Tetracycline (Oxytetracycline)

Crops

Identification of Petitioned Substance

Chemical Names: 34
4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydro-6-methyl-1,11-dioxo-2-naphthalencarboxamide
35
4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydro-6-methyl-1,11-dioxo-2-naphthalencarboxamide
monohydrochloride

CAS Numbers:
79-57-2
7179-50-2
2058-46-0

Other Codes:
6304 (U.S. EPA PC code, oxytetracycline)
6321 (U.S. EPA PC code, oxytetracycline calcium)
6308 (U.S. EPA PC code, oxytetracycline hydrochloride)
3145 (HSDB number; oxytetracycline)

Other Name:
agricultural terramycin
calcium oxytetracycline
oxytetracycline calcium complex
oxytetracycline hydrochloride
hydroxytetracycline monohydrochloride

Trade Names:
Fireman
Mycoshield
Fireline 17 WP – also marketed as FlameOut
Mycoject Tree Tech OTC
Bacastat Tree Injection

Characterization of Petitioned Substance

Composition of the Substance:
Tetracyclines are a group of human and animal broad-spectrum antibiotics with similar chemical structures and mechanisms of action (Chopra and Roberts, 2001). This group includes both naturally occurring compounds that are produced by the Streptomyces genus of bacteria, such as tetracycline, oxytetracycline, and chlortetracycline, as well as several semisynthetic compounds (Chopra and Roberts, 2001). Oxytetracycline is used as a human and animal antibiotic as well as a pesticide to control bacteria, fungi, and mycoplasma-like organisms on pears, apples, peaches, and nectarines. It is derived from the soil bacterium Streptomyces rimosus. It is marketed as oxytetracycline calcium complex (C_{22}H_{22}N_{2}O_{9}Ca) and oxytetracycline hydrochloride (C_{22}H_{22}N_{2}O_{9}HCl). The molecular structure of oxytetracycline is shown in Figure 1.
Although the National List of Allowed and Prohibited Substances (hereafter referred to as the National List) allows all forms of tetracycline for use in organic crop production, oxytetracycline is the only tetracycline antibiotic approved by the U.S. Environmental Protection Agency (EPA) to be used as a pesticide. Therefore this technical report focuses on oxytetracycline (CAS No. 79-57-2) and pesticides containing oxytetracycline calcium (CAS No. 7179-50-2) or oxytetracycline hydrochloride (CAS No. 2058-46-0) for use in plant disease control in organic crop production. The Organic Materials Review Institute (OMRI) Products List (OMRI, 2011) lists only one oxytetracycline product, Mycoshield®, which contains 31.5% oxytetracycline calcium complex (equivalent to 17% oxytetracycline).

The term “oxytetracycline” is often used broadly to include oxytetracycline, oxytetracycline calcium, and oxytetracycline hydrochloride (hydroxytetracycline monohydrochloride), which all have unique CAS numbers and EPA Pesticide Chemical (PC) Codes (EPA 1988, 1993). The EPA concluded in 1993 that the toxicity of all three oxytetracyclines (oxytetracycline, oxytetracycline calcium, and oxytetracycline hydrochloride) is expected to be similar, and data generated on one compound can be used to assess exposure and associated risks of the other two compounds (EPA, 1993). The term “tetracycline” refers to the compound tetracycline (CAS # 60-54-8) and the more general term “tetracyclines” refers to the group of related antibiotics which include tetracycline, oxytetracycline and many other tetracycline-derivatives. Tetracycline and its derivatives are generally used more commonly for veterinary and medical uses rather than for agricultural applications (HSDB, 2002).

Properties of the Substance:

Oxytetracycline calcium is produced as a wettable powder and is dark to light brown in color. Oxytetracycline hydrochloride is also produced as a wettable powder and is pale yellow to tan in color. The powders are considered odorless and stable under normal storage conditions and use (EPA, 1993). Oxytetracycline calcium is slightly soluble in water and is slightly acidic (pH between 3.5 and 5.0) (Nufarm Americas Inc., 2004). Oxytetracycline hydrochloride is considered to be very soluble in water (HSDB, 2006). Oxytetracycline is susceptible to photodegradation, but is not expected to undergo hydrolysis in the environment (Xuan et al., 2010; HSDB, 2006). At high temperatures (above 180°C), it can decompose and form toxic gases. Based on its chemical properties, oxytetracycline is expected to strongly adsorb to soil particles and have moderate to no mobility in soil (HSDB, 2006). The environmental fate and degradation of oxytetracycline is discussed in more detail in the response to Evaluation Question #4.

Specific Uses of the Substance:

In agricultural applications, oxytetracycline is used as a prophylactic treatment (i.e. when disease is expected on the basis of previous experience, predictive systems, or recommendations of local agricultural advisors) for bacterial diseases in plants (Vidaver, 2002). The substance is an effective treatment because it interferes with the ability of bacteria to produce proteins vital to the bacterium’s ability to grow and multiply. In crops, oxytetracycline is mainly used to control fire blight in apples and pears and bacterial...
spot in peaches and nectarines (EPA, 2008). Fire blight is a destructive bacterial disease that affects certain species in the Rosaceae family (Koski and Jacobi, 2009). It is caused by the bacterium *Erwinia amylovora*, which is capable of infecting blossoms, fruits, vegetative shoots, woody tissues, and rootstock crowns (Norelli et al., 2003). Oxytetracycline products can also be used to control lethal yellowing of coconut palm, lethal decline of pritchardia palm, and pear decline (EPA 1993). These compounds are commonly used to control diseases caused by *Pseudomonas* and *Xanthomonas* species in stone tree fruit, pome fruit, and turf (HSDB, 2006).

Application of oxytetracycline calcium or oxytetracycline hydrochloride to crops including apples and pears usually occurs by wetting the powder and then applying the solution as a foliar spray on the ground or with the assistance of aircraft (EPA, 2006b). For control of fire blight, spraying begins at early bloom and may be repeated every 3 to 6 days for apples or 4 to 6 days for pears (Nufarm Americas, Inc., 2008). Application may also occur by injection into the tree trunks using an injection device and an aqueous solution of oxytetracycline calcium or oxytetracycline hydrochloride. The timing of application is critically important to prevent infection. Once the disease spreads from the blossoms, there are no available cures. In aquaculture, oxytetracycline calcium and/or oxytetracycline hydrochloride compound are added to marine paints and act as an antifoulant to prevent the growth of barnacles. In the United States, oxytetracycline is used as an antibiotic in lobster and fish operations (HSDB, 2006).

