Spinosad
Crops

Executive Summary

Spinosad is an aerobic fermentation product of the soil bacterium, *Saccharopolyspora spinosa*. This review focuses on plant crop production.

The reviewers all agreed that the material is nonsynthetic. Although a chemical mutant is used for production, excluded methods are not employed, and chemical structures are not changed during isolation and purification.

Reviewers generally agreed that the toxicological profile for spinosad is relatively benign when compared with other insecticides. All found it compatible with organic production and believed that it has a place in organic agriculture. However, all expressed concerns about the effects on beneficial organisms such as bees, aquatic organisms, earthworms, soil micro-organisms, and parasitoids. Though spinosad is quickly photodegraded on leaf surfaces, it is degraded very slowly in aquatic environments, and may be accumulated by oysters and fish due to its fat solubility. Though soil micro-organisms degrade the original material quickly, metabolites are biologically active and persistent in the soil.

Because the reviewers considered spinosad to be nonsynthetic, it could only be added to the National List as a Prohibited Nonsynthetic with precisely defined exceptions to permit limited use. One reviewer suggested this course of action. Another reviewer felt there should be clear guidelines to restrict spinosad applications around water bodies, and that formulations should be restricted or adapted to have minimal impact on bees. The third reviewer suggested that spinosad 'should be used in production systems rich in microbial activity to ensure that the pesticide does not build up in soil.' The third reviewer also suggested that the primary breakdown products should be more fully studied and researched as to their 'ecological toxicity and impacts to beneficial organisms.'

Other concerns raised included fat solubility of spinosad; persistence of the substance and its toxicologically significant metabolites in soil; possible negative impacts on the organic market; and the persistence of spinosad in manure. The reviews advise the NOSB to not categorically prohibit spinosad's use in organic production, but should establish restrictions to mitigate environmental and other concerns raised by the use of the substance.

Summary of TAP Reviewer's Analyses[1]

Synthetic/ Nonsynthetic	***Allow without restrictions?***	***Allow only with Restrictions? (See Reviewers' comments for restrictions)***	***Prohibit for all uses***
Synthetic (0) Nonsynthetic (3)	Yes (2) No (1)	Yes (1) No (2)	Yes (0) No (3)

Identification

Chemical Names: The name spinosad is derived from combining the characters from spinosyn **A** and spinosyn **D**. The material is a mixture of about 85% Spinosyn A and 15% Spinosyn D. **Spinosyn A** is 2-[(6-deoxy-2,3,4-tri-O-methyl-*alpha*-L-mannopyranosyl)oxy)-13-[(5-dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl)oxy)-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-14- methyl-1H-as-indaceno(3,2-d)oxacyclododecin-7,15-dione. **Spinosyn D** is 2-((6-deoxy-2,3,4-tri-o-methyl-*alpha*-L-mannopyranosyl)oxy)-13-((5-(dimethylamino)tetrahydro-6-methyl-2H- pyran-2-yl)oxy)-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1H-as-indaceno (3,2-d)oxacyclododecin-7,15-dione (Dow 1997; Jacheta 2001).

Other Names:
DE-105; XDE-105; DE-105 Factors A and D; A83543.

Trade Names: Tracer, Success, Conserve, Spintor.

CAS Numbers:
Spinosyn A: 131929-60-7, Spinosyn D: 131929-63-0

Other Codes: None

[1] *This Technical Advisory Panel (TAP) review is based on the information available as of the date of this review. This review addresses the requirements of the Organic Foods Production Act to the best of the investigator's ability, and has been reviewed by experts on the TAP. The substance is evaluated against the criteria found in section 2119(m) of the OFPA [7 USC 6517(m)]. The information and advice presented to the NOSB is based on the technical evaluation against that criteria, and does not incorporate commercial availability, socio-economic impact, or other factors that the NOSB and the USDA may want to consider in making decisions.*

Characterization

Composition: Technical Spinosad contains 90% spinosyns and about 10% residual materials from the fermentation broth (see below). The spinosyn component is about 85% spinosyn A and 15% spinosyn D with other spinosyns as minor impurities.

Spinosyn A, Empirical Formula $C_{41}H_{65}NO_{10}$; MW 731.98
Spinosyn D, Empirical Formula $C_{42}H_{67}NO_{10}$, MW 745.99

Chemically, spinosyns are macrocyclic lactones with two sugars attached, one to the lactone ring and the other to a complex 3-ring structure. Spinosyn D has one more methyl group than Spinosyn A.

Properties: Technical spinosad is composed of tan or white low melting crystals (Spinosyn A, m.p. 84-99.5°C; Spinosyn D, m.p. 161-170°C), which have low volatility and an earthy odor. Crystals are soluble in a number of organic solvents. Solubility is higher in polar solvents such as acetone, dichloromethane, acetontrile, and methanol than in non-polar solvents such as hexane.

Crystals have low solubility in water, though spinosyn A is more soluble than spinosyn D. Water solubility increases as solutions become more acidic. The aqueous solutions are basic with pKa's about 8, and the spinosyns react with acids to form salts that have higher water solubility (Thompson et al., 2000).

How Made: The spinosyns are fermentation products produced by one or more chemical mutants of the naturally occurring actinomycetes soil bacterium *Saccharopolyspora spinosa* (Boek et al., 1994).

