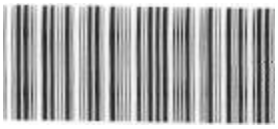
FORT DODGE ANIMAL HEALTH



Z154314

Environmental Assessment

CYDECTINÒ moxidectin 0.5% Pour-On for Cattle

Fort Dodge Animal Health

June 1997

ÒRegistered trademark of American Cyanamid Company

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Environmental Assessment

CYDECTIN moxidectin 0.5% Pour-On for Cattle

1. Date: June 12, 1997

2. Name of Applicant: Fort Dodge Animal Health

3. Address: Corporate Administrative Offices:

Fort Dodge Animal Health
9401 Indian Creek Parkway
Overland Park, Kansas 66210

Product Development and Regulatory Affairs Offices:

Fort Dodge Animal Health
Cyanamid Agricultural Research Center
PO Box 400
Princeton, New Jersey 08543-0400

4. Description of the Proposed Action:

a. Intended Product Use

A single topical application at the recommended dose level of 1 mL for each 22 lb body weight (0.5 mg moxidectin/kg body weight), is effective in the therapeutic treatment of cattle infected/infested with the internal and external cattle parasites included on the product label. In addition, the product will prevent reinfection by the endoparasites, *Ostertagia ostertagi* for 28 days and *Dictyocaulus viviparus* for 42 days following treatment. CYDECTIN moxidectin 0.5% Pour-On will be used for beef and nonlactating dairy cattle throughout the United States and is appropriate for all management systems.

b. Need for Product

Internal and external parasitism cause large production losses to cattle raised in the United States. Serious health consequences and in some cases death, can result if effective antiparasitic therapy is not provided to affected cattle. CYDECTIN moxidectin 0.5% Pour-On effectively treats and controls a broad spectrum of endo- and ectoparasites. The persistent activity of moxidectin in preventing larval infection can reduce the number of treatments required to control parasitic disease.

c. Manufacturing Locations

Three manufacture sites will be employed in the production of moxidectin and CYDECTIN moxidectin 0.5% Pour-On for Cattle. The manufacturing process begins with the aerobic fermentation of nemadectin (alternatively referred to as LL-F28249-α or F-α), a natural derivative of *Streptomyces cyaneogriseus* ssp. *noncyanogenus.* Fermentation of nemadectin will be carried out in Cyanamid Italia S.p.A's plant located in Catania, Italy. The nemadectin obtained in this proprietary fermentation process is then refined and chemically converted to moxidectin. This process will be done at facilities operated by Cyanamid de Argentina SA in Varela, Argentina Formulation, packaging and labeling of the finished product, CYDECTIN moxidectin 0.5% pour-on for Cattle, will be accomplished at Fort Dodge Animal Health's manufacturing plant located in Fort Dodge, Iowa.

5. Identification of Chemical Substances:

a. Active Drug -moxidectin

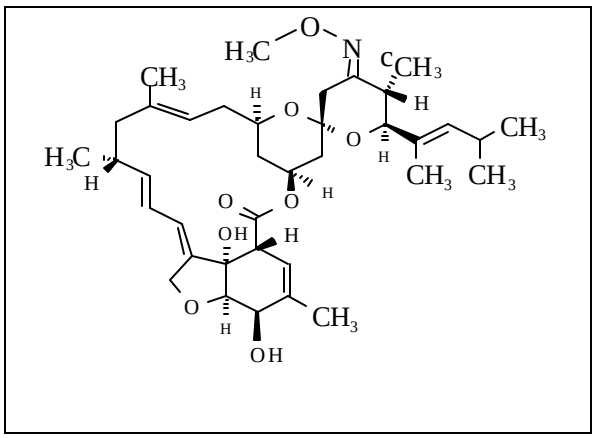
Nomenclature: moxidectin (USAN designation); 23-(O-Methyloxime)-F28249-α or 3-(O-Methyloxime)-F28249-alpha; CL 301,423

CAS Reg No.: 113507-06-5

Molecular weight: 639.8

Molecular formula: $C_{37}H_{53}NO_8$

Structural formula :



Physical description:

Appearance - white to pale yellow powder
Melting point (liquefaction) - 145 to 154°C
Vapor Pressure - $<10^{-7}$ (limit of detection)
Volatility (% by volume) - negligible
n-Octanol/water partition coefficient - 58,300
UV visible absorption spectrum – 2 45 nm peak
Evaporation rate - negligible
Solubility in water - 0.51 mg/L
Solubility in organic solvents (mL solvent/g moxidectin)
dichloromethane - 1.64
diethyl ether - 1.19
ethanol (95%) - 0.81
acetonitrile - 0.62
ethyl acetate - 0.47
Purity - >90%

b. Finished Product -CYDECTIN moxidectin 0.5% Pour-On for Cattle

Physical description -Deep violet colored oily solution with a characteristic aromatic odor.

Composition -The finished product contains 0.5% (w/v) moxidectin (active ingredient). Inactive ingredients make up the balance of the formulation.

6. Introduction of Substances into the Environment as the Result of Use

a. Administration

CYDECTIN moxidectin 0.5% Pour-On for Cattle is a ready-to-use formulation for direct topical application to cattle. It is applied to the hair and skin located along the midline of the treated animal's back from the withers to the base of the tail. The recommended dose level is 0.5 mg moxidectin/kg body weight which is equivalent to 1 mL of product for each 22 lb of body weight. Assuming the average animal weighs 300 kg, then the average dose would be 30 mL of formulation containing 150 mg moxidectin.

b. Metabolism and Excretion in Cattle

Excreta from cattle treated with the commercial product will be the major source of moxidectin introduction into the environment. A metabolism study conducted with moxidectin 0.5% pour-on demonstrated that feces are the primary route of excretion.

The majority of excreted drug residue was unaltered moxidectin (51%) with at least five metabolites formed, none of which accounted for greater than 9% of the total radioactive residue.

A "worst-case" approach has been used in calculation of PEC's (predicted Environmental Concentrations). Although the product will be used in cattle maintained on pasture and in feedlots, calculations have been based on a feedlot management system because this will result in the highest concentration of fecal moxidectin. Furthermore, all calculations assume that the entire recommended dose of 0.5 mg moxidectin/kg body weight is excreted as unaltered parent compound.

7 Fate of Emitted Substances in the Environment

a. Environmental Chemistry Summary

The physical properties of moxidectin which influence its movement and degradation in the environment are summarized in the table below.

Physical Properties

Melting Point	145-154°C
Vapor Pressure	$< 10^{-7}$ torr.
Ultraviolet- visible absorption spectra	peak at 245 nm, only slight absorption above 300 nm.
n-Octanol/Water Partition Coefficient	Kow = 58,300 (Log Kow = 4.766)
Solubility in Water	0.51 mg/L
Solubility in Organic Solvents	(mL of solvent/g moxidectin)
Dichloromethane Diethyl	1.64
Ether	1.19
Ethanol. (95%)	0.81
Acetonitrile	0.62
Ethyl Acetate	0.47

The melting point and very low vapor pressure of moxidectin indicate that it is non-volatile and will not move through the atmosphere from areas of use. The very weak adsorption of light in the region above 300 nm indicates the potential for photodegradation of moxidectin. The large *n*-octanol/water partition coefficient of moxidectin indicates that the compound is lipophilic. Because of the lipophilic nature of moxidectin, it has a very low solubility in water and binds tightly to soil.

b. Environmental Fate Summary

The various environmental factors which influence the fate and distribution of moxidectin in the environment are summarized in the table below.