Oxytetracycline is also registered with the U.S. Food and Drug Administration (FDA) as a medicine to treat bacterial diseases in animals and humans.

**Approved Legal Uses of the Substance:**

Oxytetracycline, oxytetracycline calcium, and oxytetracycline hydrochloride are registered pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), which is administered by EPA. EPA issued a Registration Standard for all three compounds in December of 1988, a Reregistration Eligibility Decision (RED) in March of 1993 (EPA, 1993), and a Tolerance Reassessment Progress and Risk Management Decision (TRED) in June 2006 (EPA, 2006b). Oxytetracycline pesticides are currently under registration review by EPA, and this review is scheduled to be complete in 2014 (EPA, 2009). EPA has established tolerances (maximum legal residue levels) of 0.35 parts per million (ppm) for residues of oxytetracycline pesticides in or on raw peaches, apples, and pears (40 CFR 180.337).

No pesticide products containing oxytetracycline are currently registered with the EPA, although two previously registered products are listed as transferred. Several pesticide products with the active ingredient oxytetracycline calcium or oxytetracycline hydrochloride are currently registered with EPA. Mycosheild®, the first product containing oxytetracycline calcium complex as the active ingredient, was registered with EPA in 1979 and is included in the OMRI Products List (OMRI, 2011). Products that are not included in the OMRI products list but are currently registered with EPA and available for use in organic crop production are Fireline 17 WP (also marketed as FlameOut), Mycoject, Fireman, Tree Tech OTC, and Bacastat Tree Injection (NPIRS, 2011).

The FDA establishes the tolerances for the sum of residues of tetracycline (including chlortetracycline, oxytetracycline, and tetracycline) in beef and dairy cattle, calves, swine, sheep, chickens, turkeys, finfish, and lobster (21 CFR 556.500). Tolerances are established for the sum of residues of the tetracyclines in tissues and milk as follows: 2 ppm in muscle; 6 ppm in liver; 12 ppm in fat and kidney; and 0.3 ppm in milk (HSDB, 2006). In addition, the FDA has placed a number of regulatory restrictions on the amount and use conditions of oxytetracycline in livestock production. For example, 400 g/ton of dry feed is allowed for use in chicken production for control of chronic respiratory disease (CRD) and air sac infection caused by *M. gallisepticum* and *E. coli* susceptible to oxytetracycline (21 CFR 558.450).

The FDA regulates tetracycline and oxytetracycline as prescription drugs that can be administered orally, topically or by injection. The currently available forms of these drugs are oxytetracycline hydrochloride and tetracycline hydrochloride (FDA, 2011). Medicines containing oxytetracycline or tetracycline may only be dispensed with a prescription from a physician (USDA, 2006). Veterinary and aquaculture uses of
Tetracycline, oxytetracycline, and chlortetracycline are also regulated by the FDA (21 CFR Chapters 520, 522, 524 and 529).

**Action of the Substance:**

Tetracyclines, including oxytetracycline, interfere with the ability of bacteria to produce proteins that are essential for growth and multiplication. Historically, tetracycline compounds are characterized by their antimicrobial efficacy against a wide range of both Gram-positive and Gram-negative bacteria (Klajn, 2001). Tetracyclines can also alter the bacterial membrane, causing compounds and genetic material to leak from the cell (Klajn, 2001).

**Combinations of the Substance:**

Oxytetracycline is not a precursor or component of any other substances on the National List. Streptomycin (streptomycin sulfate) is another antibiotic on the National List approved for use in control of fire blight. Apple and pear producers may alternate the use of these two antibiotics in different seasons. Also, there is evidence to suggest that some producers are applying these two antibiotics in combination to apple and pear trees when streptomycin-resistant strains are present in the orchard (Johnson, 2010). Copper sulfate, fixed copper mixtures (such as Bordeaux mix), and peracetic acid are all included on the National List and may be used for control of fire blight in apples and pears. Based on recommendations, it is unlikely that producers are applying these in combination or close succession with oxytetracycline (Univ. of Illinois Dept. of Crop Sciences, 2005; Koski and Jacobi, 2009). Some biological control agents may be applied to organic apple and pear trees in combination or close succession with oxytetracycline (see response to Evaluation Question #11 for a description of the available biological control agents).

Several degradation products of oxytetracycline may exist in combination with oxytetracycline calcium or oxytetracycline hydrochloride in agricultural products. These compounds are discussed in more detail in the response to Evaluation Question #4.

**Status**

**Historic Use:**

In 1948, oxytetracycline was isolated from soil containing the bacteria *Streptomyces rimosus* and was the second of the tetracycline antibiotics to be discovered (Klajn 2001). For over fifty years oxytetracycline and similar compounds have been used in human and veterinary medicine to treat bacterial infections. It has been used as an agricultural pesticide for over thirty years (USDA, 2006).

In agriculture, oxytetracycline compounds have historically been effective in controlling bacterial disease caused by *Pseudomonas, Erwinia, and Xanthomonas* species. Current organic agriculture standards permit the use of tetracycline for fire blight control only and for use only until October 21, 2012. No pesticide products containing tetracycline have been registered with the EPA. Pesticide products containing oxytetracycline compounds were first registered with EPA in 1974. The most recent registration of a new oxytetracycline pesticide product occurred in 2010 (NPIRS, 2011).

In human and veterinary medicinal uses, tetracycline and oxytetracycline stop the spread of the infection and the remaining bacteria are killed by the immune system or eventually die. Medications having tetracycline hydrochloride or oxytetracycline hydrochloride as an active ingredient are generally administered via injection, orally or are applied to the eye in liquid drops. These substances are used to treat a large variety of human bacterial infections including Rocky Mountain spotted fever, sinusitis, skin and skin structure infection, syphilis, infections caused by chlamydia, trachoma, typhus infections, urinary tract infections, ocular infections, acne, etc. (HSDB, 2006; HSDB, 2002).
Tetracycline and oxytetracycline are broad spectrum antibiotics that are active against a wide variety of bacteria. However, some strains of bacteria have developed resistance to these antibiotics, which have reduced their effectiveness for treating some types of infection (Chopra and Roberts, 2001).

In aquaculture, oxytetracycline is used as an antibacterial for fish and lobster production. The substance is also used as a dye to mark fish.

Historically, tetracycline, oxytetracycline, and chlortetracycline have been used as livestock food additives to promote growth in poultry, calves, cattle, and swine. Current national organic agricultural standards prohibit this use.

