THE ENVIRONMENTAL AND MAMMALIAN SAFETY PROFILE OF NATURALYTE INSECT CONTROL

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Abstract

This is an updated summary of the environmental and toxicological properties of spinosad, the first product in the naturalyte class of insect control products, in relation to expected environmental or human exposure. Safety assessments to a number of environmental endpoints, farm workers and human dietary exposure are presented to demonstrate the large margins of safety associated with the use of this new product in agricultural crops, particularly cotton.

Spinosad

Insect control products in the new naturalyte class are highly efficacious with a unique mode of action derived as a natural fermentation product. Another feature common to all naturalyte products is a large margin of safety to man and the environment. In this paper, spinosad, which is isolated from the actinomycete bacteria, Saccharopolyspora spinosa, is used to demonstrate the safety margins associated with naturalytes.

Physical Properties

The physical properties of spinosyns A & D are shown in Table 1. With the exception of water solubility and melting point, the physical properties of spinosyns A & D are very similar. In general, spinosad has very low vapor pressure indicating a non-volatile material, and a relatively high Kow, indicating the predominant hydrophobic character of the molecule. Spinosyn A is higher in water solubility and lower in melting point than spinosyn D which is perhaps a result of conformational differences attributed to the presence of a methyl group.

Environmental Fate

The environmental properties of spinosad are compared in Table 2 to those of chemicals known to possess physical properties associated with soil leaching. Although the water solubility of Spinosyn A is greater at pH 5 and pH 7 than the standard, the soil adsorption coefficient, Kd, generally occurs in a range that demonstrates strong soil sorption with little expected mobility. These data, along with a supplementary dataset showing the half life of spinosyn A to be 1/2 day or less in an actual field study, indicates very little potential for leaching.

In summary, the properties of spinosad are not similar to pesticides, some of which are known to leach through soil. Soil degradative routes are fast and soil sorption is moderately strong which will limit potential movement to ground or surface water.

Levels of Concern

A standard methodology to evaluate possible environmental risk is to use the U.S. EPA's technique of calculating Levels of Concern. A ratio, UQ, of an expected environmental concentration to a biological effect level (usually an LC50) is calculated and a safety factor of 5 to 20 is built in, based on an environmental end point. A level of concern for avian and terrestrial mammals exists if Q>0.2 for non-endangered species and Q>0.1 for endangered species.

Spinosad Safety to Avian Species

Maximum expected environmental exposure levels based on several species of birds' foraging habits and maximum expected use rates for spinosad are shown in Table 3 along with acute toxicity data for oral, dietary, and reproductive toxicity. Calculated Q values demonstrate very large safety margins. Based on these calculations, spinosad can be classified as practically non-toxic to birds.

Spinosad Safety to Wild Mammals

Similar calculations are shown in Table 4 for expected exposure levels to terrestrial mammals. Q values were calculated for several species based upon acute LD50 values which were extrapolated from the acute rat studies. The values demonstrate very large margins of safety. Again, spinosad can be characterized as practically non-toxic to terrestrial mammals.

Spinosad Safety to Aquatic Organisms

Spinosad safety to a variety of aquatic organisms can be evaluated in a worse case shallow pond Tier 1 assessment. The levels of concern, shown in Table 5 are calculated based on the LC50 values and aquatic expected environmental concentration based upon a typical use scenario or a maximum use scenario. In general, the levels of concern are well below the trigger values of Q=0.1 for non-endangered or Q=0.05 for endangered species.

Ecotoxicology of Spinosad

Data demonstrating the toxicity of spinosad to terrestrial invertebrates and beneficial organisms is summarized in Table 6. Spinosad, in the technical grade form is highly toxic to bees, however, evaluation of 24 hour acute contact

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data from the formulated product shows a moderated level of activity to honey bees. High levels of safety are observed to other beneficial organisms and to earthworms.

Cotton Metabolism/Residues with Spinosad

In studies conducted evaluating the metabolism and characterization of the 14C residues in spinosyn A and spinosyn D treated cottonseed, there was no detection of any spinosyn A, spinosyn D or related metabolites. Evidence was obtained which demonstrated that the residues in seed and fiber resulted from the reincorporation of 14C activity into natural components such as fatty acids, glucose and protein. These findings suggest that the spinosyn A and spinosyn D molecules are extensively degraded to 14CO2 which is taken up by the plant and used for the biosynthesis of natural plant constituents. Residue trials were conducted in a number of cotton growing regions with maximum use rates and a 28 day PHI. Assay of the cotton seed from 17 trials showed no detectable residues of spinosyn A or D at a detection limit of 0.004 ug/g. In addition, no residues have been observed in cotton residue trials conducted at exaggerated rates.

