Product & Regulatory Associates, L.L.C.

October 10, 2007

National Organic Standard Board
c/o Robert Pooler
Agricultural Marketing Specialist
USDA/AMS/TM/NOP
1400 Independence Avenue SW
Room 4008-So.
Ag Stop 0268
Washington, DC 20250-0268

Subject: Petition for Inclusion of a Synthetic Substance Allowed for Use in Organic Crop Production
Your facsimile July 19, 2007

Dear Mr. Pooler:

On behalf of AgroSource, Inc, I am submitting a respond to the subject facsimile which indicated that there were two deficiencies in the request for modification of the restrictions to Tetracycline included within Section 205.601 of the National Organics Program's (NOP), National List of Allowed and Prohibited Substances (National List)

There was an omission in the original petition of Section 9. The Section 12 A information was expanded to provide more detail. Both these are included in revised petition.

Enclosed with this cover letter are duplicate copies of the NOP Tetracycline Petition. There are also two copies of the NOP tetracycline Petition with the Confidential Business Information (CBI) redacted.

If you have any questions in regards to this petition or need more information, please contact me at (856) 424-1528 or jwrightch@comcast.net. I thank you in advance for assistance in handling this petition.

Sincerely,

John F. Wright

cc: Taw Richardson, AgroSource, Inc.

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NOP Tetracycline (Oxytetracycline Hydrochloride Complex) Petition

Confidential Business Information Deleted

Executive Summary

A petition is submitted for tetracycline (oxytetracycline hydrochloride complex) for consideration with respect to the National Organics Program (NOP), Subpart G Section 205.601(i) synthetic substance allowed for use in organic crop protection as plant disease control. The use would be for all diseases on the crops registered with U.S. Environmental Protections Agency (EPA). Currently tetracycline (oxytetracycline calcium complex) is listed in Section 205.601(i)(10) but for fire blight control only.

Oxytetracycline is a broad-spectrum antibiotic produced from the actinomycete Streptomyces rimosus. Two related final forms, hydroxytetracycline monohydrochloride (also known as oxytetracycline hydrochloride) and oxytetracycline calcium are registered as pesticides for use in preventing the growth of or killing bacteria, fungi and mycoplasma like organisms. Specifically oxytetracycline hydrochloride and oxytetracycline calcium are registered for use as bactericide/fungicides to control bacterial diseases, e.g fire blight and bacterial spot on nectarines, peaches and/or pears with apples pending registration. The EPA considers the toxicity to humans and the environment to be similar and the data generated on one compound can be used to assess exposures and risks of the other two.

Oxytetracycline has been available in the United States as a drug for therapeutic use in humans since 1950. It is also used in veterinary medicine to prevent infections in fowl, cattle and swine. Oxytetracycline first was registered as a pesticide in 1974. The Oxytetracycline Reregistration Standard was issued 4/14/88, and the Guidance Document was issued 12/88. The Reregistration Standard and Guidance Document required that previously submitted generic and product-specific product chemistry data be updated because new requirements had been introduced. Data submitted in response to the Guidance Document were reviewed, and the available product database was summarized in the Oxytetracycline Reregistration Eligibility Document (RED) dated 12/29/92. The RED required additional generic and product-specific product chemistry data concerning oxytetracycline hydrochloride. Data submitted subsequent to the RED have been reviewed by the Agency.

The EPA finalized its Tolerance Reregistration Eligibility Decision (TRED) as required by the Food Quality Protection Act (FQPA) of 1996. **Based on these analyses, chronic aggregate risk from existing and proposed uses of oxytetracycline are below HED's level of concern for the general US population and all population subgroups.** The EPA concludes that there are no areas of concern preventing the continued registrations of existing uses of oxytetracycline and the expansion to include apples.

By including all the registered crops and uses for tetracycline (oxytetracycline hydrochloride complex) on the NOP List, then the product is acceptable for NOP labeling under Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) as described in Pesticide Regulation (PR) Notice 2003-1.

Item A

Tetracycline (oxytetracycline hydrochloride complex) is being petitioned for inclusion on the National List as a synthetic substances allowed for use in organic crop production under the National Organics Program (NOP), Subpart G Section 205.601(i) plant disease control.

Item B

1. Identification of Active Ingredient

Tetracycline (oxytetracycline hydrochloride complex) or hydroxytetracycline monohydrochloride is more commonly referred to as oxytetracycline hydrochloride. This is the statement of active ingredient on the EPA registered labels. The PC code and nomenclature of oxytetracycline hydrochloride are presented in Table 1.