**OFPA, USDA Final Rule:**

The National List includes tetracycline as a synthetic substance allowed for use in organic crop production as a plant disease control (7 CFR 205.601(i)(12)) until October 21, 2012. The listing is annotated to permit the use of tetracycline for use in the control of fire blight only.

**International**

Oxytetracycline is permitted by the Canadian General Standards Board for emergency use for bee keeping. Following use, all equipment must be properly destroyed. The treated bees do not need to be destroyed, but they must be removed from organic production (Canadian General Standards Board, 2009).

Tetracycline or oxytetracycline are not specifically listed for use in organic crop production by the Canadian General Standards Board, CODEX Alimentarius Commission, European Economic Community (EEC) Council Regulation, EC No. 834/2007 and 889/2008, International Federation of Organic Agriculture Movements (IFOAM), or the Japan Agricultural Standard (JAS) for control of fire blight or any other crop uses.

**Evaluation Questions for Substances to be used in Organic Crop or Livestock Production**

**Evaluation Question #1:** What category in OFPA does this substance fall under: (A) Does the substance contain an active ingredient in any of the following categories: copper and sulfur compounds, toxins derived from bacteria; pheromones, soaps, horticultural oils, fish emulsions, treated seed, vitamins and minerals; livestock parasiticides and medicines and production aids including netting, tree wraps and seals, insect traps, sticky barriers, row covers, and equipment cleansers? (B) Is the substance a synthetic inert ingredient that is not classified by the EPA as inerts of toxicological concern (i.e., EPA List 4 inerts) (7 U.S.C. § 6517(c)(1)(B)(ii))? Is the synthetic substance an inert ingredient which is not on EPA List 4, but is exempt from a requirement of a tolerance, per 40 CFR part 180?

A). Tetracycline (oxytetracycline) is considered a toxin derived from bacteria.

B). The substance is a synthetic ingredient and is not classified by EPA as an inert of toxicological concern.

**Evaluation Question #2:** Describe the most prevalent processes used to manufacture or formulate the petitioned substance. Further, describe any chemical change that may occur during manufacture or formulation of the petitioned substance when this substance is extracted from naturally occurring plant, animal, or mineral sources (7 U.S.C. § 6502 (21)).

Oxytetracycline is a naturally occurring compound that is produced by the soil bacterium *Streptomyces rimosus*. It is produced on a large scale by aerobic fermentation of *Streptomyces rimosus* followed by isolation and purification (HSDB, 2006). The only forms commercially available at present for use in crop production are oxytetracycline calcium and oxytetracycline hydrochloride. Agricultural antibiotics, including oxytetracycline, are formulated with water-insoluble carriers (e.g., kaolin clays) that adsorb the active ingredient (Rezzonico et al., 2009).
During large-scale aerobic fermentation, inoculum from the original culture of *Streptomyces rimosus* is transferred to a series of incubators where the total quantity of biomass is greatly increased and then to fermentation tanks. The growth medium contains suitable ingredients including a source of carbohydrates, a nitrogen source, and various salt solutions to provide nutrients to optimize growth and yield of the antibiotic. In general, during the large-scale production of antibiotics, elaborate methods for extraction and purification are necessary (Madigan et al., 2003). If an antibiotic is soluble in an organic solvent, it is purified by extraction into the solvent. If not, then it is removed from the fermentation liquid by adsorption, ion exchange, or chemical precipitation.

According to the original U.S. Patent for Terramycin (oxytetracycline), many possible extraction and purification methods can be used during the manufacture of oxytetracycline (Sabin et al., 1950). One method of recovery is by treating the filtered fermentation broth with activated carbon and then elution with butanol followed by precipitation with an acid then a base. Another method of extraction is similar but without the use of activated carbon. Oxytetracycline is extracted from the fermentation broth with a solvent at basic or acidic pH. The solvents that can be used include butanol, amyl alcohol and phenylcellulose. A method of purification is to extract or precipitate oxytetracycline using an organic acid. Various salts of oxytetracycline may be prepared by dissolving the antibiotic along with the desired acid, mineral or organic compound in water, adjusting the pH of the solution using an acid or base, and then drying the precipitate by vacuum or evaporation.

**Evaluation Question #3:** Is the substance synthetic? Discuss whether the petitioned substance is formulated or manufactured by a chemical process, or created by naturally occurring biological processes (7 U.S.C. § 6502 (21)).

Oxytetracycline is produced through a naturally occurring biological process (aerobic fermentation), but the processes used to isolate and purify the substance are not naturally occurring. Therefore, oxytetracycline is considered synthetic. See the response to Evaluation Question #2 for more details on the manufacturing process.

**Evaluation Question #4:** Describe the persistence or concentration of the petitioned substance and/or its by-products in the environment (7 U.S.C. § 6518 (m) (2)).

Once released into the soil, oxytetracycline is expected to become strongly adsorbed to soil particles and have moderate to no mobility (Kumar et al., 2005; HSDB, 2006). This means it can remain in soil for a long time following treatment. Furthermore, it is not likely to leach below the surface soil (Aga et al., 2005), however it can spread by surface run-off of sediment. Reported half-lives of oxytetracycline in soil and sediment vary from 9 to 419 days, indicating that biodegradation in some types of soil is likely to be slow (HSDB, 2006). However, the extent and kinetics of antibiotic degradation in soil is highly dependent on temperature, soil type, and antibiotic adsorption to soil (Thiele-Bruhn, 2003). One study reported no degradation of oxytetracycline in a soil and manure sample after 180 days (Thiele-Bruhn, 2003). In a field study with silt loam soil, the measured amount of oxytetracycline in the soil declined by 50% in three weeks following application of manure with oxytetracycline, however the amount of total tetracyclines did not significantly decline after 5 months (Aga et al., 2005). Another study showed that oxytetracycline residues were present in agricultural soil 10 months after fertilization with manure containing oxytetracycline (Cengiz et al., 2010). Wang and Yates (2008) found the half-life of oxytetracycline to be 33 days in manure-amended soil and 56 days in non-amended soil. Yang et al. (2009) reported half-lives for oxytetracycline between 29 and 56 days for non-sterile treatments and 99 to 120 days for sterile treatments (aerobic conditions), and between 43 and 62 days in the non-sterile soil and 69 to 104 days in sterile soil (anaerobic conditions). These results suggest that microbes can degrade oxytetracycline in agricultural soil to some extent.