Photolysis Half-life in Water	6.8 hours (late autumn)
Laboratory Soil Biodegradation Half-Life	2 months
Soil Adsorption/Desorption Coefficient (Koc), Normalized for % Organic Carbon	18,000 - 41,000
Mobility Class by Soil Thin-Layer Chromatography	1 (immobile)

Aerobic soil metabolism, adsorption to soils and sediments, and photodegradation will minimize the extent of environmental contamination by moxidectin. Laboratory studies have shown that under aerobic conditions ^{14}C-moxidectin is extensively degraded in soil, with a half-life of approximately 2 months. Moxidectin is slowly mineralized (converted to CO_2) in the soil, indicating that very extensive degradation will occur. There are at least 10 degradation products formed which are only present at trace levels. Moxidectin is strongly adsorbed by soils with Koc values of 18,000 to 41,000, and is considered immobile when examined by soil thin-layer chromatography. Because of the very high degree of adsorption to soil and its very low water solubility, only extremely low residues of moxidectin are expected to move from fields into surface water. The trace levels of moxidectin which are washed off the soil or feces will bind to other soil particles, plants and other material found in the field. This binding will result in a continuous depletion of moxidectin from solutions. Because of the very strong binding and the rapid degradation, moxidectin is not expected to move in the soil and contaminate groundwater. Moxidectin is rapidly photodegraded in water with a half-life of 6.8 hours in late fall. The half-life from the spring to early fall will be even more rapid. This rapid photodegradation in water along with the removal of moxidectin by adsorption to sediments and organic material in the water column will rapidly degrade or remove any moxidectin entering the aquatic environment.

The major sources of exposure will be through highly intensive management systems such as those found in feedlots. The predicted environmental concentrations (PEC's) in manure, soil and water are given below. These values are worst-case, conservative estimates of the potential concentrations and are based on standard values for such parameters as weights of cattle, excretion of manure per day, holding times of excreta and assumes no moxidectin metabolism in cattle or degradation in excreta which is aged before application to fields.

For feedlot systems

$$PEC_{manure}(max) = \frac{\text{Total Dose Administered (mg/animal/day) x \# Days Treated}}{\text{Total Amount of Manure Produced during Manure Production Period}}$$

$$PEC_{manure}(max) = \frac{\text{Total Dose Administered (mg/animal/day)x \# Days Treated}}{\text{Kg Excreta/Day x Manure Production Period (in Days)}}$$

$$PEC_{manure}(max) = \frac{0.5 \text{ mg/kg x } 300 \text{ kg animal x } 1 \text{ day of treatment}}{27.3 \text{ kg (wet) x } 130 \text{ Days}}$$

$$PE_{manure}(max) = \frac{150 \text{ mg}}{3549 \text{ kg (wet)}} = 0.0423 \text{ mg/kg} = 0.0423 \text{ ppm} = 42.3 \text{ ppb}$$

$$PEC_{soil}(max) = \frac{\text{Concentration in Manure (ppm) x Kg Manure Applied/Acre}}{\text{Weight of Soil in Plow Layer x Water Content of Manure}}$$

$$PEC_{soil}(max) = \frac{0.0423 \text{ ppm x } 13{,}600 \text{ Kg Manure Applied/Acre}}{910{,}500 \text{ Kg Soil in Plow Layer x } 0.48} = 1.31 \text{ ppb}$$

This calculation is worst-case because it assumes that all moxidectin applied to cattle is excreted as moxidectin during the 130-day period. The concentrations of moxidectin in soil will also be reduced from this maximum value due to degradation in the cattle prior to excretion and during the storage of manure prior to application to fields.

The maximum PEC_{water} is calculated assuming that 1% of the total drug per acre applied to 10 acres of soil moves into a 1 acre pond which is 2 m (6 feet) deep.

The mass of compound which enters the pond is calculated from:

$$\text{Mass of compound} = PEC_{soil}(max) \times 9.1 \times 10^5 \text{ kg/acre} \times 0.01 \times 10 \text{ acres}$$
$$= PEC_{soil}(max) \times 9.1 \times 10^4 \text{ kg}$$

A one-acre pond which has a depth of 2 m has a volume of 8,094,000 liters.

$$1 \text{ acre} \times 4047 \text{ m}^2/\text{acre} \times 2 \text{ m} = 8094 \text{ m}^3 \times 1000 \text{ liters/m}^3 = 8{,}094{,}000 \text{ liters}$$
$$= 8.1 \times 10^6 \text{ liters}$$

$$PEC_{water}(max) = \frac{\text{Mass of production moved into water}}{\text{Mass of water in pond}} = \frac{PEC_{soil}(max) \times 9.1 \times 10^4 \text{ kg}}{8.1 \times 10^6 \text{ liters x 1 kg/liter}}$$

$$PEC_{water}(max) = \frac{1.3 \text{ µg/kg x } 9.1 \times 10^4 \text{ kg}}{8.1 \times 10^6 \text{ kg}} = \frac{1.19 \times 10^5 \text{ µg}}{8.1 \times 10^6 \text{ kg}} = 0.147 \times 10^{-1} \text{ µg/kg}$$

$$0.0147 \text{ µg/kg} = 14.7 \text{ ppt}$$

The concentrations of moxidectin in water will be reduced from this maximum value due to degradation in cattle prior to excretion and during the storage of manure prior to application to fields. In addition, the very strong adsorption of moxidectin to soil and sediment will greatly reduce the concentration of moxidectin in surface water.

The concentration in water, corrected for adsorption, is calculated from the relationship:

$$\text{Soil/Water Partition Coefficient} = Kd = \frac{\text{Concentration in Sediment}}{\text{Concentration in Water}}$$

$$Kd = \frac{\text{Mass of Compound in Sediment/Mass of Sediment}}{\text{Mass of Compound in Water/Mass of Water}}$$

$$Kd = \frac{\text{(MA-MCW)/Mass of Sediment}}{\text{MCW/Mass of Water}}$$

Where MA = Mass of Compound Added to Pond and MCW = Mass of Compound in the Water

Rearranging the equation and solving for the mass of the compound in water:

$$MCW = \frac{\text{MA x Mass of Water}}{\text{Mass of Water + (Mass of Sediment x Kd)}}$$

$$PECwater = \frac{MCW}{\text{Mass of Water}} = \frac{MA}{\text{Mass of Water + (Mass of Sediment x Kd)}}$$

Assuming that the compound is adsorbed in the top 5 cm of the sediment: The volume of sediment is: 0.05 m x 1 acre x 4047 m^2/acre = 202 m^3.
The mass of sediment is: 202 m^3 x 1500 kg/m^3 = 3 x 10^5 kg
The mass of water is: 8.1 x 10^6 liters x 1 kg/liter = 8.1 x 10^6 kg