Vegetative inoculum is grown by a submerged aerobic fermentation process. The aqueous growth media contain proteins, carbohydrates, oils, and minerals. Corn solids, cottonseed flour, soybean flour, glucose, methyl oleate, and calcium carbonate are part of the media. Because soluble proteins are present and air is blown through the media, foaming occurs. Foaming is stopped with propylene glycol or excess soybean oil (Boek et al., 1994).

When the bacterium *Saccharopolyspora spinosa* is allowed to grow aerobically in an aqueous growth medium, it produces a number of biologically active metabolites called spinosyns. The spinosyns are large complex molecules containing mostly carbon, hydrogen, and oxygen arranged in a unique 4-ringed system, one ring of which is a macrocyclic lactone. The 4-ringed system has two sugar molecules attached, about 24 spinosyns are produced in the fermentation, and there are only minor structural differences, such as the presence or absence of a methyl group in various locations (Crouse et al., 1999). Extraction of the medium and subsequent recrystallization gives technical spinosad, which contains about 90% spinosyns and 10% impurities from the growth medium. The spinosyn fraction is about 85% spinosyn A and 15% spinosyn D.

The technical spinosad is soluble in organic solvents and can be extracted from the biomass. Dow patents specify the use of methanol as one possibility (Boek et al., 1994). The methanol solution is centrifuged or filtered to remove solids. Then it is concentrated by distillation. The spinosad in the concentrated methanol is converted to the salt by mixing with acidified water. The basic, water insoluble, spinosad is crystallized from water by adding enough base to neutralize the solution (Jachetta, 2001).

Specific Uses: Spinosad has been applied to over 200 different crops. It has been used to control caterpillars in cotton, loopers in cabbage, leafminers in various crops, leafrollers on apples, thrips in citrus, etc. (Dow 1997; Thompson et al., 2000; Bret et al., 1997).

Technical spinosad is especially insecticidal to small caterpillars by ingestion and contact, but especially by ingestion. It is not a plant systemic, but will penetrate leaves. Thus, it is active against leafminers and has activity against flies and thrips. On crops, higher application rates are needed to control thrips and leafminers than for caterpillars. It is not useful for controlling plant bugs or beetles, though some control is seen with small beetle larvae that eat lots of foliage. It has little effect on mites and sucking insects (Thompson et al., 2000; Cowles et al., 2000; Tjosvold and Chaney, 2001).

Action: Spinosad kills insects through action on their nervous systems (Salgado, 1997; Salgado, 1998). More information is found under OFPA criteria #2.

Combinations: Not sold in combinations.

Status

Historic Use:

Use of spinosad in conventional agriculture started with applications of the Tracer formulation on cotton in 1997. It was applied for caterpillars in cotton, especially in situations where the caterpillars were resistant to pyrethroids or other broad-spectrum materials (Bret et al., 1997).

OFPA, USDA Final Rule:
Spinosad is not explicitly mentioned in the OFPA or in the final Rule.

Regulatory: EPA/NIEHS/Other Sources
Websites of NIEHS and OSHA: show no regulatory information on spinosad.

EPA: An EPA factsheet issued February 1997 classifies spinosad as Category III due to the acute dermal LD_{50} in rabbit of >2000 mg/kg. For all other acute toxicological categories it is listed as Category IV. The Dow MSDS issued in 2001 shows EPA classification as Category IV even for dermal toxicity. Possibly it has been retested, and the factsheet has not been updated. Due to its low toxicity and perceived low impact on the environment, EPA registered spinosad as a reduced-risk material (DOW, 2001; EPA, 1997; Jachetta, 2001). EPA sets tolerances for residues of spinosad in food crops and livestock products at 40 CFR 180.495. These range from 0.02 ppm for grain corn, 1.0 ppm for hay, 0.2 ppm for apples, 10 ppm for brassica leafy greens, 0.02 ppm for eggs and poultry meat, 0.15 for beef meat, 7.0 ppm for forage grass, and 20 ppm for milk fat (EPA, 40 CFR 180.495).

Status Among U.S. Certifiers
California Certified Organic Farmers (CCOF)—CCOF Certification Handbook (rev. January 2000)
Section 8.3.1: A - Microbial products. Microbial products may be used on compost, plants, seeds, soils and other components of the agroecosystem. Allowed materials include Rhizobium bacteria, mycorrhizal fungi, Azolla, yeast and other microorganisms. Genetically engineered organisms or viruses are not allowed. Microbial products are prohibited if the final product contains synthetic preservatives such as sodium sulfite, or if they are fortified with otherwise prohibited plant nutrients.

Maine Organic Farmers and Gardeners Association (MOFGA) *Organic Certification Standards 2001*
Not specifically listed as permitted for crops or livestock, allows .. Microbial insecticides such as Bacillus thuringiensis for crops.

Midwest Organic Services Association (MOSA) Standards January 2001. Not specifically listed for crops or livestock, allows nonsynthetic biological, botanical or mineral substances, and synthetic substances included on the OMRI lists for use in crop production . Livestock parasite control may be through cultural and biological practices.

Northeast Organic Farming Association of Vermont (NOFA-VT) 2001 VOF Standards -- Not listed.

Oregon Tilth Certified Organic (OTCO) Generic Materials List (April 30, 1999)
Insect or Mite Pest Management, Microbiological Products, Allowed: Microbial products may be used on compost, plants, seeds, soils and other components of the agroecosystem. Allowed materials include Rhizobium bacteria, mycorrhizal fungi, Azolla, yeast and other microorganisms. Genetically engineered organisms or viruses are not allowed. Synthetic preservatives such as sodium sulfites, are prohibited in the final product. Microbiological products are prohibited if they contain other synthetic preservatives such as sodium sulfite, or are fortified with otherwise prohibited plant nutrients.