Oxytetracycline is susceptible to photodegradation. It has been detected in surface waters, although at very low concentrations (0.07 to 1.34 µg/l)(Arikan et al., 2007). It has been shown to have a relatively short
half-life in sea water (Kumar et al., 2005). The potential for bioaccumulation in aquatic organisms is low
(HSDB, 2006).

The anticipated degradation products of oxytetracycline resulting from abiotic means are alpha-apo-
oxytetracycline, beta-apo-oxytetracycline, and 4-epi-oxytetracycline at acidic pHs and iso-oxytetracycline,
N-desmethyl-oxytetracycline, and N-didesmethyl-oxytetracycline at neutral to basic pHs (HSDB, 2006).
Half-lives of these compounds in soil interstitial water were found to range between 2 to 270 days (Halling-
Sorensen et al., 2003). No other information could be found on the persistence of oxytetracycline by-
products in the environment.

Chander et al. (2005) demonstrated that even though tetracycline was tightly adsorbed to clay particles in
soil, it was still biologically active. There is a concern that the persistence of oxytetracycline residues in the
environment may contribute to the development of bacterial resistance to oxytetracycline and other
tetracyclines (Arikan et al., 2007). The topic of antibiotic resistance as it relates to the use of oxytetracycline
as a pesticide is discussed in more detail in the response to Evaluation Question #10.

Evaluation Question #5: Describe the toxicity and mode of action of the substance and of its
breakdown products and any contaminants. Describe the persistence and areas of concentration in the
environment of the substance and its breakdown products (7 U.S.C. § 6518 (m) (2)).

Oxytetracycline helps to control fire blight by decreasing the growth of the bacterial pathogen Erwinia
amyllovora. When oxytetracycline enters the cells of Erwinia amylovora, it binds to cellular components called
ribosomes and reduces their ability to correctly synthesize proteins needed for growth and survival.

Animal studies have been conducted with oxytetracycline compounds to determine the potential toxic
effects of these substances (EPA, 2006a; HSDB, 2006). Oxytetracycline hydrochloride was found to have
low acute toxicity when administered to mice. A definitive target organ of oxytetracycline toxicity has not
been identified (liver is a potential target in rats at high dose levels). The National Toxicology Program
conducted two 13-week dietary studies with an oxytetracycline. No effects were observed in rats, but a
decrease in body weight was observed in mice at the highest dose tested. In developmental toxicity
studies in rats and mice, oxytetracycline hydrochloride caused decreases in maternal weight gain and fetal
weights but no evidence of fetal malformations (HSDB, 2006). A 2-year dietary study with oxytetracycline
hydrochloride in mice showed no evidence of carcinogenicity but a decrease in body weights at the highest
dose tested. A 2-year dietary study in rats showed ambiguous evidence of carcinogenicity (in the pituitary
and adrenal glands). The carcinogenicity of oxytetracycline has not been evaluated by the International
Agency for Research on Cancer (IARC), and the EPA Carcinogen List describes oxytetracyline as ‘not
classifiable as to human carcinogenicity’ (PAN, 2010). Oxytetracycline compounds have exhibited negative
results in several genetic toxicity tests to determine their potential to interact with DNA or damage
chromosomes – indicating that they are unlikely to cause cancer. Positive results were observed in one
study (mouse lymphoma forward mutation assay), however results in live mice were not dose-related
(EPA, 2006a).

The toxicity of oxytetracycline to humans has been extensively reviewed because of its use in medicine.
HSDB (2006) summarizes the toxic effects of oxytetracycline. Such effects include GI irritation,
hepatotoxicity (at high doses of 2 g or more per day, more pronounced in pregnant women), renal toxicity
in pregnant women, brown discoloration of the teeth or depression of bone growth in children receiving
treatment or in infants whose mothers were treated during pregnancy, changes in the peripheral blood,
superinfections caused by strains of bacteria or yeast resistant to oxytetracycline, colitis due to an
overgrowth of Clostridium difficile, photosensitivity, affects to the nails, and allergic skin reactions (rare).
The FDA has categorized oxytetracycline as pregnancy category D due to the risk of renal and hepatic
effects on the mother and skeletal effects on the fetus. Pregnancy category D is for substances that have
demonstrated positive evidence of human fetal risk, and should only be given in pregnancy when the
benefit outweighs the risk. Although there is a risk to the pregnant mother and fetus following therapeutic
doses of oxytetracycline, the exposure that occurs from pesticidal use is not expected to pose a risk. The
typical therapeutic dose of oxytetracycline is 15 to 50 mg/kg body weight. EPA (2006a) has established
that chronic exposure to 0.005 mg/kg body weight per day of oxytetracycline is expected to be safe without risk of adverse effects, including risks during pregnancy. EPA (2006a) estimated the aggregate exposure to oxytetracycline due to its use as a pesticide (coming from food and water) and found it to be well below the safe exposure level.

Oxytetracycline has been shown to affect root or shoot growth in a few plants. Batchelder (1982) conducted a series of greenhouse experiments with chlortetracycline and oxytetracycline to determine their effects on growth and development of wheat, maize, radish and pinto bean in different soils. Both antibiotics only affected pinto beans (bean yields, plant heights, top and root dry weight, and Ca, Mg, K, and N contents were all decreased). Kong et al. (2007) observed that oxytetracycline significantly inhibited alfalfa shoot and root growth in a hydroponic system. Li et al. (2010) also observed a significant inhibition of root growth and numbers when wheat was grown hydroponically with oxytetracycline. Effects seen in hydroponic systems are most likely not applicable to soil situations because oxytetracycline becomes strongly adsorbed to soil components and is not available for uptake into plants. No further information was found on the potential phytotoxicity of oxytetracycline.

EPA determined that oxytetracycline is practically non-toxic to mammals, birds, freshwater fish, aquatic invertebrates and invertebrates such as honey bees on an acute oral basis (EPA, 1993, 2008). Chronic data are not available. EPA (1993) stated that due to its low toxicity and low estimated environmental concentrations resulting from pesticidal use, it is unlikely that oxytetracycline poses an undue risk to avian or aquatic organisms.

No information could be found to suggest that agricultural oxytetracycline products contain toxic contaminants or that the degradation products of oxytetracycline would result in toxic effects to humans or the environment. As stated in the responses to Evaluation Questions #4 and #10, the persistence of oxytetracycline in soil and sediments raises a concern over the development of bacterial resistance.

Evaluation Question #6: Describe any environmental contamination that could result from the petitioned substance’s manufacture, use, misuse, or disposal (7 U.S.C. § 6518 (m) (3)).