As was previously shown in the calculation of the PEC_{water}(max:) :

$$\text{Mass of compound} = PEC_{soil}(max) \times 9.1 \times 10^5 \text{ kg/acre} \times 0.01 \times 10 \text{ acres}$$
$$= PECsoil(max) \times 9.1 \times 10^4 \text{ kg}$$

$$PECwater = \frac{MA}{\text{Mass of Water + (Mass of Sediment x Kd)}}$$

$$PECwater = \frac{PECsoil(max) \times 9.1 \times 10^4 \text{ kg}}{\text{Mass of Water + (Mass of Sediment x Kd)}}$$

$$PECwater = \frac{1.31 \text{ ug/kg} \times 9.1 \times 10^{*} \text{ kg}}{8.1 \times 10^6 \text{ kg} + (3 \times 10^5 \text{ kg} \times Kd)}$$

Assuming the sediment contains 5% organic matter, which is equivalent to 2.9% organic carbon, based on the % organic carbon = % organic matter/l.724 (Hamaker, 1975) then:

Kd = 0.029 x Koc. The Koc values were 18,000 - 41,000. Using a conservative value of 20,000 for the Koc, the Kd = 580.

$$PECwater = \frac{119\ mg}{8.1 \times 10^6\ kg + (3 \times 10^5\ kg \times 580)} = \frac{119\ mg}{(8.1 + 174) \times 10^6\ kg} = \frac{119\ mg}{1.82 \times 10^8\ kg}$$

$$= 65.4 \times 10^{-8}\ mg/kg = 6.54 \times 10^{-7}\ mg/kg = 6.54 \times 10^{-7}\ ppm = 0.654\ ppt$$

This value will be further reduced due to degradation in both the soil and the pond.

8. Environmental Effects of Released Substances

In order to demonstrate the environmental safety of a compound, the potential effects on terrestrial, aquatic and avian organisms must be evaluated. In addition to the typical evaluation required to demonstrate the safety of a new compound, there are two additional areas of concern which need to be addressed in the evaluation of milbemycin and avermectin compounds and products applied via the pour-on route of administration. There have been concerns raised on the potential effects of avermectins on dung degrading insects (Wall and Strong, 1987; Herd et al., 1993). Being somewhat related to the avermectin family of compounds, it was necessary to examine these concerns as they relate to the avermectins and determine if moxidectin would be expected to potentially produce the same effects on dung insects. An additional area of potential concern arises due to the route of administration of this product. Since the occurrence of avian deaths due to exposure of birds to residues of organophosphate animal drugs that were applied in pour-on formulations (Henny, et al., 1985), similar topical formulations need to be evaluated to determine if exposure to residues from this type of formulation pose a hazard to birds.

a. Ecotoxicological Summary

The toxicity of moxidectin to a variety of organisms which are representative of groups of aquatic, avian and terrestrial organisms is summarized in the tables below.

Aquatic Organisms		
Bluegill 96-hour	LC_{50}	0.62 ppb
	NOEC	<0.52 ppb
Rainbow Trout	96-hour LC_{50}	0.16 ppb
	NOEC	<0.15 ppb
Water Flea	48-hour EC_{50}	30 ppt
	NOEC	11 ppt
Green Algae	72-hour EC_{50}	>87 ppb

Avian Organisms		
Bobwhite Quail	21-day acute oral LD_{50}	278 mg/kg bw
Mallard Duck	21-day acute oral LD_{50}	365 mg/kg bw
Chicken	14-day acute oral LD_{50}	283 mg/kg bw
Terrestrial Organisms		
Plant Phytotoxicity		inactive at 4 kg/ha
Earthworm	28-day subacute LC_{50}	37.2 mg/kg medium

b Aquatic Toxicity

Moxidectin is toxic to many aquatic species, with the water flea *(Daphnia magna)* being the most sensitive species. EC_{50} = 30 ppt

Bluegill	96-hour LC_{50}	0.62 ppb
	NOEC	<0.52 ppb
Rainbow Trout	96-hour LC_{50}	0.16 ppb
	NOEC	<0.15 ppb
Water Flea	48-hour EC_{50}	30 ppt
	NOEC	11 ppt
Green Algae	72-hour EC_{50}	>87 ppb

The concentrations at which toxicity is observed in these tests should be regarded as "worst-case" values because several factors, such as binding to sediment and suspended particulate matter, and photodegradation, which are known to reduce exposure under field conditions, are absent in these studies.

The predicted concentrations in a pond [14.7 ppt (max) and 0.65 ppt (with adsorption)] are lower (0.001 - 0.5 X) than the 96-hour LC_{50} values for these species and are at, or less than the NOEC of the water flea, the most sensitive aquatic species. The ratio of the predicted environmental concentration (PEC) to the predicted no-effect concentration (PNEC) for *Daphnia magna* (EC_{50}/Assessment factor of 100) is 0.65 ppt/(30 ppt/100) is 2. If an assessment factor of 10 is used, due to testing of four aquatic species, the PEC/PNEC ratio is less than 1. The calculation of the concentration in water assumed that there is no degradation of the compound during storage of the excreta before application to a field. However, it has been demonstrated that there will be significant degradation during storage, since the half-life in soil is approximately 60 days. Due to this degradation, the concentration of moxidectin which may be found in water due to run-off from treated fields will be greatly reduced. Thus, there will be no significant negative impact on these aquatic organisms.

A study which examined the potential for moxidectin to wash-off from cattle treated with the pour-on formulation demonstrated that approximately 1% or less of the applied dose will wash-off from treated animals with one inch of simulated rainfall being applied to treated cattle over a 30-minute period. Any of the low levels of moxidectin which do wash-off from cattle will become adsorbed onto soil or sediment where it will be degraded. This process, along with the very low amount of moxidectin in wash-off water, will not have a significant impact on the potential concentrations of moxidectin in pond water, which are already below levels of toxicological concern.

c. Avian Toxicity

The acute toxicity of moxidectin, when administered as a single oral dose, was determined in the bobwhite quail and mallard duck. LD_{50} values are 278 mg/kg and 365 mg/kg, respectively. Mortality occurred at the lowest dose levels tested in each species, 100 and 147 mg/kg, respectively. These LD_{50} values are similar to those obtained for the chicken, where the LD_{50} value was 283 mg/kg, and mortality occurred at dose levels starting at 100 mg/kg. The LD_{50} values are such that these species would have to consume many kg of soil and/or feces in order to receive a toxic dose. Thus there should be no adverse effects on birds.

The use of the pour-on formulation of moxidectin is not expected to have an adverse effect on hair eating birds. Henny et al. (1985) reported on the deaths of magpies from ingestion of cattle hair containing residues of the organophosphate famphur. Henny et al. (1985) reported that cattle hair accounted for 12% of the gizzard contents in magpies. Measured moxidectin residues in hair of beef cattle which were treated with the pour-on formulation of moxidectin had residues of 127 to 344 ppm, which is in the range of the LD_{50} values for the three species of birds tested. If a 200 g bird were to consume 20 g of feed per day of which 12% (2.4 g) was cattle hair, this would represent a maximum consumption of 0.826 mg.

