activated sludge metabolism information per Sections 163.62-7(b) and 163.62-8(g), respectively, of EPA's Proposed Guidelines for Registering Pesticides (July 1978).

(1) PHYSICO-CHEMICAL TRANSFORMATION 163.62-7

(A) Hydrolysis 163.62-7(b)

Hydrolysis data are required to support the registration of all manufacturing-use products regardless of the intended end uses of products formulated from the manufacturing-use product.

No data on the hydrolysis of 4-aminopyridine are available.

Data Gaps

All data specified in Section 163.62-7(b) are needed to assess the hydrolysis properties of manufacturing-use 4-aminopyridine.

(B) Photolysis 163.62-7(c)

Photodegradation studies in water are required to support the registration of all formulated products intended for terrestrial (except greenhouse and domestic outdoor), aquatic, terrestrial/aquatic (forest), or aquatic impact (except indirect pesticide discharges and discharges into wastewater treatment systems) uses.

Studies in soil are required to support the registration of all formulated products intended for crop uses and terrestrial/aquatic (forest) uses.

No data on the photolysis of 4-aminopyridine are available.

Data Gaps

All data specified in Section 163.62-7(c) are needed to determine the effect of light on 4-aminopyridine.

- 1) $t_{1/2}$ -life
- 2) materials balance

(2) METABOLISM 163.62-8

Data on metabolism are required to determine the nature and availability of pesticide residues to rotational crops and to help in the assessment of potential disposal and reentry hazards.

(A) Soil 163.62-8(b,c)

Aerobic metabolism studies are required to support the registration of all formulated products intended for terrestrial uses or terrestrial/aquatic (forest) uses. Anaerobic soil metabolism studies are required to support the registration of all formulated products intended for field and vegetable crop uses.

Three soil metabolism studies were reviewed and two were considered valid. Starr and Cunningham (MRID 05003185) investigated the degradation of 4-aminopyridine in various soil types (loamy sand, sandy loam, loam, and sandy clay loam) under aerobic and flooded conditions as measured by $^{14}\text{CO}_2$ evolution. In soil under aerobic conditions, 4-aminopyridine applied at 10 ppm exhibited half-lives ranging from 3 months in loamy sand to 32 months in sandy clay loam (Starr and Cunningham, MRID 05003185). A lag period of over 7 days was needed before extensive degradation to CO_2 occurred. However, under flooded conditions, very little (<0.5%) [^{14}C]4-aminopyridine degradation was detected over 43 days.

Rates of metabolism of [^{14}C]4-aminopyridine in soil under aerobic conditions increased with increasing organic matter and pH (Starr and Cunningham, MRID 05003185). For two slightly acidic (pH 5.6-5.8) loam soils containing 16% clay, [^{14}C]4-aminopyridine was degraded to $^{14}\text{CO}_2$ almost 3 times faster ($t_{1/2} = 8$ months) in the soil with the greater level of organic matter (5%) than it was in a similar soil with 2.9% organic matter ($t_{1/2} = 22$ months). Soil pH also influenced 4-aminopyridine

metabolism. Over a 3-month period, recovered $^{14}\text{CO}_2$ was minute (0.35%) for a highly acidic loam (pH 4.1) but much greater (4.88%) for an alkaline sandy clay loam with similar levels of organic matter and clay. It should be noted that degradation of 4-aminopyridine was only measured by $^{14}\text{CO}_2$ recovery and no attempt was made to identify intermediate degradation products.

Betts et al. (MRID 05003407) investigated the degradation of [2- ^{14}C]-4-aminopyridine (10 ppm) in sandy loam, loamy fine sand, and clay soils under aerobic and flooded conditions. A lag period of 20 days occurred before extensive degradation to CO_2 was observed. Under aerobic conditions, between 5 and 24% of the applied radioactivity was recovered as $^{14}\text{CO}_2$ after 60 days. The greatest degradation occurred in the clay soil and the least degradation occurred in the sandy loam soil. Under flooded conditions, 21% of the applied radioactivity was recovered from the sandy loam and 24% was recovered from the clay (studies were not conducted with flooded loamy sand). No degradation products were detected in extracts from soils under either aerobic or flooded conditions.

Data Gaps

Additional aerobic and anaerobic soil metabolism studies are needed in the following areas:

- Identification of degradation products greater than 10% of the initial application, or 0.01 ppm, whichever is greater.
- Material balance, including nonextractable residues.
- The above studies should continue until a 90% loss of the pesticide occurs and until patterns of formation and decline of metabolic products are established.