Organic Crop Improvement Association International (OCIA) Certification Standards, July 2001
2.10.2 f Microbial insecticides as found in the OCIA material list are acceptable:
Microbial Products--Naturally occurring microbes only. Including rhizobia bacteria, mycorhizzae fungi, azolla, Azotobacter, yeast, and other microorganisms. Microbial products may be used on compost, plants, seeds, soils, and other components of the agroecosystem. Genetically engineered organisms or viruses are not allowed. No synthetic preservatives or fortifications are allowed. The liquid preparations often contain sodium sulfites which are NOT allowed.
9.3.1 Livestock Production Materials List--Biological Controls, Allowed, insects, nematodes, plants and animals. No genetically engineered organisms.

Quality Assurance International (QAI)
QAI Program, Section 5.2 Acceptable and Prohibited Materials: Until full implementation of the NOP, the general criteria used by QAI for determining the acceptability of materials is that specified by the Organic Materials Review Institute.

Texas Department of Agriculture (TDA) Organic Certification Program Materials List
Biological controls: Crops-Living organisms that benefit plant production through reducing pest populations. Including but not limited to: viruses, bacteria, protozoa, fungi, insects, nematodes, plants and animals. Genetically engineered organisms are prohibited.

Microbial products, regulated. Crops: Microbial products may be used on compost, seeds, soils and other components of the agroecosystem. Allowed materials include Rhizobium bacteria, mycorrhizal fungi, Azolla, yeast and other microorganisms. Genetically engineered organisms or viruses are not allowed. Microbial products are prohibited if the final product contains synthetic preservatives such as sodium sulfite, or if they are fortified with otherwise prohibited plant nutrients. Product review may be needed to verify compliance with standards.

Parasiticides, regulated. Livestock: Products must be reviewed on case by case basis. Ivermectin allowed in dairy and breeding stock with extended withdrawal period. Use in slaughter stock is prohibited. Fenbendazole and levamisole are prohibited.

Washington State Department of Agriculture Organic Food Program
Chapter 16-154 WAC Organic Crop Production Standards:
WAC 16-154-080 Insect pest control materials and practices. 1. Approved materials and practices, d. biological control organisms, n. microbial products. Microbial products cannot contain any synthetic ingredients, such as synthetic forms of nitrogen. Genetically engineered organisms and their products are prohibited.

Chapter 16-162 Animal Production Standards for Organic Meat and Dairy Products: no mention of microbial/biological materials; synthetic parasiticides prohibited.

International
CODEX — B. Livestock & Livestock Products; Health Care; 22. a) where specific disease or health problems occur, or may occur, and no alternative permitted treatment or management practice exists, or, in cases required by law, vaccination of livestock, the use of parasiticides, or therapeutic use of veterinary drugs are permitted.

EU 2092/91— Not specifically listed.

IFOAM — Basic Standards, Appendix 2, "bacterial preparations" is listed with no restrictions.

Canada —Not specifically listed.

Japan —Not specifically listed.

Section 2119 OFPA U.S.C. 6518(m)(1-7) Criteria

1. *The potential of the substance for detrimental chemical interactions with other materials used in organic farming systems.*
   There is no evidence that spinosad interferes with the action of Bt and neem. Studies conducted by the petitioner show that it shows little tendency for detrimental actions on actions such as foliar sprays of fertilizer, administration of sulfur, and other agronomic interactions (Jachetta, 2001). However, adverse impacts against beneficial organisms are a potential concern. Fresh sprays could kill honeybees, trichograma and other parasitoids (Suh et al., 2000; Tillman and Mullrooney, 2000; Bret et al., 1997).

2. *The toxicity and mode of action of the substance and of its breakdown products or any contaminants, and their persistence and areas of concentration in the environment.*
   Mammalian toxicity. Toxicity of spinosad to humans and other mammals is summarized in (4) below.

   Ecotoxicology. Spinosad shows slight toxicity to birds, moderate toxicity to fish, and slight to moderate toxicity to aquatic invertebrates. It is highly toxic to bees in laboratory tests and is highly toxic to oysters (EPA, 1997) and other marine mollusks (Dow, 2001). Care must be taken with honeybees when spray applications are being made. After residues have dried, it is much less toxic to bees (Bret et al. 1997).

   Mode of Action. Spinosad kills insects through activation of the acetylcholine nervous system through nicotinic receptors. The mode of action is unique and incompletely understood. Continuous activation of motor neurons causes insects to die of exhaustion. There may be some effects on the GABA and other nervous systems (Thompson et al., 2000; Salgado, 1997; Salgado et al., 1998ab).

Soil Persistence. Soil microbes demethylate both spinosyn A and spinosyn D, giving these compouds half-lives of about 9-17 days. Spinosyn A is converted to spinosyn B, which is then hydroxylated. Spinosyn D is converted to N-demethylated spinosyn D, which is hydroxylated. Although spinosyns A and D degrade quickly, spinosyn B produced from the degradation of spinosyn A can persist 4 months later under certain field conditions (Hale and Portwood, 1996; Australia National Registration Authority for Agricultural and Veterinary Chemicals, 1998). Spinosyn B is almost as insecticidal as Spynosyn A (Crouse et al., 1999; Hale and Portwood, 1996). About half of the spinosyn D remained as the demethylated metabolite 4 months later. A maximum of 20% of spinosyn A had totally degraded to CO_2 1 year later (Hale and Portwood, 1996). Soil microbes degrade spinosad into other spinosyns that are more persistent and are biologically active. Repeated applications could lead to some build-up of spinosyns in soil, though the original material is rather quickly degraded.