344 mg/kg (highest hair residue) x 2.4 g of hair as feed = 0.826 mg

This represents a maximum daily intake of 4.1 mg/kg, which is 1.1 to 1.5% of the LD_{50} for the bobwhite quail and mallard duck, respectively.

0.826 mg/200 g bird = 4.1 mg/kg

In one day hair-eating birds would have to consume many times their weight in cattle hair with moxidectin residues in order to be exposed to potentially toxic levels of moxidectin. In addition these calculations were the worst case for exposure since they assume that all of the consumed hair is from the treated areas on cattle. In the real-world their exposures would be even lower due to ingestion of non-treated hair. The exposure of raptors which might eat the magpie is even lower due to the lower

maximum concentrations of moxidectin in the magpie (4.1 mg/kg). Thus, it is not expected that exposure of hair-eating birds to moxidectin residues in hair from treated cattle would have a negative impact on birds.

d. Toxicity to Terrestrial Organisms

Plants

Moxidectin was inactive against a wide variety of plants when applied either preemergence to soil, or postemergence to the weeds, at a rate of 4 kg active ingredient/ha, which is approximately 2,500 times greater than the maximum concentration in the soil, assuming no metabolism in cattle, excreta, or soil. The absence of any visible effects of moxidectin on the ability of the plants to germinate or to damage leaves of growing plants indicates that moxidectin will have no impact on the environment when manure from treated animals is applied to fields or pastures. Similar results have been found in the literature for the avermectins (Halley, et al. 1993; Wislocki et al. 1989).

Earthworms

The 28-day LC_{50}, based on nominal concentrations, was determined to be 37.2 mg/kg. After 28 days of aging, the measured concentration was 81.9% of the nominal concentration for the 40 mg/kg sample. Therefore, the actual LC_{50} would correspond to approximately 30 mg/kg. The report noted that behavioral and morphological changes were generally observed in earthworms at concentrations above 1 mg/kg which also corresponded to the no effect level (as determined by observations of weight gain). This value is approximately 800 times the maximum predicted concentration in the soil (1.31 ppb). The ratio of the predicted environmental concentration (PEC) to the predicted no-effect concentration (PNEC) for earthworms (LC_{50}/Assessment factor of 10) is 1.31 ppb/(30,000 ppb/l0) is <1. Thus, moxidectin is not expected to have any negative impact on earthworms.

Dung Insects

Dung beetles play a role in the degradation of feces deposited on pastures by both domesticated animals and wildlife. As a result of this activity, they are an important part of the pasture ecosystem. The toxicity of the avermectins towards developing dung beetle larvae has been demonstrated by numerous investigators. Although moxidectin is a milbemycin, its similarities in structure and spectrum of activity to the avermectins warranted investigation of moxidectin toxicity to dung beetles. Therefore, studies were conducted to examine the potential effects of moxidectin on dung insects.

A pivotal study was conducted to determine if feces from cattle treated with moxidectin pour-on had any negative effects on adult *Onthophagus gazella* and *Euoniticellus intermedius* exposed directly to the feces or their progeny developing in brood balls produced from this fecal material. In a blinded study, four mixed beef breed steers were treated with 0.5% moxidectin pour-on formulation at a dose of 0.5 mg/moxidectin/kg body weight and a control group of four steers was dosed with a blank formulation which did not contain moxidectin. At 1, 3, 7, 10, 14, 17 and 21 days after treatment fecal samples were collected and frozen. The collected fecal samples were thawed and placed on top of an 18 cm deep layer of sandy loam soil. For each of the two species, two pairs of beetles which were at least 10 days old were placed into each sample. Progeny beetles were collected from 23 through 40 days after the beetles were introduced. Moxidectin concentrations were measured in feces collected from individual animals on the various sampling days.

The moxidectin concentration in all samples was less than the limit of quantification (100 ppb moxidectin). Feces from cattle treated with moxidectin pour-on had no deleterious effect on adult beetles exposed directly to the feces or their progeny developing in brood balls produced from this fecal material.

In addition to this previously described study, a series of supportive studies had similar findings. One study (Doherty et al., 1994), which compared the activity of moxidectin and abamectin mixed directly into cattle feces, against the development of *Onthophagus gazella* larvae. This study demonstrated that moxidectin had no adverse affects on dung beetle larvae at concentrations less than or equal to 128 ppb. Moxidectin at 256 and 512 ppb reduced larval development to adults by 16%, and 90%, respectively. Abamectin was more toxic to dung beetle larvae, with reductions in larval development of 22% at only 4 ppb, 94% at 8 ppb, and 100% at 16 and 32 ppb. In this study, moxidectin was approximately 64-fold less toxic to developing *Onthophagus gazelle* larvae than abamectin.

A study examined the effects of moxidectin 1% injectable on the dung beetles, *Onthophagus gazella* and *Euoniticellus intermedius* (Fincher and Wang, 1992). Dung from cattle treated with a moxidectin 1% injectable formulation at a rate of 0.2 mg/kg had no effect from 1 to 42 days posttreatment on adult beetles, the mean number of brood balls produced or the percent eclosion of the two species of dung beetles included in this study.

In a blinded field study dung from cattle treated with moxidectin 1%. injectable at 0.2 mg moxidectin/kg or ivermectin 1% injectable at 0.2 mg ivermectin/kg, was collected and placed on a pasture in a randomized grid of 2 kg pats (Strong and Wall, 1994). The colonization of the pats with insect fauna was evaluated. Dung from cattle treated with moxidectin 1% injectable had no effect, at any time posttreatment, on the development of *Aphodius* spp. larvae. Dung from cattle

treated with ivermectin 1% injectable prevented development of *Aphodius* spp. larvae for at least seven days posttreatment. Moxidectin treatment had no effect on the number of cyclorrhaphous dipteran larvae in fecal pats; however, these larvae were absent from dung of ivermectin treated cattle for up to 14 days posttreatment.

9. Use of Resources and Energy

The manufacture and disposal of moxidectin and the formulated pour-on product will not require any unusual amounts of resources or energy.

10. Mitigation Measures

No adverse impact on the environment is expected from the proposed action; therefore, no mitigation measures are required. Moxidectin 0.5% Pour-On for Cattle will be packaged in 500 mL, 1 L and 2.5 L polyethylene bottles. Consistent with the container disposal pattern for similar animal drug products, individuals purchasing and administering this product will be instructed to dispose of empty bottles and any residual content in an approved landfill or by incineration. Instructions for proper handling and container disposal are clearly stated in the "Environmental Safety" and "Disposal" sections of the CYDECTIN moxidectin 0.5% Pour-On for Cattle label which follows below:

Environmental Safety

Studies indicate that when moxidectin comes in contact with the soil it readily and tightly binds to the soil and becomes inactive. Free moxidectin may adversely affect fish and certain aquatic organisms. Do not contaminate water by direct application or by improper disposal of drug containers.

Disposal

Dispose of containers in an approved landfill or by incineration.

11. Alternatives to Proposed Action

No potential adverse environmental impacts have been identified for this proposed action. As a result, no alternative actions are necessary.