TABLE 1. Oxytetracycline Hydrochloride Nomenclature	
PC Code 006308	
Common name	Oxytetracycline hydrochloride; hydroxytetracycline monohydrochloride
Molecular Formula	$C_{22}H_{25}ClN_2O_9$
Molecular Weight	496.9
IUPAC name	2-Naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12, 12a-hexhydroxy-6-methyl-1,11-dioxo-, monohydrochloride, [4S-(4α,4aα,5α,5aα, 6β,12aα)]
CAS name	2-naphthacenecarboxamide, 4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12, 12a-hexhydroxy-6-methyl-1,11-dioxo-, monohydrochloride, (4S,4aR,5S,5aR,6S,12aS)- (9CI)
CAS #	2058-46-0
ANSI name	oxytetracycline
Chemical classification	Antibiotic
EPA Reg. No.	80990-2
Trade Names	Fireline™ Fungicide/Bactericide Agricultural Oxytetracycline FlameOut™ Fungicide/Bactericide

The physicochemical properties of oxytetracycline hydrochloride are listed in Table 2.

TABLE 2. Physicochemical Properties of Oxytetracycline hydrochloride		
Parameter	Value	Reference
Oxytetracycline hydrochloride (PC Code 006308)		
Physical state	Crystalline powder	MSDS
Color	Pale yellow to tan	MSDS
Melting point	Decomposes above 180 °C	RED 12/29/92
pH	2.4 (1% aqueous solution)	RED 12/29/92
Density, bulk density, or specific gravity	5.0 lbs/ft^3 1.98 g/mL (bulk density)	RD D289846, 9/9/03, S. Malak D167892, 9/22/92, F. Toghrol
Water solubility	Freely soluble in water	RD D289846, 9/9/03, S. Malak
Solvent solubility	Sparingly soluble in alcohol	RD D289846, 9/9/03, S. Malak
Vapor pressure	N/A; water soluble salt	RD D289846, 9/9/03, S. Malak
Dissociation constant, pK	N/A; water soluble salt	RD D289846, 9/9/03, S. Malak
Octanol/water partition coefficient	N/A; water soluble salt	RD D289846, 9/9/03, S. Malak

2. The manufacturer is:

AgroSource, Inc.
P. O. Box 1341
Mountainside, New Jersey 07092-0341
U. S. A.
Telephone: (908) 931-9001

3. The intended use of oxytetracycline hydrochloride is as bactericide/fungicide to control bacterial diseases, specifically fire blight and bacterial spot on nectarines, peaches and/or pears with apples pending registration.

4. The list of crops, application rate and method of application are listed in Table 3.

Table 3. Overall Use Patterns for Oxytetracycline				
Oxytetracycline hydrochloride				
Crop	Max Single Rate (Lbs/ai/A)	Applications per Year	Application Equipment	Preharvest Interval (days)
Pear	0.183	10	Ground	60
Peach, Nectarine	0.685	9	Ground Airblast or handheld single nozzle	21
Apple	0.275	6	Airblast	60

5. Manufacturing **CBI Deleted**

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6. There are no previous reviews by State or private certification programs or other organizations of oxytetracycline hydrochloride.

7. Information regarding EPA and FDA

EPA completed its tolerance reassessments for oxytetracycline. Tolerances for residues of oxytetracycline in/on pears, peaches and apples are expressed in terms of the parent compound, [(4*S*,4a*R*,5*S*,5a*R*,6*S*,12a*S*)-4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,5,6,10,12,12a-hexahydroxy-6-methyl-1,11-dioxonaphthacene-2-carboxamide], as the residue of concern [40 CFR 180.337]. A summary of the oxytetracycline tolerance assessments is presented in Table 4

TABLE 4. Tolerance Reassessment Summary for Oxytetracycline

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comments
Pears	0.35	0.35	--
Peaches	0.35	0.35	--
Apples	--	0.35	Proposed

There are currently no livestock tolerances for oxytetracycline as there is no reasonable expectation that residues of concern will transfer to livestock tissues [40 CFR §180.6(a)(3)].

Use of oxytetracycline as a drug in food animals is regulated by the FDA according to 21 CFR 556.500. The FDA has established the following tolerances for the sum of residues of the tetracyclines including chlortetracycline, oxytetracycline, and tetracycline: 2 ppm in muscle (meat) of cattle, swine, sheep, poultry, fish and lobsters; 6 ppm in liver, 12 ppm in fat and kidney, and 0.3 ppm in milk.