Spinosyn A is more water soluble than the other component of spinosad, spinosyn D, and thus was made the subject of soil mobility studies. Spinosyn A and its soil metabolites bind to soil and have low soil mobility. A 10-month field study in California and Mississippi showed that no degradation products were found in soil below 24 inches (Saunders and Brett, 1997). Research was not found that evaluated the impact of manure from spinosad treated animals on soil metabolites, mobility, or micro fauna.

Leaf Surfaces. Spinosad is applied to plants at the rate of about 540 g/ha (Jachetta, 2001). Spinosad is quickly converted to degradation products by sunlight on leaf surfaces. Half-lives for spinosyn A were 1.6 to 16 days depending on the amount of sunlight received (Saunders and Brett, 1997).

Water. When spinosad is applied to water, very little hydrolysis occurs, and the substance can be persistent. In the absence of sunlight, half lives of spinosyn A and D are at least 200 days. In water exposed to sunlight, photodegradation occurs (Saunders and Brett, 1997).

3. *The probability of environmental contamination during manufacture, use, misuse, or disposal of the substance.*

Environmental contamination could come through release of the organism or processing solutions or waste products into the environment. The manufacture occurs in large, closed fermenters. Air used in the process is treated by catalytic incineration to insure that odors or live organisms are not released.

Excess water and residual extraction solution are recovered by distillation. Solvents are recovered and recycled for subsequent use. Prior to release, contaminated water is treated with activated carbon, anaerobic and aerobic digestion. The biomass concentrate is stabilized with lime and buried in a landfill (Jachetta, 2001).

Risk of spills during transport seems low. In case it spilled, it would present low risk to the public due to its low acute toxicity.

Shelf life is about three years (Thompson et al., 2000). After that, users would want to get rid of it. Most likely, even the old material would be applied to crops. Otherwise, it would probably have to be carried to a hazardous waste dump like any other pesticide.

4. *The effects of the substance on human health.*

Acute toxicity. A search of Medline and Toxline revealed no published incidences of human poisoning with spinosad. Spinosad has low acute toxicity in rats. The oral LD_{50} in male rats is 3,738 mg/kg. The oral LD_{50} in female rats is >5,000 mg/kg. According to an EPA factsheet, acute dermal doses in rabbits are >2,000 mg/kg. A Dow technical factsheet gives >5,000 mg/kg. In any case acute toxicity through this route is low. The rat inhalation LC_{50} is >5.18 mg/liter (EPA, 1997; Jachetta, 2001; Dow, 1997).

Metabolism. Spinosad is rapidly absorbed and extensively metabolized in a rat. Within 48 hours of dosing, 60-80% of spinosad or its metabolites are excreted through urine or feces (EPA, 1997; Dow, 1997).

Chronic Toxicity. 13-week dietary studies showed no-effect levels of 4.98 mg/kg/day in dogs, 6 mg/kg/day in mice and 8.6 mg/kg/day in cats. No dermal or systemic toxicity occurred in a 21-day repeated dose dermal toxicity study in rabbits of 1,000 mg/kg/day. Based on these data the EPA set the reference dose in humans at 0.0268 mg/kg/day. Presumably, daily doses of this amount would cause no harm (EPA, 1997),

Cancer and Developmental. There was no evidence of carcinogenicity in two rodent species at all dosages tested. Mutagenic studies show no mutagenic activity. There were no development effects in rats and rabbits up to the highest dose tested. No effect levels were 10mg/kg/day. Neonatal effects at 100 mg/kg/day were attributed to maternal toxicity (EPA, 1997).

Neurotoxicity. Spinosad did not cause neurotoxicity in rats in acute, subchronic, or chronic toxicity studies (EPA, 1997).

5. *The effects of the substance on biological and chemical interactions in the agroecosystem, including the physiological effects of the substance on soil organisms (including the salt index and solubility of the soil), crops and livestock.*

Effects of spinosad on earthworms and soil microorganisms have been performed in the laboratory. Results indicated that application rates of 540 g/ha should not cause significant effect on soil microflora respirations. Both spinosad and the Tracer formulation demonstrated safety for earthworms. The LD_{50} for earthworms was greater than 970 mg/kg (Jachetta, 2001). No research was found on the impact of spinosad on insect soil detritovores and their predators. There are many insects, including ants and springtails, in this group that could be impacted by the insecticidal activity of spinosad (Brady, 1974).

Spinosad is non-phytotoxic for most crops (Jachetta, 2001). It is metabolized and excreted fairly quickly by mammals. Within 48 hours of dosing, 60-80% of spinosad or its metabolites are excreted through urine or feces (EPA, 1997; Dow, 1997). It does show a tendency to accumulate in fat. Food containing 10 ppm concentrations of spinosyn A was given each day for 3 days to lactating goats. At 24 hours after the last dose, concentration of residues in fat were 3.6 ppm (Rainey et al., 1996). Food containing spinosyn A concentrations of 10 ppm when fed to hens for 5 days led to residues in eggs. "Residues in eggs increased steadily throughout the dosing period and ranged from 0.319-0.377 ppm in the final samples collected" (Magnussen et al., 1996).