12. List of Preparers:

Frank Guerino
Product Development Manager
Ph.D., Animal Science, 1989
Seven years experience in development of animal health products

Gary D. Mangels
Associate Research Fellow
Ph.D., Environmental Science, 1985
Nineteen years experience in conducting risk assessments and environmental fate research

Andrew T. Palmeter
Associate Director
DVM, Veterinary Medicine, 1980
Twelve years experience in regulatory affairs

13. Certification:

The undersigned official certifies that the information presented in this Environmental Assessment is true, accurate, and complete to the best of the knowledge of Fort Dodge Animal Health.

Signed by
Frank Guerino, Ph.D.
Product Development Manager Animal Health Research Development Fort Dodge Animal Health

Date June 12, 1997

14. References

Doherty, W.A. N.P. Stewart, R.M. Cobb and P.J. Keiran. 1994. *In vitro* comparison of the larvicidal activity of moxidectin and abamectin against *Onthophagus gazella* (F) (Coleoptera: Scarabaeidae) and *Haematobia irritans exigua* De Meijere (Diptera: Muscidae). J. Aust. Ent. Soc. 33:71-74.

Fincher G. T. and G. T. Wang. 1992. Injectable moxidectin for cattle: Effects on two species of dung beetles. Southwestern Entomologist. Vol. 17(4):303-306.

Hamaker, J.W. 1975. Environmental Dynamics of Pesticides, Plenum Press, NY pp. 115-133.

Halley, B.A., W.J.A. VandenHeuvel, and P.G. Wislocki. 1993. Environmental effects of the usage of avermectins in livestock. Veterinary Parasitology 48: 109-125.

Henny, C.J., L.J. Blus, E.J. Kolbe and R.E. Fitzner. 1985. Organophosphate insecticide (famphur) topically applied to cattle kills magpies and hawks. J. Wildl. Manage. 49: 648- 658.

Herd, R., L. Strong and K. Wardhaugh. 1993. Special Issue: Environmental impact of avermectin usage in livestock. Veterinary Parasitology, 48: 1-343.

Strong, L. and R. Wall. 1994. Effects of ivermectin and moxidectin on the insects of cattle dung. Bulletin of Entomological Research 84:403-409.

Wall, R. and L. Strong. 1987. Environmental consequences of treating cattle with the antiparasitic drug ivermectin. Nature, 327:418-421.

Wislocki, P.G., L.S. Grosso, R.A. Dybas. 1989. Environmental aspects of abamectin use in crop protection. In: W.C. Campbell (ed.) Ivermectin and Abamectin. pp. 182-200. Springer- Verlag, New York.

15. Appendices

a. Data Summary Charts

Physical Properties

Melting point (liquefaction)	145-154°C
Vapor pressure	$< 10^{-7}$ torr
UV /Visible absorption spectrum peak	245 nrn
n-Octanol/water partition coefficient	Kow = 58,300 (Log Kow = 4.766)
Solubility in water	0.51 mg/L

Solubility in organic solvents	mL solvent/g moxidectin
Dichloromethane	1.64
Diethyl ether	1.19
Ethanol (95%)	0.81
Acetonitrile	0.62
Ethyl acetate	0.47

Environmental Fate

Photodegradation half-life in water	6.8 hours (late Autumn)
Soil biodegradation half-life	~ 2 months
Soil Adsorption/desorption (Koc)	18,000-41,000 (immobile)
Mobility class by soil thin layer chromatography	1 (immobile)

Environmental Toxicology

Aquatic organisms

Bluegill 96-hour LC_{50}	0.62 ppb
NOEC	<0.52 ppb
Rainbow trout LC_{50}	0.16 ppb
NOEC	<0.15 ppb
Water flea 48-hour EC_{50}	30 ppt
NOEC	11 ppt
Green algae 72-hour EC_{50}	>87 ppb

Avian organisms

Bobwhite quail 21-day acute oral LD_{50}	278 mg/kg bw
Mallard duck 21-day acute oral LD_{50}	365 mg/kg bw
Chicken 14-day acute oral LD_{50}	283 mg/kg bw

Terrestrial Organisms

Earthworm 28-day subacute LC_{50}	37.2 mg/kg medium
Plant phytotoxicity @ 4 kg moxidectin/ha	inactive

b. Summary of Individual Studies

Physical Properties

Melting Point PD-M 28-17

The melting point of moxidectin was determined by the capillary tube method to be 145 to 154°C.

Vapor Pressure PD-M 28-10

The vapor pressure of moxidectin was determined to be < 10^{-7} torr, the limit of detection, at 25°C using the gas saturation technique, which is used to determine the vapor pressure of compounds with vapor pressures from 10 to 10^{-7} torr.

Ultraviolet-visible absorption spectra PD-M 27-51

The ultraviolet-visible absorption spectra of moxidectin was determined in a series of water/acetonitrile solutions using several concentrations of moxidectin. An absorption peak was observed at 245 nm, while there was only slight absorption above 300 nm.

n-Octanol/Water Partition Coefficient PD-M 28-20

The *n*-octano/water partition coefficient was determined to be 58,300 (Log Kow = 4.766) using the shake flask method and initial concentrations of 753 and 79.7 ppm.

Solubility in Water and Organic Solvents PD-M 28-40

The solubility of moxidectin in water and various organic solvents was determined using the shake-flask method. The water solubility was determined to be 0.51 mg/L. The solubility in various organic solvents is given in the table below.

Solvent	(mL of solvent/g moxidectin)
Dichloromethane	1.64
Diethyl Ether	1.19
Ethanol (95%)	0.81
Acetonitrile	0.62
Ethyl Acetate	0.47

Environmental Fate Studies

Laboratory Soil Biodegradation

PD-M 28-23

A soil degradation study was conducted by adding ^{14}C-moxidectin to each of three soils and aging them under aerobic conditions for 63 days. The properties of the soils are given below:

	Composition						
Type & Texture	% Sand	% Silt	% Clay	% O.M.	% O.C.	pH	C.E.C
Sassafras sandy loam[1]	62.8	25.6	11.6	1.0	0.58	6.9	5.9
Piano loam[2]	32.8	47.6	19.6	2.4	1.39	7.1	7.46
Tippeecanoe silt loam[3]	32.8	49.6	17.6	3.1	1.80	6.9	20.06

Soil origin: [1]New Jersey, [2]Wisconsin, [3]Indiana

During the aging period the ^{14}C-moxidectin was extensively degraded, with 5.24%, 1.59% and 1.16% of the applied dose being mineralized (converted) to $^{14}CO_2$ in soils from Indiana, New Jersey and Wisconsin, respectively. After 63 days of incubation, moxidectin accounted for 47, 44, and 57% of the applied dose in the Indiana, New Jersey and Wisconsin soils. There were at least 10 degradation products formed, most of which were at trace levels. Half-lives of approximately two months under these conditions indicate that moxidectin is not expected to persist in the environment.