Spinosad Mammalian Toxicology

Examination of some of the toxicology data, shown in Table 7, that has been developed to support the registration of spinosad shows very low levels of acute toxicity to the rat and rabbit with very safe levels of >2000 mg/kg/day and >5000 mg/kg/day, respectively. Similarly in subchronic and chronic studies, very safe NOELs are observed when compared to traditional insecticides. Spinosad has also been shown to be non-mutagenic, non-teratogenic, non-carcinogenic, and non-neurotoxic in a number of lab studies. Overall, spinosad possesses an excellent toxicology package with high margins of safety for most mammalian toxicological endpoints.

Dietary Exposure

Based on the toxicology studies and the cotton residue trials, dietary safety factors can be calculated. Magnitude of residue studies have shown no detectable residues at the limit of quantitation (LOQ) of 0.01 ppm, and hence a tolerance of 0.02 ppm (2X the LOQ) is appropriate. Metabolism studies in poultry and a ruminant have indicated that there will be no spinosad or its metabolites observed in meat, milk, or eggs at a reasonably attainable detection limit.

Based on chronic toxicity studies, a reference dose, RfD, of 0.025 mg/kg/day is recommended using an uncertainty factor of 100 and the NOEL of 2.5 mg/kg/day in the 1 year dog feeding study. Assuming residues in cotton seed at the proposed tolerance level, and that 100% of the crop is treated with spinosad, it was determined that the use on cotton will result in dietary exposure to human populations of less than 0.002% of the RfD.

Worker Exposure

An assessment of potential exposures and risks to workers associated with the use of spinosad, on apples and cotton has been determined. Exposures have been estimated by using the Pesticide Handlers Exposure Database and assuming maximum label use of spinosad and typical size orchards and fields.

Table 8 estimates worker exposure and margins of exposure for apple orchard workers who mix and load airblast equipment and those who just apply insecticides with airblast equipment.

Table 9 does the same for cotton workers who mix and load aerial application equipment, pilots who apply insecticide, flaggers who mark the fields during aerial application, and the farmer who mixes, loads, and applies the product by ground.

The margin of exposure for cotton and apple workers (Table 8 and Table 9), are well above the value of 100 which is usually deemed to be acceptable for agricultural workers. Since it is unlikely that 100% of the spinosad that contacts the skin will be absorbed by the human body, allowance for dermal absorption would likely increase these margin of exposure values by 1 or 2 orders of magnitude.

On this basis, it was concluded that spinosad can be used on cotton and apples without any significant hazard to agricultural workers.

Favorable Regulatory Attributes of Spinosad

In conclusion, spinosad has highly favorable environmental and toxicological attributes. It is applied at low rates compared to traditional pesticides reducing the environmental loading of the compound. Very large margins of safety are observed for workers or through dietary consumption; the material is safe to beneficials and non-target organisms, yet has very little potential to contaminate surface or ground water.

After reviewing these and other factors, the U.S. EPA concluded that spinosad meets the criteria necessary to be placed in the reduced risk category.

Table 1. Physical Properties of Spinosad

State	Vapor Pressure
Crystalline solid	spinosyn A=2.4×10^{-10} mmHg
Color	spinosyn D=1.6×10^{-10} mmHg
light gray to white	Melting Point
Odor	spinosyn A: 84-99.5◦ C
Slightly stale water	spinosyn D: 161.5-170◦ C

Water Solubility			Octanol/Water (Kow)		
pH	spinosyn A	spinosyn D	pH	spinosyn A	spinosyn D
5.0	290 ppm	29 ppm	5.0	log P = 2.8	log P = 3.2
7.0	235 ppm	0.332 ppm	7.0	log P = 4.0	log P = 4.5
9.0	16 ppm	0.053 ppm	9.0	log P = 5.2	log P = 5.2
		DI H_2O		log P = 3.9	log P = 4.4

Table 2 Environmental Properties of Spinosad Compared to Those of Pesticides Known to Leach

Pesticides		Spinosad	
Property	Known to Leach	Spinosyn A	Spinosyn D
Water Solubility	> 30 ppm	pH 5 290 ppm pH 7 235 ppm pH 9 16 ppm	pH 5 28 ppm pH 7 0.329 ppm pH 9 0.040 ppm
Kd	<5.0 (Usually < 1.0 or 2.0)	5.4 - 323	---
Speciation	Negatively Charged	Positive Charge	Positive Charge
Henry's Constant	< 10^2 atm-m^3/mol	pH 5 7.96×10^{-10} pH 7 9.82×10^{-10} pH 9 1.44×10^{-8}	pH 5 5.47×10^{-9} pH 7 4.87×10^{-7} pH 9 2.96×10^{-6}
Hydrolysis	> 25 weeks	pH 5 Stable pH 7 Stable pH 9 200 days	pH 5 Stable pH 7 Stable pH 9 259 days
Aqueous Photolysis	> 1 week	< 1 day	< 1 day
Soil t1/2 (lab)	> 2-3 Weeks	9.4-17.3 Days	14.5 Days