No current information could be found on the possible environmental contamination resulting from the manufacture of agricultural oxytetracycline products. The following information was included in the 2006 Technical Report for Tetracycline (Oxytetracycline calcium complex). The commercial fermentation of antibiotics usually takes about two to seven days and may require the use of several chemicals, such as solvents and antifoaming agents (Sengha, 1993). In 1998, EPA revised its water effluent limitations guidelines and standards for the pharmaceutical manufacturing industry to control water pollution discharged from these facilities (EPA 1998). Based on information EPA collected from 244 facilities, fermentation operations may use solvents to isolate the substance from the broth and other impurities. Usually, the solvents are recovered and reused, but small amounts of the solvents may remain in the broth “washes” that are discharged into the facility’s wastewater. The solvents most frequently used in fermentation operations, according to the data collected, include acetone, methanol, isopropanol, ethanol, amyl alcohol, and methyl isobutyl ketone. Specific information for the production of oxytetracycline calcium or oxytetracycline hydrochloride was not provided, so it is unclear whether manufacturers of these substances actually use solvents. Other pollutants that could be discharged from fermentation processes include detergents and disinfectants used to clean equipment. Nitrogen and sulfur oxide gases may also be produced, which are regulated by EPA. Assuming oxytetracycline manufacturers comply with applicable water and air regulations, it is unlikely that environmental contamination will result from fermenting processes. The Pollution Prevention and Abatement Handbook: Pharmaceuticals Manufacturing (IFC, 1998) includes a general discussion of environmental pollution and opportunities to diminish pollution associated with the manufacture of pharmaceuticals, including antibiotics such as oxytetracycline.

As stated in the response to Evaluation Question #4, oxytetracycline residues have the potential to persist in soil and sediments for many months. Therefore, environmental contamination could result from use, misuse, or improper disposal of oxytetracycline products. No reports of environmental contamination could be found specifically relating to the use of oxytetracycline on crops. However, the potential for
environmental contamination with oxytetracycline and other veterinary antibiotics resulting from application of antibiotic-contaminated manure to agricultural soils is a subject of growing interest to the scientific community (Wang and Yates, 2008; Thiele-Bruhn and Peters, 2007). Oxytetracycline has been detected in agricultural soils for extended periods of time following application of oxytetracycline-contaminated manure (Cengiz et al., 2010; Kay et al., 2004).

Evaluation Question #7: Describe any known chemical interactions between the petitioned substance and other substances used in organic crop or livestock production or handling. Describe any environmental or human health effects from these chemical interactions (7 U.S.C. § 6518 (m) (1)).

No information was available to assess whether spray-applied oxytetracycline or its byproducts will cause chemical interactions with other substances used in organic crop production. There is evidence to suggest that some producers are applying oxytetracycline in combination with streptomycin sulfate to apple or pear trees when streptomycin-resistant strains are present in the orchard (Johnson, 2010). No chemical interactions are expected to occur between these two antibiotics.

No information could be found on interactions in the agro-ecosystem following the use of oxytetracycline specifically for control of fire blight in apples and pears. However, information is available on effects following general application of tetracyclines (including oxytetracycline) to the soil, and most of the studies are related to land application of manure containing tetracyclines.

The studies reviewed for this Technical Evaluation Report employed various concentrations of tetracyclines or oxytetracycline in soil. For comparison purposes, according to the manufacturer of Mycoshield®, the recommended amount and concentration of oxytetracycline used for control of fire blight in apples and pears is approximately 50 gallons of a 200 ppm solution per acre (Nufarm Americas, Inc., 2008). This results in 0.5 lbs of oxytetracycline applied per acre. EPA estimated the rate of application of oxytetracycline for control of fire blight in apples and pears to be 0.64 lbs. per acre (EPA, 2006b). The current tolerance (maximum residue limit) for oxytetracycline on or in apples and pears is 0.35 ppm.

Soil Microorganisms:

Although oxytetracycline, as an antibiotic, is toxic to some microorganisms in the soil, it is already present in soil due to production by naturally occurring bacteria. Thiele-Bruhn (2003) reported that, in general, the effects of an antibiotic on soil organisms are essentially influenced by the bioavailability of the antibiotic, which depends on soil properties, availability of nutrients, and presence of root exudates. Tetracyclines exhibit strong adsorption to soil components such as clay and organic matter and form strong bonds with metals in the soil. These interactions limit the bioavailability of tetracyclines to microorganisms in the soil (Lui et al., 2009). Tetracycline can persist in soil for long periods of time without showing antimicrobial activity, and high concentrations can be achieved (Popowska et al., 2010). Upon later release from soil components, it can exhibit antimicrobial activity. Factors that may result in a release of tetracycline from the soil include changes in organic material composition of the soil, shifts in microorganism populations, or changes in soil pH (Aga et al., 2005).

Piotrowska-Seget et al. (2008) demonstrated in a laboratory experiment that three successive applications of 3 mg oxytetracycline per gram of soil (on Days 0, 42, and 84) significantly reduced the number of culturable bacteria measured 10 days after each treatment (in sandy loam soil from a pine forest). A small but statistically significant reduction in fungal numbers was also observed after the first two treatments. The total fungal biomass and fungal/bacterial biomass ratio were decreased on Day 60 (but not Day 10). Furthermore, the results indicated that oxytetracycline reduced the rate of nitrification, presumably by inhibiting the activity of soil nitrifying bacteria. One important finding from this study is that the magnitudes of these effects after one treatment were not increased with two more applications.
According to Kumar et al. (2005), broad-spectrum antibiotics like tetracyclines would be expected to inhibit the nitrification process in soil. Furthermore, these authors reported pinto bean plants exhibited 67% fewer root nodules when grown in the presence of oxytetracycline (from application of a manure containing 11.3 ppm of oxytetracycline to the soil).

Colinas et al. (1994) applied a combination of oxytetracycline/penicillin to forest soil in a laboratory experiment at a rate of 10 ppm for each antibiotic and tested the effects on soil populations of active and total bacteria, active and total fungi, protozoa, nematodes, and microarthropods. Active and total bacteria were significantly reduced by oxytetracycline/penicillin, along with the lengths of active hyphae. The other soil organisms were not significantly affected by application with oxytetracycline/penicillin. Bossuyt et al. (2000) reported that application of oxytetracycline to soil at a rate of 1500 ppm did not lead to reduced macroaggregate (i.e., soil structure) formation, but did disturb the fungal biomass. No further information could be found on the potential effects of oxytetracycline on the mycorrhizal fungi.