References

Betts, P.M., C.W. Giddings, and J.R. Fleeker. 1976. Degradation of 4-aminopyridine in soil. J. Agri. Food Chem. 24(3):571-574. (MRID 05003407)

Starr, R.I., and D.J. Cunningham. 1975. Leaching and degradation of 4-aminopyridine-¹⁴C in several soil systems. Arch. Environ. Contam. Toxicol. 3(1):72-83. (MRID 05003185)

(B) Aquatic 163.62-8(d,e)

An aerobic aquatic metabolism laboratory study using radioisotopic techniques is required to support the registration of all formulated products intended for aquatic uses and aquatic impact uses that result in direct discharges into the aquatic environment.

An anaerobic aquatic metabolism laboratory study using radioisotopic analytical techniques is required to support the registration of all formulated products intended for aquatic, terrestrial/aquatic (forest), and aquatic impact uses that result in direct discharges into the aquatic environment.

No data are required on the aquatic metabolism of 4-aminopyridine because the use pattern indicates that direct discharge into the aquatic environment is unlikely.

(C) Microbiological 163.62-8(f)

Data on the effects of microbes on pesticide degradation and the effects of pesticides on microbes are required to support the registration of all formulated products intended for the following uses: terrestrial noncrop, tree fruit/nut crop, field/vegetable crop, aquatic food crop and noncrop, terrestrial/aquatic (forest), and direct discharge aquatic impact.

Microbiological - Effects of Microbes on Pesticides 163.62-8(f)(2)

One study was reviewed on the ability of soil microorganisms to metabolize 4-aminopyridine (Betts et al., MRID 05003407). Pure cultures of Aspergillus niger, Pseudomonas fluorescens, Enterobacter aerogenes, Streptomyces griseus, and Agrobacterium tumefaciens failed to metabolize 4-aminopyridine when incubated in the presence of the compound at 10 and 100 µg/ml for 5-6 days. Microbiological growth rates in the pure cultures were not retarded by the pesticide. *(These data are considered insufficient because not enough microorganisms and cultural conditions were examined to draw any conclusions about the effect of microorganisms on 4-aminopyridine.)*

Data gaps

All data specified in Section 163.62-8(f)(2) are needed to determine the effect of microorganisms on 4-aminopyridine.

Reference

Betts, P.M., C.W. Giddings, and J.R. Fleeker. 1976. Degradation of 4-aminopyridine in soil. J. Agri. Food Chem. 24(3):571-574. (MRID 05003407)

Microbiological - Effects of Pesticides on Microbes 163.62-8(f)(3)

In one study, preliminary data were reviewed. A study by Betts et al. (MRID 05003185) indicated that 4-aminopyridine did not retard the growth of A. niger, P. fluorescens, E. aerogenes, S. griseus, and A. tumefaciens when incubated in the presence of 4-aminopyridine at 10 or 100 µg/ml for 5-6 days. These data are considered insufficient because not enough microorganisms (viz., typical soil flora) were examined to draw any conclusions about the effect of 4-aminopyridine on microbial populations and functions.

Data gaps

1 study not enough to satisfy guidelines but the one study is valid -

All data specified in Section 163.62-8(f)(3) are needed to assess the effects of 4-aminopyridine on microorganisms.

Reference

Betts, P.M., C.W. Giddings, and J.R. Fleeker. 1976. Degradation of 4-aminopyridine in soil. J. Agri. Food Chem. 24(3):571-574. (MRID 05003407)

(D) Activated Sludge 163.62-8(g)

A laboratory study of the effects of pesticides on the wastewater treatment process is required to support the registration of all manufacturing-use products and all formulated products that are indirectly discharged into wastewater treatment systems or are used as treatments in wastewater treatment systems.

No data on the activated sludge metabolism of 4-aminopyridine are available.

Data Gaps

All data specified in Section 163.62-8(g) are needed to assess the effects of the manufacturing-use formulation of 4-aminopyridine on waste treatment facilities.

(3) MOBILITY 163.62-9

Data on mobility are required to determine pesticide residue movement in the environment.

(A) Leaching 163.62-9(b)

Leaching data are required to support registration of formulated products intended for terrestrial noncrop, tree fruit/nut crop, field/vegetable crop, and terrestrial/aquatic (forest) uses.

Three leaching studies were reviewed and are discussed below.