Dairy cattle were fed food containing concentrations up to 10 ppm spinosad for 28 days, and the highest residues were found in fat and cream. Concentration in cream was 1.9 ppm and in beef fat was 5.7 ppm (Rutherford et al., 2000). Hens consumed feed that contained up to 5 ppm spinosad for 42 days. Maximum concentrations of 0.227 ppm were found in eggs on the 13th day (Rutherford et al., 2000).

The petitioner has applied for use of spinosad as an external parasiticide in organic livestock production. It would be applied to cattle at 2 mg/kg body weight by topical administration (Jachetta, 2001). According to the petitioner, spinosad shows slow and incomplete dermal absorption (Dow, 1997). No evidence is presented by the company to show the amount of spinosad that would appear in meat and milk for a typical agronomic use pattern in livestock.

6. *The alternatives to using the substance in terms of practices or other available materials.*

Spinosad is especially effective for caterpillars, though it does have activity for thrips, flies, and for the larval forms of some beetles that eat lots of foliage. Organic alternatives for caterpillars are Bt, neem, parasitoids, predators, pheromone mating disruption, and pyrethrins. Another alternative to spinosad is the ecosystem management approach to insect control (Lewis, 1997; Johnston, 1994). This approach includes a variety of management tools including the use of year round insect refugia, cover crops integrated with conservation tillage, unsprayed strips, and crop rotation. Spinosad does not seem to offer any advantage over Bt, but it might be faster than neem and cause less damage to beneficials than pyrethrins. It is also less toxic to humans than pyrethrins (Meister, 1999).

Predaceous mites and Orius bugs can provide biological control for thrips. A microbial alternative is *Beauveria bassiana* and pyrethrins would be the last resort.

Bt is available for the citrus leafminer, and neem and parasitoids are sold to control other leafminers.

Organic apple farmers currently control apple maggot flies by red sticky traps. However, "considerable labor, expense and messiness are associated with employing and maintaining sticky spheres." Spinosad might be a worthwhile alternative. However, use as an insecticide in localized baits showed it relatively ineffective (Prokopy et al., 2000). To be effective for fruit flies, it would have to be applied as a protein bait spray. Field tests have shown that spinosad bait sprays, though less effective than malathion, gave significant levels of control (Peck and McQuate, 2000).

Fly traps and parasitoids are alternatives for livestock flies. Natural pyrethrins are used externally for lice and other parasites (OMRI, 2001).

7. *Its compatibility with a system of sustainable agriculture.*

To be compatible with a system of sustainable agriculture, an insecticidal material should be selective, killing the target pest and sparing the beneficial insects that provide biological control. In addition to the criterion of insecticidal selectivity, compatibility with sustainable agriculture means that the material or practice should move crop production in the direction of a systems approach to agriculture (Lewis et al., 1997). Spinosad is somewhat selective, as it spares predatory bugs such as Nabis bugs and Geocoris sp. Spinosad shows less mortality than pyrethroids and OPs, but is more toxic than Bt or emamectin benzoate to these beneficial bugs (Boyd and Boethel, 1998ab). Though spinosad spares predatory bugs and beetles, it can have a negative impact on parasitoid populations (Tillman and Mulrooney, 2000; Elzen, 2001; Suh, et al., 2000).

TAP Reviewer Discussion

Reviewer 1 *[M.S. agronomy. Provides technical services to growers. Extensive experience in organic and sustainable agriculture. Midwest.]*

The petitioner requests approval to use spinosads for control of external parasites. It is a bit disconcerting that none of the research provided appears to address [one of the]the applications the petitioner proposes, i.e., pour-on & livestock spray. While I have no great suspicions that the active ingredient might cause contamination problems or raise animal health and welfare issues, I hope we're not missing some important information.

Interactions

. . . [T]here appears to be little or no negative interactions with other materials—fertilizers, pest control products—used in organic production. However, the easy compatibility of spinosads with other organic materials can increase the hazard to beneficial organisms when producers start to combine various pesticides and fertilizers in order to save on trips through the field and increase efficacy. Since spinosad can present a hazard to pollinators during and immediately after application, guidelines for its use must be made clear and adhered to by the farmer. Ideally, details of use of spinosad would be outlined in the Organic Farm Plan…but this might be too much to expect.

Toxicity

. . . Persistence in the soil should be of no concern since application rates are low and degradation should be accelerated in the more biologically active soils we expect under organic management. Likewise, persistence on leaf surfaces is short and the low toxicity of spinosads leaves little reason for concern. The persistence of spinosads in low-sunlight aquatic environments, however, raises some concerns since there is low but documented toxicity to fish and aquatic invertebrates. These should be addressed by clear guidelines for use that restrict applications around water bodies.

Human Health

. . . [T]he observations regarding accumulation in the fat (discussed in section 5) *[might not be appropriate to extrapolate to humans]*. The research was done on animals but implications to human health are implied.

Agroecosystem Interaction

. . . [T]he impacts on the predator/parasite complex within agroecosystems ought to be addressed here. There is considerable research pointing out that spinosad is hard on select beneficials among the insect predators and parasites. Specifically noted are Trichogramma and Braconid wasps. It appears that there is much less impact on other species—the true bugs (Hemiptera), lacewings, and beetles. While the negative effects should not be discounted, they are consistent with the performance of many other approved materials, especially the botanicals and insecticidal soaps, which also impact non-target beneficials.