Soil Adsorption/Desorption

PD-M 28-7

The adsorption of moxidectin onto four different soils was investigated using the batch equilibrium technique. Initial concentrations of ^{14}C-moxidectin of 0.044, 0.084, 0.455 and 0.983 ppm in 0.01 M calcium chloride were used. The soil and the moxidectin solutions were mixed, shaken continuously for two days at room temperature, centrifuged and the concentration of moxidectin in the adsorption solution was measured. Fresh 0.01 M calcium chloride was added and the desorption of moxidectin from soil was studied using the same procedures used in the adsorption phase. After the desorption phase, the amount of ^{14}C-moxidectin remaining in the soil was determined. The adsorption coefficients, normalized for the % organic carbon in the soil (Koc), are shown in the table below.

		Composition						
Type & Texture	Sand	% Silt	% Clay	% O.M.	% O.C.	pH	C.E.C	Koc
Buelah loamy sand[1]	80.0	15.6	3.6	0.5	0.29	6.5	3.4	41379
Sassafras sandy loam[2]	62.8	25.6	11.6	1.0	0.58	6.9	5.9	28448
Piano loam[3]	32.8	47.6	19.6	2.4	1.39	7.1	7.46	20215
Tippeecanoe silt loam[4]	32.8.	49.6	17.6	3.1	1.80	6.9	20.06	18666

Soil origin: [1]Arkansas, [2]New Jersey, [3]Wisconsin, [4]Indiana

Mobility in Soil by Thin-Layer Chromatography PD-M 27-24

The mobility of moxidectin (^{14}C-Iabeled) was assessed in four different soils using soil thin layer chromatography. Soil coated (1 mm) plates were used with water as the mobile phase.

	Composition %							
Tvpe & Texture	Sand	Silt	Clay	O.M.	O.C.	pH	C.E.C	RF
Buelah loamy sand[1]	80.8	15.6	3.6	0.5	0.29	6.5	3.4	0.07
Sassafras sandy loam[2]	62.8	25.6	11.6	1.0	0.58	6.9	5.9	0.08
Piano loam[3]	32.8	47.6	19.6	2.4	1.39	7.1	7.46	0.07
Tippeecanoe silt loam[4]	32.8	49.6	17.6	3.1	1.80	6.9	20.06	0.07

Soil origin: [1]Arkansas, [2]New Jersey, [3]Wisconsin, [4]Indiana

All four soil types tested were given a 1 classification under the Helling method which characterizes moxidectin as an immobile compound, which is consistent with the results of the adsorption/desorption study.

Photolysis in Water PD-M 28-22

The photo degradation of moxidectin in aqueous solutions was studied using both sunlight and a high-pressure xenon-arc lamp which was filtered to remove light <290 nm to simulate sunlight. The sunlight study was conducted in NJ in late autumn (November). Due to the low solubility of moxidectin in water (i.e., < 1 ppm), acetonitrile (1%) was used as a cosolvent to help keep moxidectin in solution. Foil wrapped samples were used as dark controls. The initial concentration of moxidectin was measured and additional determinations made every two hours until termination of the study after 14 hours exposure. There was a reduction in the measured moxidectin concentration from 97% to 22% of the applied dose after 12 hour exposure to natural sunlight, and a reduction from 94% to 19% of the applied dose after 14 hour exposure to the xenon-arc lamp. The calculated half-lives were 6.8 hours and 5.6 hours, respectively. The half-life from the spring to early fall would be even more rapid due to the longer and more intense exposure to sunlight. Therefore, the use of a half-life of 6.8 hours clearly represents a worst-case value for direct photolysis. This rapid photodegradation in water will rapidly degrade any moxidectin entering the aquatic environment. Several photodegradation products were observed, but were not identified since each accounted for less than 10% of the applied dose.

Absorption, Distribution. Excretion & Biotransformation From Cattle PD-M-29-43

Two groups of three steers each were treated with a single dose of the pour-on formulation of ^{14}C-moxidectin at 0.5 mg/kg body weight. Urine and feces were collected daily and assayed. Animals were sacrificed at two and fourteen days posttreatment. This study demonstrated that feces are the primary route of excretion. The majority of excreted drug residue was unaltered moxidectin (51%) with at least five metabolites formed, none of which accounted for greater than 9% of the total radioactive residue.

Environmental Toxicology

Aquatic Toxicity

Bluegill ECO 971-90-149

The toxicity of moxidectin to the bluegill *(Lepomis macrochirus)* was determined using a flow-through test over 96 hours of exposure. The test was conducted in accordance with US EPA guidelines, and used a control, a solvent control and solutions of moxidectin at nominal concentrations of 0.65, 1.1, 1.8, 3.0 and 5.0 ug ai/L. The mean measured concentration ofmoxidectin were 0.52, 0.71, 1.1, 2.0 and 3.2 ug ai/L, respectively. For each concentration studied, 20 fish were used with monitoring conducted at 24-hour intervals. The 96-hour LC_{50}, based on measured concentrations was 0.62 ppb, while the NOEC was < 0.52 ppb, the lowest concentration tested.

Rainbow trout ECO 971-90-150

The toxicity of moxidectin to the rainbow trout *(Oncorhynchus mykiss)* was determined using a flow-through test over 96 hours of exposure. The test was conducted in accordance with US EPA guidelines, and used a control, a solvent control and solutions of moxidectin at nominal concentrations of 0.26, 0.43, 0.72, 1.2 and 2.0 ug ai/L. The mean measured concentration of moxidectin were 0.15, 0.22, 0.43, 0.71 and 1.2 ug ai/L, respectively. For each concentration studied, 20 fish were used with monitoring conducted at 24-hour intervals. The 96-hour LC_{50}, based on measured concentrations was 0.16 ppb, while the NOEC was < 0.15 ppb, the lowest concentration tested.

Water Flea *(Daphnia magna)* ECO 971-90-151

The toxicity of moxidectin to the water flea *(Daphnia magna)* was determined using a flow-through test over 48 hours of exposure. The test was conducted in accordance with US EPA guidelines, and used a control, a solvent control and solutions of moxidectin at nominal concentrations of 6.5, 11, 18, 30 and 50 ng ai/L. For each concentration studied, 20 daphnia were used with monitoring conducted at 24-hour intervals. The 48-hour LC_{50} was 30.2 ng/L (ppt), while the NOEC was 11 ng/L (ppt).

Green Algae ECO 954-92-101

The effects of moxidectin on the growth of green algae *(Selenastrum capricornutum)* were studied over three days in accordance with OECD Guideline G 201. The effects were studied using a control, a solvent control and solution of moxidectin at nominal concentrations of 9.38, 18.8, 37.5, 75.0 and 150 µg ai/L in a synthetic algal assay nutrient medium. The mean measured concentration of moxidectin were 5.1, 10.0, 17.6, 39.5 and 86.9 µg ai/L, respectively. The highest concentration studied corresponding to the maximum solubility level in the test medium. The test was conducted under static, non- renewal conditions at 24 ± 2°C with continuous illumination (4306 lux). Test vessels (500 mL Erlenmeyer flasks with 100 mL of test solution) were continually shaken. The effects on growth were evaluated by comparing the area under the growth curves in the treated solutions with the control groups. A statistical difference was noted

between the blank and solvent controls. Therefore, the percentage growth inhibition was calculated against the growth in the solvent control. The 3-day EC_{50}, based on measured concentrations was > 87 ppb, the limit of its solubility in the test medium, which was the highest concentration tested. During the study there were significant decreases in the concentration of moxidectin from the treatment solutions. This decrease is consistent with the finding that moxidectin is rapidly photodegraded.