Studies by Starr and Cunningham (MRID 05003185; MRID 00004001) indicate that 4-aminopyridine is relatively immobile in the soils studied. Seven different alkaline and acidic soils (Table 1) were fortified with [^{14}C]4-aminopyridine at 10 ppm. After application of approximately 7 inches of water over a 20-day period to columns containing the fortified soil, detectable radioactivity was found in the leachate from only one of the four acidic soils and in the leachate from all three of the alkaline soils. Total detectable radioactivity in the leachate never exceeded 0.2% of the initial ^{14}C application. Analysis of the soil columns after the leaching treatment showed, for all soils, that more than 95% of the recoverable ^{14}C was in the upper 1-inch soil layer. Soils A, B, C, and D were packed into columns, and a corn seedling was planted in each column. The soils were fortified with [^{14}C]4-aminopyridine at 10 ppm and leached with a total of 5.8 inches of water over a 7-day period. Less than 0.03% of the applied radioactivity leached through the soils during the 7-day treatment period. Analysis of radioactivity in all of the soils at the conclusion of the leachate experiments showed that greater than 97% of the total radioactivity found was in the top 1 inch of the soil. However, because the experimental soils were leached with less than half the amount of water suggested by the Proposed Guidelines, a conclusion that the compound is immobile is premature.

Table 1. Leaching of [¹⁴C]4-aminopyridine (10 ppm) from soil columns after elution with 7 inches of water over 20 days.^a

Soil	Soil type	pH (paste)	Organic matter (%)	Sand (%)	Silt (%)	Clay (%)	Radioactivity recovered from leachate (%)	Radioactivity remaining in upper inch of soil column ^b (%)
Alkaline soils								
A	Loamy sand	7.8	2.9	77	16	7	0.18	95
B	Sandy clay loam	7.7	4.0	61	19	20	0.02	99
C	Sandy clay loam	7.6	1.9	47	27	26	0.09	98
D	Loam	7.6	2.5	59	30	11	0.01	-- ^c
Acidic soils								
E	Loam	5.8	2.9	46	38	16	<0.01	>99
F	Loam	5.6	5.0	50	34	16	--	>99
G	Sandy loam	5.6	4.0	53	33	14	--	>99
H	Loam	4.1	1.4	31	44	25	--	>99

^a Adapted from Starr and Cunningham (MRID 05003185; MRID 00004001).

^b Percent of total recovered from soil columns.

^c Not measured.

Data Gaps

The following additional studies are needed to assess the ability of 4-aminopyridine to leach:

- Data regarding 4-aminopyridine leaching after the pesticide has been aged in soil under aerobic conditions for 30 days prior to elution with the equivalent of 0.5 acre-inch of water per day for 45 days.
- EPA's Proposed Guidelines require that, in column leaching studies, soil columns be eluted with 20 acre-inches of water. Because the submitted studies employed 10 inches or less of water, additional studies are needed with the specified amount of water. One of the above studies should include a soil having an organic matter content of less than 1%.

References

Starr, R.I., and D.J. Cunningham. 1975. Leaching and degradation of 4-aminopyridine-¹⁴C in several soil systems. Arch. Environ. Contam. Toxicol. 3(1):72-83. (MRID 05003185)

Starr, R.I., and D.J. Cunningham. 1970. Translocation and degradation of 4-aminopyridine in corn plants--its movement and degradation in soil systems. Third Periodic Report, Avitrol Concentrate. (Unpublished study received April 24, 1970, under 224-EX-3. Prepared by U.S. Fish and Wildlife Service, Denver Wildlife Research Center; submitted by Phillips Petroleum Co., Bartlesville, Okla. CDL:122744-H.) (MRID 00004001)

(B) Volatility 163.62-9(c)

Laboratory volatility studies using nonradioisotopic analytical techniques are required to support the registration of all formulated products intended for greenhouse use.

Starr and Cunningham (MRID 00004001) reported that approximately 14, 15, and 18% of applied radioactivity (10 ppm of [¹⁴C]4-aminopyridine) was lost after 7 days from nonaerated nutrient solution, aerated nutrient solution, and aerated water media, respectively. This loss could have been due to either microbiological degradation or volatilization.

Volatility data are only required for pesticides used in greenhouses. Therefore, data are not required on the volatility of 4-aminopyridine because no formulated products of 4-aminopyridine have yet been proposed for greenhouse use.