Some notation might also be made on the potential for repeated use of this pesticide to encourage the development of resistance among targeted pests. However, as with the matter of impacts on non-target beneficial insects, this is an expected phenomenon with selective pesticides and has been well documented with other approved materials such as Bt.

Alternatives

Again, I agree with the overall evaluation. It is especially important that the biological control alternatives be stressed as has been done; pesticides should remain as the fallback option. That said, there are several additional issues, however, worthy of note. First, the ovicidal action of spinosads is not mentioned. This trait can be of great value in pest management and make the spinosad option more unique than most natural pesticides.

Similarly, spinosads are said to penetrate the leaf cuticle giving it additional flexibility in controlling leaf miners (Boucher, 1999).

While Bt would likely be a preferred option where lepidopteran control is needed, the future efficacy of Bt is in question with the proliferation of genetically engineered Bt crops. *[Some predict widespread]* . . . pest resistance . . ., and it is uncertain whether industry could keep pace with new organically acceptable Bt formulations that would be efficacious.

Compatibility

. . . It would be of particular value if growers could be better guided to product use based on the specific knowledge of predator/parasite impacts. Spinosad appears an excellent option in instances where the primary beneficials are non-susceptible predatory species, e.g. thrips management. Alternatively, it could be discouraged from use in crops and systems where these are the principal biocontrol agents, e.g. earworm control in sweetcorn.

Reviewer 1 Conclusion

Spinosads should be allowed in organic production systems as long as the process meets all non-GMO requirements. This pest control product can be manufactured using allowed methods and it presents little to no environmental hazard when used according to existing guidelines. If used intelligently within an IPM framework, it should have minimal impact on beneficial organisms within the agroecosystem. Spinosads could prove to be a very valuable pest management tool due to some of its unique characteristics and in light of the threat to Bt products posed by genetically engineered crops.

Reviewer 2 [*Ph.D. plant pathology, M.S. soil science. Research, consulting, and administrative activities related to waste treatment and reuse of waste as soil amendments and fertilizers. Southeast US*]

Interactions

This reviewer would like to know what is the impact of spinosad treatment of poultry or other animals on the manure they produce. What is the spinosad content of the manure? Are the degradation times and by-products similar to those in soil? What happens to any spinosad content during manure composting?

Toxicity

In the ecotoxicology section, add that the material is highly toxic to [other] marine mollusks . . . [besides] oysters (Dow, 2001).

Soil Persistence: It should be stated that the degradation product Spinosyn B has almost as much insecticidal activity as Spinosyn A, not just that it has insecticidal activity (Crouse et al., 1999).

The issue of spinosad content in manure and its fate after land application needs to be considered. The National Organic Program Final Rule Listings October, 2001 allows the application of raw manure under specific conditions (e.g., nonfood crops and prior soil incorporation with food crops). In coastal areas, the application of manure from animals treated with spinosad could have impacts on marine mollusks and the oysters industry.

Agroecosystem Interactions

Other than the mention of earthworms there is no discussion of the impact on soil detritivores and their predators. There are many insects, including ants and springtails, in this group that might be impacted by the insecticidal activity of spinosad (Brady, 1974).

Alternatives

Another alternative to spinosad is the ecosystem management approach to insect control (Lewis, 1997; Johnston, 1994). This approach includes a variety of management tools including the use of year round insect refugia, cover crops integrated with conservation tillage, unsprayed strips, and crop rotation. To utilize the ecosytem management approach it is important to understand why a pest has become a pest.

Compatibility

In addition to the criterion of insecticidal selectivity, compatibility with sustainable agriculture means that the material or practice should move crop production in the direction of a systems approach to agriculture (Lewis et al., 1997).

Reviewer 2 Conclusion

Spinosad is a natural (nonsysthetic) material produced by Saccharopolyspora spinosa when it is grown in a submerged aerobic fermentation system (Boek et al, 1994).

Spinosad is less toxic to many non-target organisms than some natural insecticides such as pyrethrum that are currently on the National Organic Program Final Rules Listings (Farm Chemicals Handbook, 1999). According to the definition in the Federal Register (2001) organic agriculture is a system that incorporates "cultural, biological, and mechanical practices that foster cycling of resources, promote ecological balance and conserve biodiversity." Spinosad's reduced toxicity to many organisms has the potential to increase ecological balance and conserve biodiversity. However, it is not without toxicity. In particular, it is toxic to bees and they should not be in contact with the material until it has dried in the field. It is also toxic to oysters and other marine mollusks (Dow, 2001).

While Spinosad is an improvement over some compounds currently used in organic agriculture, it is not necessarily an ideal material. It attacks broad categories of insects. The orders Lepidoptera, Hymenoptera, and Diptera are susceptible. In addition to insect pests these orders contain native pollinators. It is also toxic to parasitoids in the Coleoptera and other orders (Tillman and Mulrooney, 2000).

Organic agriculture is a practice still very much in development toward an ecosystem based management approach. Many organic agriculture practices still represent an interventionist approach rather than one based on understanding the agroecological system (Lewis et al., 1997). Spinosad, while an improvement over some materials, is still fairly broad spectrum and not representative of an ecological approach.

These review comments should not be taken to be an evaluation of the patented formulation of Spinosad containing inert compounds. The petitioner for this review did not present information on the current content of inerts. This is a review of the fermentation product Spinosad.