Codex MRLs have not been established or proposed for residues of oxytetracycline in or on any food/feed commodity; therefore, no questions regarding compatibility between U.S. tolerances and Codex MRLs exist.

8. The CAS Number for oxytetracycline hydrochloride is 2058-46-7. The technical grade or manufacturing use product is AgroSource Oxytetracycline Technical Fungicide/Bactericide Agricultural Oxytetracycline, EPA Reg. No. 80990-2. It is formulated into a wettable powder product containing 18.3% w/w oxytetracycline hydrochloride, with 17% equivalent oxytetracycline. It is sold under the following brand names:

- Fireline™ 17 WP Fungicide/Bactericide Agricultural Oxytetracycline, EPA Reg. No. 80990-1

- FlameOut™ Fungicide/Bactericide Agricultural Oxytetracycline, EPA Reg. No. 80990-1-82695
- FlameOut™ Fungicide/Bactericide Agricultural Oxytetracycline, EPA Reg. No. 80990-1-4581

9. Oxytetracycline Physical Properties and Chemicals Mode of Action

Oxytetracycline is a broad-spectrum antibiotic produced from the actinomycete Streptomyces rimosus. Oxytetracycline is a member of the tetracycline family of antibiotics. Oxytetracycline is a human and animal antibiotic drug which, in various forms, is used primarily to control bacteria, fungi, and mycoplasma-like organisms. In agriculture, oxytetracycline is used to help control fire blight and/or bacterial spot on pears, peaches, nectarines, and apples.

As a pesticide product, this material has been used extensively in agricultural environments since 1974. This would also include interaction with the subset of products used in organic production. If detrimental chemical interactions with other materials used in agriculture practices were identified, these would normally appear as advisory or prohibition statements on the label. There are always concerns of potential phytotoxicity with pesticides to new sensitive cultivars of plants so a general precautionary statement appears on the end use label. This is standard label language. Other than this, no other detrimental interactions have been raised in the past.

All requirements for fate data on oxytetracycline were waived during the reregistration process since oxytetracycline had a limited use pattern and because it was expected to pose low risk (Office of Pesticide Programs, 1993). Product chemistry studies offer data on water solubility (MRID 44219401, 46109401, 43262301, and 41602001). A peer-reviewed study from the open literature on the soil to water partition coefficients of oxytetracycline in 30 soils of the eastern United States provides the information on mobility that is used in this assessment (Jones *et al.*, 2004). .

Oxytetracycline has uses regulated by the FDA that may lead to environmental and irrigation reservoir exposure, such as concentrated animal feeding operations (CAFO), concentrated aquatic animal production facilities (CAAPF), aquaculture, and silviculture operations. These uses require an NPDES permit to discharge pollutants; although oxytetracycline has not been found to be a listed pollutant [40 CFR 122 (2004)]. Studies have shown that antibiotics mixed in aquaculture feed tend to accumulate in and persist in the sediment below, where wild fish and invertebrates can uptake them into their tissues to levels unacceptable for human consumption (Milewski, 2001; Capone *et al.*, 1996). .

As a pharmaceutical and pesticide, the manufacturing use and disposal of this product is highly regulated. The pesticide manufacturing use is regulated in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit.

The toxicity to humans is well defined for this product since it also has drug applications. EPA estimates that the pharmaceutical oxytetracycline exposure a user is expected to

receive from a typical therapeutic dose (25 mg/kg/day for children) is 50,000 to 200,000 times greater than the estimated dietary exposure from the pesticidal sources of oxytetracycline (0.000121 mg/kg/day to 0.000473 mg/kg/day). Therefore, because the pesticide exposure has no more than a minimal impact on the total dose to a pharmaceutical user, EPA believes that there is a reasonable certainty that the potential dietary pesticide exposure will result in no harm to a user being treated therapeutically with oxytetracycline. FDA is aware of EPA's conclusions regarding pesticide exposure in users receiving treatment with a pharmaceutical oxytetracycline drug product and FDA's June 7, 2006 response to EPA is available the public docket (EPA-HQ-OPP-2005-0492).