Avian toxicity

Chicken --14-Day Acute Oral LD_{50} A90-42

The acute toxicity of moxidectin, when administered as a single oral dose, was determined for the chicken. The calculated LD_{50} value was 283 mg/kg. Mortality was observed at dose levels starting at 100 mg/kg. This study demonstrated that moxidectin is moderately toxic towards avian species.

Bobwhite Quail --21-Day Acute Oral LD_{50} BLAL 90QD 156

The test was conducted in accordance with US EPA protocol FIFRA Guideline No. 71-1. The acute toxicity of moxidectin, when administered as a single oral dose, was determined for the bobwhite quail. The calculated LD_{50} value was 278 mg/kg. Mortality occurred at the lowest dose tested, 100 mg/kg. These figures indicating that moxidectin is moderately toxic towards avian species.

Mallard Duck --21-Day Acute Oral LD_{50} BLAL 90DD79

The test was conducted in accordance with US EPA protocol FIFRA Guideline No. 71-1. The acute toxicity of moxidectin, when administered as a single oral dose, was determined for the mallard duck. The calculated LD_{50} value was 365 mg/kg. Mortality occurred at the lowest dose tested, 147 mg/kg. These figures indicating that moxidectin is moderately toxic towards avian species.

These LD_{50} values are similar to those obtained for the chicken, where the LD_{50} value was 283 mg/kg, and mortality occurred at dose levels starting at 100 mg/kg. The LD_{50} values are such that either species would have to consume many kg of soil and/or feces in order to receive a toxic dose. Thus, there should be no adverse effects on birds.

Terrestrial Organisms

Plants PD-M 28-24

Moxidectin was inactive against a wide variety of weeds when applied either preemergence to soil, or postemergence to the weeds, at a rate of 4 kg active ingredient/ha. The weeds were: *Abutilon theophrasti* (velvetleaf), *Ambrosia artemisiifolia* (common ragweed), *Avena fatua* (wild oats), *Brassica kaber* (wild mustard), *Calystegia arvensis* (hedge bindweed), *Cyperus rotundus* (purple nutsedge), *Digitaria sanguinalis* (large crabgrass), *Echinochloa crus-galli* (barnyardgrass), *Elytrigia repens* (quackgrass), *Ipomoea* sp. (morningglory), *Setaria viridis* (green foxtail), *Sida spinosa* (prickly sida). The absence of any visible effect of moxidectin on the ability of the plants to germinate or damage leaves of growing plants indicates that moxidectin will have little or no impact on the environment when manure from treated animals is deposited on pastures or applied to fields.

Earthworm *(Eisenia foetida)* ECO 91-118

A 28-day subacute toxicity test was conducted on earthworms using a mixture of ^{14}C- labeled and non-labeled moxidectin in accordance with FDA Guideline No. 4.12 "Earthworm, Subacute Toxicity Test". After a range finding test, eight concentrations of moxidectin were used ranging from 1 to 1280 mg/kg (nominal). Observations of mortality were taken at 7, 14, 21 and 28 days after application.

Samples were prepared by mixing a solution of moxidectin in acetone (11.8 mL) with cow manure (50 g) and deionized water (27.3 mL). The manure slurry was held in a fume hood overnight to evaporate the solvent. The slurry was then mixed with artificial soil (1000 g, dry weight) using a mechanical mixer. Samples were held in 2 L covered glass beakers with 10 earthworms per test container. Samples were kept at 20±2°C, with four replicates per concentration.

After 28 days of exposure the LC_{50}, based on nominal concentrations, was determined to be 37.2 mg/kg. Analysis of the 40 mg/kg sample indicated that at the conclusion of the test, the actual value was 81.9% of the nominal concentration. Therefore, the actual LC_{50} would correspond to approximately 30 mg/kg. Behavioral and morphological changes were generally observed in earthworms at concentrations above 1 mg/kg, which also corresponded to the no effect level, as determined by observations of weight gain.

Dung Insects

Dung beetles *(Onthophagus gazella* and *Euoniticellus intermedius)* GASD 04-18.00

Four mixed beef bred heifers were treated with 0.5% moxidectin pour-on formulation at a dose level of 0.5 mg/moxidectin/kg body weight. A control group was dosed with a blank formulation which did not contain moxidectin. At 1, 3, 7, 10, 14, 17 and 21 days after treatment fecal samples were collected and frozen. Subsamples of this excreta were assayed for moxidectin. For the bioassay, the collected fecal samples were thawed and placed on top of an 18-cm deep layer of sandy loam soil. For each of the two species, two pairs of beetles which were at least 10 days old were placed into each sample. Progeny beetles were collected from 23 through 40 days after the beetles were introduced. The moxidectin concentrations in all samples was less than the limit of quantification (100 ppb). There were no statistical differences for either beetle species in the number of intact brood balls produced from feces of control or treated cattle. This study demonstrated that feces from cattle treated with moxidectin pour-on had no deleterious effect on adult beetles exposed directly to the feces or their progeny developing in brood balls produced from this fecal material.

Exposure Studies

Residue Levels in Cattle Hair GASD 02-18.00

Ten Hereford crossbred steers were treated with 0.5% moxidectin pour-on formulation at a dose level of 0.5 mg/moxidectin/kg body weight. Hair was taken in a band at 4 inches from the midline of the treated cattle at 1, 3, 7, 21, and 42 days after treatment. Residues in the hair from treated cattle ranged from 127 to 344 ppm throughout the study, with considerable variation between animals. Due to this variation, depletion of moxidectin in hair from treated areas could not be determined.

Wash-off Potential from Treated Cattle GASD 04-12.00

Six mixed beef-breed heifers were treated with 0.5% moxidectin pour-on formulation at a dose level of 0.5 mg/moxidectin/kg body weight. At one, two and six hours after treatment two animals were exposed to 30 minutes of simulated rainfall which delivered one inch of rain. The animals were placed in a stainless steel apparatus which allowed the water to be collected. Water which washed-off the animals was collected and the apparatus was washed with methanol. The water and the washes were assayed to determine the concentrations of moxidectin in the water. At 1, 2 and 6 hours after treatment, the mean percentage of applied moxidectin which washed-off from the cattle was 0.60, 0.71 and 1.49.

c. Material Safety Data Sheet

Material Safety data Sheet (MSDS), Mosidectin Pour-On, American Cyanamid Company, Wayne NJ 07470 dated June 02, 1997. MSDS No. AG07187-2

AMERICAN CYANAMID *CO.*
PARSIPPANY, NJ 07054

MSDS NO. AGO7187-2
MATERIAL SAFETY DATA SHEET CAS NO. Mixture

DATE: JUN 02, 199

EMERGENCY TELEPHONE: (973) -683-3100 (U.S.A.)
(800) -424-9300 (CHEMTREC)

PRODUCT IDENTIFICATION	TRADE NAME:	Moxidectin Pour-On (Violet)
	SYNONYMS:	
	CHEMICAL FAMILY:	Milbemycin Derivative
	MOLECULAR FORMULA:	$C_{37}H_{53}NO_6$
	MOLECULAR WEIGHT:	639.800
	USAGE:	Pour-On for Cattle

WARNING STATEMENTS	CAUTION: Keep out of reach of children. Avoid contact with eyes, skin or clothing. Avoid contact with sprays or mists.