Reviewer 2 Suggested Annotation

Spinosad should be added to the list as prohibited non-synthetic, restricted. Its use should be restricted due to its toxicity to bees and other beneficials represented in the orders Hymenoptera, Lepidoptera, Coleoptera, Diptera and possibly others (Liu and Yue, 2000; Suh et al., 2000; Shelton et al. 2000; Tillman and Mulrooney, 2000). Its toxicity to oysters is also a concern in coastal areas where manure might be used. No information on Spinosad residue in manure was provided with the review material. Spinosad B, the degradation byproduct of Spinosyn A, is almost as insecticidal as Spinosyn A and persists in the soil longer (Crouse et al.; Hale and Portwood, 1996). Soil degradation studies of Spinosad did not look at toxicity to soil insects.

Reviewer #3 [Environmental toxicology researcher, M.A. Environmental Policy. West Coast]

Toxicity

All pesticides achieve 'toxicity' at some dose, and given the NOSB Principles of Organic Production and Handling (adopted October 17, 2001), the objective should be to only use pesticides that are effectively non-toxic—the relevant standard being a dosage that can be tolerated without adverse effects while promoting "biodiversity, biological cycles, and biological activity." NOSB principles and guidelines sanction the inclusion of pesticides in crops and livestock that *enhance* the biological diversity of an ecosystem, and reinforce the biological needs of livestock.

When evaluating the potential toxicological effects, both human and ecological, of a substance, certain factors of toxicity should be measured by means of categorization into acceptable, marginally acceptable, and unacceptable ecological features that could establish impacts to an organic production system. These factors include, though are not limited to, persistence, bioconcentration, a substance's hydrophilic/lipophilic partition, toxicity to sensitive species, toxicity to beneficial organisms, and toxicity of primary breakdown products.

The standard dosage for acceptable human toxicity is commonly referred to as the Reference Dose (RfD), which is an estimate of a "presumably safe" level of exposure or ingestion. RfD's should be conservative (i.e., relatively high) and should reflect ecological safety because it is based on toxicity assessment in the most susceptible animal species and in turn the most vulnerable organ system. Thus, the RfD reflects a sensitive endpoint for ecosystem vertebrate toxicity.

Pesticides with RfDs of .01 mg/kg/day or greater are generally considered an acceptable risk. Pesticides with RfDs of <.01 are generally less acceptable and should be excluded from sustainable and environmentally sound systems of production. The level of .01 mg/kg/day is selected because several pesticides with RfDs at this level or higher have been thoroughly studied and found likely to produce short-lived or no ecological damage. Chemicals with lower RfDs are generally indicative of greater ecological toxicity and hence should be avoided.

As shown in Table 1, spinosyns A and D both are highly persistent, but only when applied to pre-sterilized soils. Otherwise, the half-life of 9-17 days presents an acceptable persistence profile. Theoretically, if spinosyns A and D are used in organic production systems, the soils would not be pre-sterilized and thus would contain sufficient microbial activity to break down the pesticide quickly. Spinosyns A and D's primary metabolites do appear to be persistent and should be given consideration in assessing the toxicity profile.

Table 1: Spinosad Toxicological Assessment

Chemical	Half Life	Log K_{ow}	RfD	LD50	LC50	BCF
Spinosyn A	9-17 days 128-240 (pre-sterilized soils)	**4.0** (pH7) **5.2** (pH9)	.0268	3793 **.0029** (honeybee)	5.18 5.9 (bluegill)	19 (whole fish)
Spinosyn B *Primary metabolite*	9-17 100-356					
Spinosyn D	14 days **177** (pre sterilized soils)	4.5 (pH7) 5.2 (pH9)	.0268			33 (whole fish)
Mono-N-demethyl spinosyn D *Primary metabolite*	**100-356**					

Sources: Hale and Portwood, 1996; Australia National Registration Authority for Agricultural and Veterinary Chemicals, 1998.

Bold indicates an exceedence of acceptable toxicological criterion

The bioconcentration factor measures the likelihood of a pesticide's ability to biomagnify. The bioconcentration factor is the ratio of the concentration of a given pesticide in the flesh of a species and its living environment. When the bioconcentration factor exceeds 1000, the pesticide should be excluded. Spinosyns A and D do not have high bioconcentration factors.

Soil Persistence

The standard description of persistence relies on a determination of a pesticide's half-life, meaning its time following application to a particular environment needed to degrade, dissipate, and destroy half of an applied dose of the chemical in question. A standard definition of "persistent" includes the following half-life criteria (Kamrin, 1997):

A. Non or weakly persistent................................<30 days
B. Moderately persistent ....< 30-100 days
C. Strongly persistent .... > 100 days

Based on its half-life, any pesticide that, under the conditions of use, persists or can reasonably be expected to persist in its originally used formulation or a toxicologically active form (including its primary breakdown products) for 100 days or more shall be considered "persistent" and therefore would not fall within the acceptable standards of organic agriculture. Moderately persistent pesticides should pass stringent toxicological criteria to receive acceptance. This criteria includes measures of non-toxicity and non-bioconcentration for acceptance. It is well understood that environmental and soil conditions, including aerobic soil qualities and quantities, temperature, as well as pH affect the actual length of time a pesticide remains in the environment. Even with a relatively short half-life, significant amounts of pesticide still remain in the environment after three months (90 days) when a percentage of the originally applied dose will still in theory remain. Relatively non-toxic pesticides, which remain biologically active after 100 days, should be given special consideration since they are likely to continue their impact on non-target species in the applied treatment area.