Product chemistry studies indicate that the water solubility of hydrochloride salt is 1g in 2 mL (500,000 mg L^{-1}) and that oxytetracycline base and calcium salt are slightly soluble (MRID 41602001, 46109401, 43262301, 44219401). They also report that the 0.1% solution pH of the calcium salt is 7.5 to 10.0, which implies that the water solubility is somewhat near 10 g L^{-1} (10,000 mg L^{-1}; MRID 44219401). Therefore, these compounds are soluble enough to dissolve in surface water and groundwater. However, their exact water solubilities are not well defined.

Soil to water partition coefficients (K_d) for oxytetracycline in 30 eastern U.S. soils representing five soil orders and 28 soil series have been published in a peer-reviewed study (Jones *et al.*, 2005). The study concluded that soil texture, cation exchange capacity, and iron oxide content appeared to most influence oxytetracycline sorption in soils with organic carbon content of 0 to 4%. Soil organic carbon content negatively correlated with compound sorption in those soils, but not with a single soil of 9% organic carbon. K_d values ranged from 486 L kg^{-1} to 12,047 L kg^{-1} (pH 5.5). Data from this study were used to generate EDWCs for this assessment.

The following studies from open literature may offer insight regarding the degradation of oxytetracycline. The USGS Kansas Water Science Center (http://ks.water.usgs.gov) published a study on the chemical degradation of antibiotics in anaerobic swine lagoons, which found that oxytetracycline hydrolysis rates generally increase as pH deviates from 7 and as temperature increases in synthetic systems (Loftin *et al.*, 2004). A kinetics study of oxytetracycline found that high temperatures, light exposure, alkaline conditions, the presence of a substrate, and the presence of organic matter each led to decreased concentrations of the compound in deionized water as compared to contrasting conditions (Doi and Stoskopf, 2000).

Monitoring studies of oxytetracycline were not found in a brief literature search. Oxytetracycline and related tetracyclines are not analytes listed in the U. S. Geological Service (USGS) National Water Quality Assessment (NAWQA) database[1], National Stream Quality Accounting Network (NASQAN) database (http://water.usgs.gov/nasqan), or the California Department of Pesticide Regulation (DPR) Surface Water Database (http://www.cdpr.ca.gov/docs/sw/surfdata.htm).

States and federal agencies have no oxytetracycline monitoring data reporting requirements specified by statute, regulation, or guidance. Consequently, oxytetracycline is not listed in the EPA Safe Drinking Water Information System (SDWIS) database (http://www.epa.gov/safewater/data/getdata.html), nor is it found in EPA Unregulated Contaminants Monitoring Regulation (UCMR) chemical monitoring databases (http://www.epa.gov/safewater/data/ucmrgetdata.html). Groundwater monitoring studies from 1971 to 1991 listed in the EPA Pesticides in Ground Water Database (USEPA, 1992) did not include oxytetracycline as an analyte.

Based on the soil to water partitioning data (Jones *et al.*, 2005), carbon filtering may reduce oxytetracycline concentrations, as other chemicals with high soil to water or octanol to water partition coefficients tend to be hydrophobic and are removed well with activated carbon filtering. Flocculation and sedimentation removal may be effective at reducing oxytetracycline concentrations as well. These processes use the affinity of the compound to organic matter to collect and remove it from water. However, the mobility study by Jones *et al.* (2005) referenced above found that oxytetracycline sorption to soils negatively correlated with soil organic carbon content in soils with 0 to 4% organic carbon. Consequently, the chemical complexity of oxytetracycline may render treatment processes such as carbon filtering, flocculation, and sedimentation ineffective.

Hydrolysis rates for oxytetracycline may increase as pH deviates from 7 (Loftin et al., 2004). Therefore, softening may substantially reduce oxytetracycline concentrations (via alkaline hydrolysis), as softening raises the pH of the water as high as 11.

An avian acute oral toxicity test on bobwhite quail (Colinus virginianus) revealed that calcium oxytetracycline has an $LD_{50} > 2{,}000$ mg/kg and is practically non-toxic. In dietary studies performed on the bobwhite quail (Colinus virginianus) and the mallard duck (Anas platyrhynchos), calcium oxytetracycline was found to be practically non-toxic with $LC_{50} >$ 5,620 ppm ai.

Freshwater fish toxicity test revealed that oxytetracycline hydrochloride has a $LC_{50} > 116$ ppm for the rainbow trout) Oncorhynchus mykiss) and a $LC_{50} > 95$ ppm for bluegill sunfish (Lepomis macrochirus). These LC_{50} values are classified as practically non-toxic.

In Europe, furunculosis, a major disease of salmonid fish caused by Aeromonas salmonicida, is treated with the use of oxytetracycline.