Reference

Starr, R.I., and D.J. Cunningham. 1970. Translocation and degradation of 4-aminopyridine in corn plants--its movement and degradation in soil systems. Third Periodic Report, Avitrol Concentrate. (Unpublished study received April 24, 1970, under 224-EX-3. Prepared by U.S. Fish and Wildlife Service, Denver Wildlife Research Center; submitted by Phillips Petroleum Co., Bartlesville, Okla. CDL:122744-H.) (MRID 00004001)

(C) Adsorption/Desorption 163.62-9(d)

A laboratory study using radioisotopic or nonradioisotopic analytical techniques is required to support the registration of all formulated products intended for all terrestrial uses, terrestrial/aquatic (forest) uses, aquatic uses, and aquatic impact uses (if the pesticides are discharged directly into the aquatic environment).

No data on the adsorption/desorption of 4-aminopyridine are available.

Data Gaps

All data specified in Section 163.62-9(d) are needed to evaluate the adsorption/desorption of 4-aminopyridine.

(D) Water Dispersal 163.62-9(e)

A field study tailored to one or more representative sites is required to support the registration of all formulated products intended for aquatic uses and aquatic impact uses (if the pesticides are discharged directly into aquatic sites).

No data on the water dispersal of 4-aminopyridine are required because the use pattern indicates that a direct discharge into the aquatic environment would not occur.

(4) FIELD DISSIPATION 163.62-10

A field dissipation study under actual use conditions is required to support the registration of all formulated products intended for terrestrial (except greenhouse) uses, aquatic uses, and terrestrial/aquatic (forest) uses.

(A) Terrestrial 163.62-10(b)

Terrestrial field dissipation data are required to determine the rate at which each pesticide formulation dissipates in the environment.

No data on the terrestrial dissipation of 4-aminopyridine are available.

Data Gaps

All data specified in Sections 163.62-10(b)(1,4,5) are needed to determine the terrestrial dissipation rate of 1.00, 0.50, 0.05, 0.03, and 0.02% ai granular, and 50 and 25% ai dust formulations of 4-aminopyridine.

(B) Aquatic 163.62-10(c)

Data are necessary to determine rate, mobility, and accumulation under field conditions for each pesticide formulation.

No data on the aquatic dissipation of 4-aminopyridine are available.

No data are required on the aquatic dissipation of 4-aminopyridine because the use pattern indicates that introduction into the aquatic environment would not occur.

(C) Terrestrial/Aquatic (Forest) 163.62-10(d)

Terrestrial/aquatic environments such as forests and reforestation sites require a special ecosystem residue study using the formulated pesticide product to assess environmental fate and hazards.

No data on the terrestrial/aquatic dissipation of 4-aminopyridine are available.

Data Gaps

All data specified in Section 163.62-10(d) are needed to determine the dissipation rate of 4-aminopyridine (25% ai dust and 1.00, 0.5, 0.05, 0.03, and 0.02% ai granular) in a forest environment.

(D) Aquatic Impact Uses 163.62-10(e)

Data are required for each formulated product to determine dissipation rate, mobility, and accumulation of residues discharged or dispersed into the aquatic environment.

No data are required on the aquatic impact of 4-aminopyridine because the use pattern indicates that introduction into the aquatic environment would not occur.

(E) Combinations and Tank Mixes 163.62-10(f)

Data are required to support the registration of all combinations and all formulated products intended for tank mixtures.

4-Aminopyridine is not used in combination with other pesticides; therefore, no data are required for this section.

(5) ACCUMULATION 163.62-11

Data on accumulation are required to determine accumulation in food webs.

(A) Rotational Crops 163.62-11(b)

Rotational crop studies are required to support the registration of all formulated products intended for field/vegetable and aquatic food crop uses.

No data on the accumulation of 4-aminopyridine in rotational crops are available.

Data Gaps

All data specified in Section 163.62-11(b) are needed to determine whether 4-aminopyridine will accumulate in rotational crops.

(B) Irrigated Crops 163.62-11(c)

A crop residue study under actual field use conditions is required to support the registration of all formulated products intended for aquatic food or aquatic noncrop uses, or for use in holding ponds or effluent and other discharged sources used to irrigate crops.

No data are required on the accumulation of 4-aminopyridine in irrigated crops because the use pattern indicates that 4-aminopyridine would not be used in irrigated crops.

(C) Fish 163.62-11(d)

This laboratory study employing radioisotopic or nonradioisotopic analytical techniques is required to support the registration of all formulated products intended for terrestrial noncrop, tree fruit/nut crop,

and field/vegetable crop uses; aquatic food crop and noncrop uses; terrestrial/aquatic (forest) uses; and aquatic impact (direct discharge) uses.

No data on the accumulation of 4-aminopyridine in fish are available.

Data Gaps

All data specified in Section 163.62-11(d) are needed to determine if 4-aminopyridine will accumulate in fish.