The effects of tetracyclines on soil bacteria have been tested by measuring respiration and enzymatic activities in the soil. Lui et al. (2009) observed little effect on soil microbial respiration and phosphatase activity following application of two tetracyclines (chlortetracycline and tetracycline) at various concentrations (1 to 300 ppm soil). Measurements were made up to 23 days following treatment and no obvious effects on these parameters were noted. Thiele-Bruhn and Beck (2005) found no effect on soil dehydrogenase activity even with oxytetracycline applied at 500 ppm soil (topsoils from grasslands). By contrast, Boleas et al. (2005) observed a significant effect on soil microbial enzymatic activities (phosphatase and dehydrogenase) following applications of oxytetracycline at 0.01, 1, or 100 ppm soil in a multi-species soil system.

Popowska et al. (2010) demonstrated in a laboratory experiment that the presence of tetracycline in three different types of soils affected the ecological balance in the soil, causing the elimination of some bacterial populations. In this study, varying concentrations of tetracycline (1–9 ppm) were added to three different soil types in a laboratory setting: forest soil from a pine forest, fertile arable agricultural soil, and garden compost. The soils were then incubated for 14 days. The authors found that 2 ppm and higher concentrations of tetracycline caused a significant reduction in bacterial count and many bacterial species were eliminated from the soils. The eliminated species were described as beneficial bacteria involved in various metabolic processes, mineralization of organic compounds, degradation of toxic compounds, or creating soil structure. This study also isolated from the soils many strains of bacteria demonstrating resistance to tetracycline, including opportunistic pathogens of humans and/or animals.

**Soil Fauna:**

Baguer et al. (2000) tested the effects of oxytetracycline on three species of soil fauna (earthworms, springtails, and enchytraeids). No effects were observed at environmentally relevant concentrations. The No Effect Concentration Levels for springtails and the earthworms were greater than the highest concentration tested (5000 ppm soil) while the No Effect Concentration Level for enchytraeids was 3000 ppm soil. Reproduction of each species (measured as number of offspring) did not significantly differ from controls at any concentration tested. Even though oxytetracycline exhibited low toxicity to the soil fauna in this experiment, the authors noted that it is not possible to exclude the possibility of indirect effects on soil fauna caused by changes in the microbial community following application of oxytetracycline.

Based on the available data, it is still uncertain whether the use of oxytetracycline for control of fire blight has significant negative effects on interactions in the agro-ecosystem, including soil organisms. Based on laboratory experiments, there appears to be a potential for negative effects on fungal biomass in the soil, length of active hyphae, nitrifying bacteria, root nodules, and biodiversity of soil bacterial populations. There are no studies available in the field following application of oxytetracycline for control of fire blight. Furthermore, no information was found regarding potential effects on the Salt Index and solubility of the soil, mites, grubs, pH levels, nutrient availability, or endangered species.
Evaluation Question #9: Discuss and summarize findings on whether the petitioned substance may be harmful to the environment (7 U.S.C. § 6517 (c) (1) (A) (i) and 7 U.S.C. § 6517 (c) (2) (A) (i)).

EPA’s Pesticides Registration Eligibility Document (RED) for oxytetracycline concluded that oxytetracycline products, labeled and used according to EPA regulations, will not pose unreasonable risks or adverse effects to the environment (EPA, 1993). However, as part of EPA’s current registration review of oxytetracycline, new data are being called for to complete an updated ecological and endangered species risk assessment. These data include environmental fate data to determine the persistence of oxytetracycline in the environment, oyster acute toxicity – shell deposition, mysid acute toxicity, freshwater invertebrates acute toxicity, freshwater and saltwater fish acute toxicity, avian reproduction, terrestrial plant toxicity data, and aquatic plant toxicity data (EPA, 2009). The registration review is scheduled to be complete in 2014.

Oxytetracycline is moderately persistent in soil and sediments, which results in a certain level of environmental contamination. Manufacture of oxytetracycline may release solvents, disinfectants, detergents, gases, and the compound itself into the environment. Assuming manufacturers comply with applicable water and air regulations, it is unlikely that environmental contamination will result from the manufacture of oxytetracycline products. There is a high probability that oxytetracycline resistant bacteria are present in the environment as a consequence of pesticidal use of oxytetracycline which may have negative health consequences for humans (EPA, 2006).

Evaluation Question #10: Describe and summarize any reported effects upon human health from use of the petitioned substance (7 U.S.C. § 6517 (c) (1) (A) (i), 7 U.S.C. § 6517 (c) (2) (A) (i)) and 7 U.S.C. § 6518 (m) (4)).

EPA’s Tolerance Reassessment Progress and Risk Management Decision (TRED) for oxytetracycline concluded that “there is reasonable certainty that no harm to any population subgroup will result from exposure to oxytetracycline” (EPA, 2006b, p. 4).

The current tolerance (maximum residue limit) for oxytetracycline on or in apples and pears is 0.35 ppm. Assuming that the maximum amount of oxytetracycline residues are present in all types of food which may contain residues, EPA determined that chronic aggregate dietary exposure from oxytetracycline residues in food and water is not considered to be a human health concern (EPA, 2006b). Exposure to oxytetracycline through pharmacological uses in addition to chronic dietary exposure is also not considered a human health concern (EPA, 2006b).

Workers may be exposed to oxytetracycline while applying products containing this pesticide or while working in fields where crops have recently been treated. The Health Effects Division (HED) Chapter of the TRED states that there were almost no reports of ill effects from exposure to oxytetracycline in the available data bases (EPA, 2006a). In order to mitigate the risk to workers, personal protective equipment is advised to prevent skin or eye contact with oxytetracycline. Furthermore, workers are not permitted re-entry into treated areas for at least 12 hours.