INGREDIENTS

COMPONENT	CAS. NO.	%	PEL/TLV
Aromatic 100	64742-94-5	15.00	100 ppm
Inerts		84.50	
Moxidectin	113507-0605	0.50	None Established

REFERENCE:	Aromatic 100	Exxon 1987
	Inerts	
	Moxidectin	None

PHYSICAL PROPERTIES

APPEARANCE AND ODOR:	Deep violet colored oily solution with a characteristic aromatic odor
BOILING POINT:	162 – 164 ^{O} C
MELTING POINT:	-17.9 - -10.4 ^{O} C
VAPOR PRESSURE:	not available
DENSITY:	0.918 g/ml
VAPOR DENSITY:	not available
% VOLATILITY (BY VOL.) :	16.3 % (as aromatic 100)
OCTANOL / H_2O PARTITION COEF.:	not applicable
PH:	not applicable
SATURATION IN AIR (BY VOL.) :	not available
EVAPORATION RATE:	0.07 (n-butyl acetate = 1)
SOLUBILITY IN WATER:	insoluble

FIRE AND EXPLOSION HAZARD INFORMATION	FLASH POINT:	150 ^{O}F
	FLAMMABLE LIMITS (% BY VOL.)	not available
	AUTOIGNITION TEMP:	not available

FIRE EXTINGUISHING MEDIA:
Use water, foam, dry chemical or carbon dioxide to extinguish fires.

FIRE CONTROL TACTICS:
Wear self-contained, positive pressure breathing apparatus and full fire fighting protective clothing.

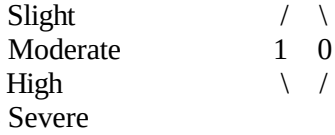
Keep unnecessary people away. Use as little water as possible. Dike area of fire to prevent run-off. Use spray or fog -solid stream may cause spreading.

Conduct fire fighting and rescue operations from upwind of the fire area. Evacuate people downwind who may come in contact with smoke, fumes, or contaminated surfaces. Do not decontaminate personnel or equipment, or handle broken packages or containers without protective equipment as specified in the Exposure Control Section. Decontaminate emergency personnel with soap and water before leaving the fire area.

Avoid breathing dusts, vapors and fumes from burning materials. Alert medical personnel to be ready to treat for poisoning. Control run-off water - if water enters a drainage system, advise the authorities downstream.

NFPA HAZARD - RATING

0 Least
1 Slight
2 Moderate
3 High
4 Severe



REACTIVITY DATA	INCOMPATIBLE MATERIALS:	not available
	HAZARDOUS DECOMPOSITION PRODUCTS:	not available

HEALTH HAZARD INFORMATION

TOXICITY DATA AND EFFECTS OF OVEREXPOSURE:

ACUTE TOXICITY DATA:
The acute oral LD_{50} in rats for the combined sexes was shown to be greater than 5000 mg/kg b.w indicating that the material is relatively non-toxic by ingestion in single doses.

The acute dermal LD_{50} in rabbits for the combined sexes was shown to be greater than 2000 mg/kg

(cont from pg. 2)	b.w., indicating that the product is no more than slightly toxic by skin contact in a single dose. This formulation was determined to be slightly irritating to both skin and eyes in appropriate primary irritation studies in rabbits. Within 48 hours signs of irritation had completely disappeared in all cases. EMERGENCY AND FIRST AID PROCEDURES: IF SWALLOWED: Do not induce vomiting. See notes to physician. IF IN EYES: Flush eyes with large amounts of water. Seek medical attention if irritation persists. IF ON SKIN: Wash skin with plenty of soap and water. Seek medical attention if irritation persists. IF INHALED: Remove to fresh air. NOTES TO PHYSICIAN: Because of increased risk of chemical pneumonia and/or pulmonary edema due to aspiration of aromatic hydrocarbons into the lungs, vomiting should be induced only under professional supervisor.
EXPOSURE CONTROL METHODS	Work shall be conducted in ventilated areas. The use of hoods with a minimum average capture velocity of 125 FPM or point source exhaust. When engineering controls cannot capture airborne contaminants, a respirator with a pesticide cartridge or an air supplied respirator should be worn. Personal protective equipment including lab coats or Tyvek coveralls or other protective clothing, eye protection and neoprene or nitrile gloves must be worn. Work shall be conducted in ventilated areas. The use of hoods with a minimum average capture velocity of 125 FPM or point source exhaust.
SPILL OR LEAK PROCEDURES	Wearing appropriate protective clothing and equipment (*See* "Exposure Control" section), dike spill area to prevent spill from spreading, absorb with an inert absorbent material, (e.g. granular clay or sawdust), and shovel/sweep into covered containers for proper disposal *(See* "Waste Disposal" section). Rinse spill area and tools several times with soapy water. Contain and absorb rinsate with inert absorbents and place into the same disposal container as spilled material. Small spills to the soil can be shoveled directly into disposal containers. In the event *of* a large spill, contact Cyanamid for guidance on available clean-up options.

Depending on the quantity released to the environment notifications to regulatory authorities may be required. This material could be highly toxic to aquatic organisms. If spill is to a water body, immediately notify applicable authorities downstream, so that contingencies can be taken, if necessary.

WASTE DISPOSAL: To avoid disposal, all attempts should be made to utilize the product completely, in accordance with its intended and/or registered use. If - this is not possible, handle with care, and dispose in a safe manner.

Empty containers may retain some product residues. DO NOT REUSE. Rinse thoroughly, render container unusable by crushing and/or puncturing, and dispose in a safe manner. Do not allow rinsate to be discharged directly to water bodies due to potentially high toxicity to aquatic organisms.

It is the ultimate responsibility of the waste generator to determine at the time of disposal whether the product (and/or "empty" container residue) meets any hazardous waste criteria. Follow all applicable Federal, State, Provincial, and Local regulations regarding waste management methods.

Cyanamid's recommended disposal method for this product is detoxification according to Company procedures, followed by biological waste treatment. As an alternative, incineration can be used.

SPECIAL PRECAUTIONS

HANDLING AND STORAGE:

Do not contaminate water, food, or feed by storage or disposal. Store in a secure, dry, cool well-ventilated separate room, building or covered area.

Not for use or storage in or around the home.

Keep away from sources of ignition and protect from exposure to fire and heat.

Segregate from oxidizers and incompatible materials listed in the Reactivity Data Section.

APPENDIX

The information and statements herein are believed to be reliable but are not to be construed as a warranty or representation for which we assume legal responsibility. Users should undertake sufficient verification and testing to determine the suitability for their own particular purpose of any information or products referred to herein. NO WARRANTY OF FITNESS FOR A PARTICULAR PURPOSE IS MADE.

SOURCE AND DATE INFORMATION

SHEET NO.: AG07187-2
DATE: JUN 02, 1997