Table 3. Calculated Q Values for Several Avian Species

Bird		Bob White	Mallard	Field Sparrow	Mourning Dove	Blue Tit
EEC	Oral, mg/ft^2	1.17	1.17	1.17	1.17	1.17
	Dietary, ppm	26.9	26.9	26.9	26.9	26.9
Acute Toxicity	Oral, mg/bird	340	2400	27.8	200	22.0
	Dietary, ppm	5253	5156	5970	17857	6670
	Repro. ppm	550	550	2985	8929	3333
Q	Oral	0.0034	0.0005	0.0420	0.0058	0.0531
	Dietary	0.0051	0.0051	0.0045	0.0015	0.0040
	Repro	0.0489	0.0489	-	-	-

Table 4. Calculated Q Values for Several Terrestrial Mammal Species

Animal	Dietary EEC, ppm	Dietary LC50, ppm	Dietary Q
Vole (Herbivore)	26.9	6120	0.0044
Mouse (Granivore)	3.70	23100	0.00016
Shrew (Insectivore)	3.70	3400	0.0011

Table 5. Calculated Q Values for Aquatic Organisms in Worse Case Aerial Deposition Pond Scenarios

		Q Max Rate	Q Typical Rate
Organism, LD50	Toxicity , ppm	0.5 ft POND*	0.5 ft POND*
Bluegill, 96 hr	5.9	0.00140	0.00083
Rainbow Trout, 96 hr	30.0	0.00027	0.00016
Rainbow Trout, 21d	4.8	0.00170	0.00102
Daphnia (Death)	92.7	0.00009	0.00005
Carp, 96 hr	5.0	0.00160	0.00099
N. pelliculosa	0.14	0.06100	0.03630
Green Algae	106.0	0.00008	0.00005
Blue Green Algae	8.1	0.00100	0.00061
Grass Shrimp, 96 hr	9.8	0.00084	0.00050
Sheepshead Mnw, 96 hr	7.9	0.00100	0.00063
S. costatum	0.3	0.03600	0.02170
Eastern Oyster	0.3	0.02700	0.01640

* EEC(ppm)=0.00822 (max); 0.00492 (typical)

Table 6. Ecotoxicology of Spinosad to Beneficial Organisms

Terrestrial Invertebrates

SPINOSAD	Honey Bee
48-hour LD50 (ug/bee)	0.0025
	Earthworm
NOEC (mg/kg)	>970

("Highly Toxic to Bees")

Beneficial Organisms

24 HR ACUTE CONTACT LC50 (PPM)

	NAF-85
Honey Bee	11.5
Encarsia formosa	29.1
Minute Pirate Bug	200
Convergent Ladybird Beetle	>200
Phytoseiulus persimilis	>200
Green Lacewing	>200

Table 7. Summary of Spinosad Mammalian Toxicology

Acute Toxicity
Rat, Rabbit - >2000 - >5000 mg/kg/day

Eye & Dermal Irritation (rabbit) - slight to none

Subchronic toxicity
Rat, Mouse, Dog - 13 week NOEL = 5-50 mg/kg/day

Chronic Toxicity
Rat, Mouse, Dog: 12-24 mos. NOEL=2.5 - 11.0 mg/kg/day

Rat, Mouse, Dog: 12-24 mos. NOEL=2.5 - 11.0 mg/kg/day

Other Toxicity
Non-mutagenic
Non-teratogenic
Non-carcinogenic
Non-neurotoxic

Table 8. Estimated Margin of Exposure for Apple Orchard Workers

Worker & Task(s)	Est. Exposure mg/kgBW/d	Margin of Exposure
Mixer/loader (airblast)	0.0148	331
Applicator (airblast)	0.00249	1968

Table 9. Estimated Margins of Exposure for Cotton Workers

Worker & Task(s)	Est. Exposure, mg/kgBW/d	Margin of Exposure
Mixer/loader - aerial	0.0028	1,800
Aerial - pilots	0.00036	14,000
Aerial - flaggers	0.00072	6,900
Groundboom - M/L/A	0.0016	3,100