As stated in the response to Evaluation Question #9, there is a high probability that oxytetracycline resistant bacteria are present in the environment as a consequence of pesticidal use of oxytetracycline and the persistence of oxytetracycline in soil and sediments (EPA, 2006a). Although there have been reports of oxytetracycline resistant strains of E. amylovora in apple orchards, the extent of this resistance is unknown at present time (EPA, 2006a). Furthermore, resistance to oxytetracycline has been observed in other plant surface-associated bacteria (Vidaver, 2002). As stated in the response to Evaluation Question #8, Popowska et al. (2010) demonstrated in a laboratory experiment that the addition of 2 ppm and higher concentrations of tetracycline to different soil types caused many bacterial species to be eliminated from the soils, including beneficial species. At the same time, many strains of bacteria demonstrating resistance to tetracycline were isolated from the treated soils, including opportunistic pathogens of humans and/or animals.
Microorganisms that become resistant to one tetracycline often exhibit resistance to other tetracycline antibiotics (EPA, 2006a). Most strains of gram-positive bacteria that cause human diseases are resistant to tetracyclines, and many of the aerobic gram-negative bacilli (e.g., enterobacteriaceae) are also resistant to tetracyclines. Despite this, tetracycline and oxytetracycline remains important in modern medicine, and an increase in tetracycline-resistant bacteria in the environment and in humans may lead to adverse human health consequences. Tetracycline and oxytetracycline are used today in medicine to treat a wide variety of bacterial infections and as prophylactic treatment following surgery or injury. Oxytetracycline is also used as a second line of defense for bacteria that pose significant health threats, such as anthrax. It is important to note that there are alternatives available to treatment with oxytetracycline. In regard to other tetracyclines, the CDC has indicated that resistance to tetracyclines has not yet occurred in important pathogens including chlamydia, mycoplasmas, rickettsiae, and spirochetes (EPA, 2006a).

The HED Chapter of the TRED for streptomycin includes a qualitative assessment of pesticidal uses of oxytetracycline contributing to antibiotic resistance in human health and the environment (EPA, 2006a). EPA concluded that the available data were insufficient to complete a quantitative assessment. However, EPA concluded that bacterial resistance to oxytetracycline as a result of pesticidal use has the potential to cause adverse public health consequences if human bacterial pathogens are present in orchards and develop resistance or if non-pathogenic bacteria in orchards develop resistance and later transfer the resistance to human bacterial pathogens. The assessment concluded that “the overall risk of the development of antibiotic resistance to oxytetracycline in human health and the environment is medium” (EPA, 2006a, pg. 6).

As part of its current pesticide registration review for oxytetracycline, EPA has requested from the registrant environmental fate data to further characterize the persistence of oxytetracycline in the environment, as well as the potential for antibiotic resistance to transfer from plant pathogens to human pathogens (EPA, 2009). EPA’s final registration review decision for oxytetracycline is scheduled for 2014.

Rezzonico et al. (2009) state that prohibitions and restricted uses of antibiotics in agriculture have occurred in other countries due to concerns about horizontal transfer of resistance genes from bacteria in the agricultural setting to clinically relevant bacteria. However, such a link has never been documented.

**Evaluation Question #11:** Describe all natural (non-synthetic) substances or products which may be used in place of a petitioned substance (7 U.S.C. § 6517 (c) (1) (A) (ii)). Provide a list of allowed substances that may be used in place of the petitioned substance (7 U.S.C. § 6518 (m) (6)).

**Natural (non-synthetic) Substances or Products:**

Biological control agents – Various antagonistic organisms have been studied for use in control of fire blight in apples and pears. The premise of biological control agents (such as bacteria or yeast) is that they are used to out-compete the pathogen where it occurs on the blossom. Some also decrease pathogen numbers through antibiosis (production of a substance that inhibits the growth of the pathogen) (Johnson et al., 2009). Organisms that can grow quickly and deprive *E. amylovora* of food or space without causing disease are helpful for fire blight suppression. Biological control agents are recommended to be applied to flowers at early bloom (15 to 20% bloom) and at late bloom (full bloom to petal fall) (Sundin et al., 2009). These agents are preventative and must colonize the blossom before infection occurs in order to be effective. Once the antagonistic organisms are established on the stigmas of flowers, warm temperatures (>15 °C) and pollinator activity will help to ensure colonization and increase the efficacy of the biocontrol agent (Sundin et al., 2009).

All of the commercially available biological control agents are organisms that are indigenous to apple and pear blossoms. Two different strains of the beneficial bacterium *Pantoea agglomerans* have been studied for control of fire blight and registered as the products Bloomtime Biological (Northwest Agri Products, Pasco, WA) and BlightBan C9-1 (Nufarm Americas, Inc., Burr Ridge, IL). The bacterium *Pseudomonas fluorescens* A506 is marketed as BlightBan A506 (Nufarm Americas, Burr Ridge, IL). Two different strains of the yeast *Aureobasidium pullulans* make up the product Blossom Protect (Bio-ferm, Germany) which is currently not
The efficacy of commercially available biological control agents has been widely studied. In one type of field protocol, the antagonistic organisms are sprayed at high doses onto flowers, and then several days later, the flowers are inoculated with a low dose of the pathogen E. amylovora. Control plants receive no treatment with antagonistic organisms but are still inoculated with the pathogen. Using this protocol (inoculated fire blight trials), antagonists usually produce only a 40 to 60% reduction in disease incidence when compared to control plants (Johnson et al., 2009). Results have been mixed for the product BlightBan A506. Johnson (2010) describes its effectiveness as poor to fair, stating that it has performed better in field trials with natural pathogen populations as opposed to inoculated trials (also reported in Stockwell et al., 2011). Johnson’s summary also reports that strains of Pantoea agglomerans (such as Bloomtime Biological and BlightBan C9-1) are usually the most effective biocontrol agents in fire blight suppression, with about a 50% reduction in disease incidence observed in inoculated trials (Johnson 2010). Johnson describes the effectiveness of Bloomtime Biological as poor to good and the effectiveness of both Serenade Max and the European product Blossom Protect as fair to good. By comparison, treatment with oxytetracycline calcium is described as fair to very good, and treatment with the antibiotic streptomycin is poor to excellent (the poor rating is due to widespread pathogen resistance to streptomycin within the western states).

Sundin et al. (2009) reports that treatments with BlightBan A506 and BlightBan C9-1 have produced a 40 to 80% reduction in the incidence of fire blight in several trials conducted in the Pacific Northwest of the U.S. However, trials conducted in the eastern U.S. (Michigan, New York, Virginia) have shown that BlightBan A506, BlightBan C9-1, Bloomtime Biological, and Serenade were much less effective in controlling blossom blight when compared to the standard treatment with streptomycin (Agri-Mycin). Management of fire blight is more difficult in the east because of greater rainfall and humidity. The mean percent reduction in blossom blight for the biological control agents ranged from 26.5% to 36.1%.