Environmental Contamination

Saccharospora spinosa was discovered and collected from a soil sample taken from the Virgin Islands. Successive extraction, isolation, and structural understanding led to a new family of macrocyclic lactones called the spinosyns, A and D make up the technical material and include the spinosyn factors with primary insecticidal activity. In isolating the technical spinosad and determining its structure, spinosyns A and D were naturally present in the 85:15 ratio. It is important to note that the technical spinosad is the formulation of spinosyns A and D that are naturally present in this ratio. Technical spinosad is extracted from the bacterium *Sacchorspora spinosa.*

The structural backbone of *Saccharospora spinosa* permits the manufacturer to add new and potentially chemically modified spinosyn factors. Penicillin was isolated and manufactured in a similar manner and now has additional factors added to its structural backbone, which may preclude its being considered a nonsynthetic product. However, as it is presently formulated, Technical Spinosad is not chemically synthesized nor is it the result of recombinant DNA technology.

The manufacturer may decide to convert the spinosyn molecules into its salt because they have improved solubility in water, for example. In order for the manufacturer to convert spinosyns A and D into the various salts, it will need to do so through checmical modification and thus the resulting salts may be considered synthetic. The salts would need to undergo a thorough review for use in an organic production system.

One of the accepted standard measures for a pesticide's ability to bioaccumulate in individual organisms and bioconcentrate to higher trophic levels is the octanol/water partition coefficient. This is the amount of chemical that concentrates in octanol minus the log of the concentration in water. The resulting log or K_{ow} is the measure of lipophilicity and predicts the degree of concentration of any given chemical in the fat or lipid fraction of cells or organisms. Where the K_{ow} is more than 3, the pesticide is very likely to concentrate up the food chain (Shaw and Chadwick, 1998). The K_{ow} for spinosyn A and D corresponds with an unacceptable level of concentration of the pesticide in the tissue of an aquatic species.

Human Health

Technical Spinosad carries a rather benign toxicity profile. There is a question regarding spinosyn A and its ability to concentrate in the milk fat and beef fat of dairy cattle. Cattle dosed at the highest tested level (10µg/g) resulted in the highest reflected residue of 5.7µg/g (Rutherford, 2000). Even at this level the average human consumption using an intake rate of .3720755 g/kg/day residue reflects .0021 mg/kg/day, well below the reference dose of .0268 mg/kg/day (US EPA, 1997).

Technical Spinosad should be applied to soils that have adequate microbial activity with which to beak down the product. The product should be applied in such a manner as to avoid contact with beneficial honeybees, as its toxicity to the bees is very high. Many pesticides that are effective within the lepidopteron species are also detrimental to the survival of honeybees due to the similarities of their nervous systems. EPA has requested studies regarding ecological effects to estuarine fish early life cycle, estuarine invertebrates life cycle, and honeybee toxicity residues on foliage. These studies should be completed if they have not been already and reviewed for pertinent and biologically beneficial information.

The National Library of Medicine did not have information available on Technical Spinosad's primary metabolites spinosyn B and mono-N-demethyl spinosyn D. The National Registration Authority for Agricultural and Veterinary Chemicals document regarding Tracer and Laser Naturalyte placed the primary breakdown products half-lives in the strongly persistent range. The effects of the breakdown products, generally, and to beneficial soil organisms, specifically, should be better understood. It is unclear whether due to absorption or binding if the breakdown products would be unavailable to exert a toxic influence on the ecosystem or if according to the NOSB principles there would be an optimization of soil biological activity.

The review of Technical Spinosad should explicitly be used for assessing spinosyns A and D, as other spinosyns could be manufactured and processed using the structural backbone. The new spinosyns may have varying toxicity profiles, methods of manufacture, etc. I would suggest the TAP Review heading use "Technical Spinosad (spinosyns A and D)" instead of the more broad designation of "Spinosad."

Spinosyns A and D, as described and processed, have been isolated and developed in a non-synthetic manner. The toxicity profile of spinosyns A and D is relatively benign both to humans and the ecosystem. Care should be taken when applying spinosyns A and D to mitigate any risk to honeybees. Spinosyns A and D also should be used in production systems which are rich in microbial activity to ensure that the pesticide does not build-up in the soil. Also, spinosyns A and D have primary breakdown products which should be more fully studied and researched as to their ecological toxicity and impacts to beneficial organisms.

Reviewer 3 Conclusion

Technical Spinosad (compound spinosyn A [85%] and D [15%]) is a non-synthetic substance with low toxicity and thus should be approved and allowed for National listing. Technical Spinosad, while undoubtedly obtained or revealed through use of a "chemical mutagen," was extracted from a culture that has not been [OFPA §6502 (21)] formulated or manufactured by a chemical process that would chemically change the substance.

a. The substance is not synthetic
b. For crops and livestock, the substance should be added as approved to the national list without annotation

[End of TAP Reviewer Comments]

Conclusion:

Spinosad is a combination of naturally occurring compounds. Based on the OFPA criteria, all reviewers considered it to be compatible with organic production, but also acknowledged that certain uses might be harmful to beneficial organisms and might contaminate certain organic foods. One reviewer recommended that spinosad be added to the National List of prohibited substances with an annotation to permit limited use under well-defined conditions. The other two considered that prohibition and a specific annotation was not necessary, but that the use of spinosad needed to be addressed in the context of other natural toxins used in organic agriculture.

Note: further investigation of livestock uses may be necessary.

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