Stockwell et al. (2011) reports that disease control was more consistent in field trials conducted with compatible mixtures of antagonistic organisms than with single strains. These authors tested strains of Pseudomonas fluorescens A506 (similar to BlightBan A506), a mutant strain of Pseudomonas fluorescens A506 (extracellular protease-deficient mutant), Pantoea vagans C9-1S, Pantoea agglomerans Eh252 (similar to Bloomtime Biological), and combinations of these. The treatments were applied to pear trees at 30% and 70% bloom, and then the pathogen was sprayed on the trees at full bloom. The results for fire blight treatments were compared with a control treatment of water. The strain Pseudomonas fluorescens A506 decreased disease incidence by only 16% from control on average. The Pantoea strains decreased disease incidence by 42 and 55% on average. Combinations of the mutant Pseudomonas fluorescens A506 strain with either Pantoea strain were more effective (68 and 71% disease reduction on average). Combination treatments with either Pantoea strain and the non-mutant strain of Pseudomonas fluorescens A506 were not as effective (44 and 59% disease reduction on average). The reason for this difference is that the non-mutant strain degrades a peptide antibiotic which is produced by the Pantoea strains. This peptide antibiotic is believed to be a key contributor to the efficacy of Pantoea strains against the fire blight pathogen. Antibiotic treatments were also included in these trials for comparisons. Oxytetracycline calcium and streptomycin reduced disease incidence by 39% and 81% on average, respectively.

Cao et al. (2010) of the Ohio State University have provided efficacy ratings for some of the biocontrol agents available for control of fire blight. These ratings are based on the results of one-year field studies published between 2000 and 2009 in the Plant Disease Management Reports.1 The rating are for each

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1 The Plant Disease Management Reports are available at: http://www.plantmanagementnetwork.org/pub/trial/pdmr/

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product was determined from a comparison between untreated controls and the application of each product individually. The product Bloomtime Biological was rated as “±” for fire blight control in apples and pears, meaning that evidence for disease control is mixed with some reports showing positive results and others not. The product Serenade Max was rated poorly corresponding to “no obvious response to treatment in one or more published reports.” No other biocontrol agents currently used in the control of fire blight were rated by Cao et al. (2010).

Kunz et al. (2008) describes the results of field trials with the product Blossom Protect (consisting of two strains of the yeast Aureobasidium pullulans) conducted on apple and pear orchards in Germany. Treatment with Blossom Protect resulted in an average efficiency of 82% reduction in fire blight incidence (results from six different trials). In each trial, Blossom Protect was applied to plants four times during bloom (this is twice the number of treatments typically applied for fire blight control). After the first application, one tree per plot was inoculated with the pathogen, E. amylovora. After that, the pathogen was reported to spread over the entire orchard by natural vectors. Results of disease incidence were only recorded for plants that were not inoculated. Johnson (2010) reports that he and his colleagues evaluated Blossom Protect in an inoculated fire blight trial in 2008 (also using four applications during bloom). They found this product to be nearly as effective as streptomycin (Agri-Mycin) in an orchard with high disease pressure.

As demonstrated by the data presented above, the results are mixed for biological control agents in the suppression of fire blight. While most controlled trials have shown some degree of reduction in disease incidence, the results have been inconsistent. However, research is ongoing to find new antagonistic organisms and combinations of antagonistic organisms that provide higher efficacy in suppression of E. amylovora (Pusey et al., 2009; Sholberg and Boulé, 2008; Johnson, 2010). Currently, inconsistent efficacy discourages many producers from using biocontrol agents in the fight against fire blight (Stockwell et al., 2011).

Fire blight prediction models – These computer models are based on weather patterns and can be useful in helping the grower decide when to apply a biological control agent. The two most popular models are MaryBlyt® developed by Paul Steiner and Gary Lightner at the University of Maryland and Cougarblight developed by Timothy Smith at Washington State University. These models are also widely used by growers to decide when to apply antibiotic treatments (streptomycin or oxytetracycline).

Allowed Synthetic Substances:

In addition to tetracycline, the following substances are included on the National List and are used for control of fire blight in apples and pears:

- Copper mixtures, including Bordeaux mixture (copper sulfate and lime)
- Peracetic acid
- Streptomyacin (streptomyacin sulfate)

Products with copper as the active ingredient can be applied during dormant periods up until the green tip stage. If applied to apples and pears during the blossom period and later, copper may cause phytotoxicity and russetting of the fruit (Smith, 2010). The efficacy of copper products has been described as satisfactory to insignificant. Smith (2010) reports that copper products have not performed well in fire blight trials performed by Washington State University. The level of control when applied to open blossoms varied from 20 to 40%, and the level of control when applied pre-bloom (as recommended to prevent phytotoxicity) was reported to be insignificant. Smith (2010) concludes that copper products are not reliable under conditions of high disease pressure. Adaskaveg and Gubler (2002) report that control of fire blight with copper products is only satisfactory when the threat of disease is low to moderate. No recent trials testing the efficacy of copper products in control of fire blight could be found in the published literature.

Peracetic acid is an oxidizing agent that kills bacteria upon contact. No information could be found on the efficacy of peracetic acid in control of fire blight.
Streptomycin is an antibiotic used to control fire blight in areas of the country where resistance to this compound is not widespread. The level of fire blight control in apples and pears with streptomycin has been reported to be about 80%, which is about twice that of oxytetracycline (Stockwell et al., 2008).

**Evaluation Question #12:** Describe any alternative practices that would make the use of the petitioned substance unnecessary (7 U.S.C. § 6518 (m) (6)).

Using resistant varieties of apple and pear trees is the most effective prevention method for fire blight (Koski and Jacobi, 2009). Although no cultivar is completely immune to fire blight, some are less susceptible than others. Koski and Jacobi (2009) and researchers at the University of Illinois Department of Crop Sciences (2005) list the relative susceptibility of common apple and pear cultivars and rootstocks to fire blight. Unfortunately, most of the cultivars demanded by consumers are highly or moderately susceptible to fire blight (Norelli et al., 2003; Sundin et al., 2009).

Because fire blight infestation is greatly favored by the presence of young, succulent tissues, cultural practices that favor moderate tree growth are recommended. Such practices include keeping the soil well-drained and limiting or excluding the use of manure (Sholberg and Boulé, 2008; University of Illinois, Department of Crop Sciences, 2005). In addition, careful pruning, disinfection of all tools used in pruning, and/or pruning during the winter when lower temperatures render the bacteria inactive can help prevent spreading the disease from infected to uninfected trees. Smith (2010) states that many organic growers successfully use the blossom removal method to prevent secondary bloom fire blight in pears and apples. This method involves removing secondary blossoms by hand when the conditions suggest a high risk of fire blight infection.

**References**