A 48-hour Daphnia magna toxicity test showed a 48-hour $EC_{50} > 102$ ppm and this is classified oxytetracycline hydrochloride as practically non-toxic.

An acute contact honey bee study showed that the $LD_{50\ for}$ worker honeybees exposed to calcium oxytetracycline is >> 100 ug/bee and therefore practically non-toxic.

10. Safety Information

The EPA provides information to support the issuance of a risk management decision document known as a Tolerance Reregistration Eligibility Decision (TRED) for oxytetracycline. EPA's pesticide reregistration process provides for the review of older pesticides (those initially registered prior to November 1984) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) to ensure that they meet current scientific and regulatory standards. The process considers the human health and ecological effects of pesticides and incorporates a reassessment of tolerances (pesticide residue limits in food) to ensure that they meet the safety standard established by the Food Quality Protection Act (FQPA) of 1996.

Oxytetracycline is a broad-spectrum antibiotic produced from the actinomycete Streptomyces rimosus. Oxytetracycline is a member of the tetracycline family of antibiotics. Oxytetracycline is a human and animal antibiotic drug which, in various forms, is used primarily to control bacteria, fungi, and mycoplasma-like organisms. In agriculture, oxytetracycline is used to help control fire blight and/or bacterial spot on pears, peaches, nectarines, and apples. Oxytetracycline hydrochloride and oxytetracycline calcium are registered for use as bactericide/fungicides to control bacterial diseases on nectarines, peaches and/or pears with registration pending on apples. In its review, the EPA considers oxytetracycline hydrochloride, oxytetracycline calcium, and oxytetracycline (hereafter collectively referred to as "oxytetracycline").

The toxicity of all three oxytetracyclines would be expected to be similar and shall be considered equivalent in this hazard characterization. Historically, all the toxicological data requirements for oxytetracycline have been waived. The information available on the effects of oxytetracycline in humans, supplemented with the data available on the toxicity of oxytetracycline in laboratory animals, is sufficient to evaluate the toxicity of oxytetracycline and related compounds. Based on the information available from these sources, the database is complete and there are no data gaps.

It is a broad spectrum antibiotic produced by the actinomycete *Streptomyces rimousus* and became available for use in 1950. Its use as broad-spectrum antibiotic is possible because of its activity against a wide range of disease-causing bacteria. The chemical name of oxytetracycline is 2-napthacenecarboxamide, 4-(dimethylamino)-1, 4, 4a, 5, 5a, 6, 11, 12a-octahydro- 3, 6, 10, 12, 12a- pentahydroxy- 6- methyl- 1- 11- dioxo.

Animal Data

In mice, oxytetracycline has a low acute toxicity, being a Category IV for oral toxicity (LD_{50} > 7200 mg/kg). Based on the extensive availability of human data, the data requirements for the acute dermal, inhalation, primary eye irritation, and skin sensitization studies in animals have been waived.

Oxytetracycline has low toxicity potential when administered by the oral route to animals. In the rat, the liver is a potential target organ at high dose levels (> 1, 250 mg/kg/day).

Long-term administration of oxytetracycline to male and female rats at this dose led to fatty metamorphosis of the liver. No other signs of hepatic toxicity were observed in neither the 13-week oral toxicity study nor the prenatal developmental study in rats. However, the available database did not demonstrate the potential for the liver to be the primary target organ in other animal species (e.g. mice or dogs). Clinical signs in the rat included increased incidence of respiratory signs and rough hair coat and decreased maternal survival. The most common effect in intermediate- or long-term oral exposures was a decrease in body weight and/or body weight gain. In a 13-week feeding study in mice, a decrease in body weight was observed at 7,500 mg/kg/day. In a 103-week feeding study in mice, a slight decrease in body weight (7- 9%) was observed in males at 945 mg/kg/day. No adverse effects were seen in mice at 2,100 mg/kg/day in a mouse prenatal developmental study.

Toxicity in dogs was manifested as a shift from a predominantly drug-susceptible population of enteric lactose-fermenting organisms to a multiple antibiotic resistant population in intestinal flora isolated from fecal samples in a 44-week feeding study. In a chronic toxicity study in dogs, a yellow discoloration of the thyroid was observed in all dosed animals at necropsy. No other changes in clinical signs, mortality, body weight, food consumption, macrosopy, or histopathology were reported in either of the two chronic toxicity studies in dogs.

No evidence of neurotoxicity was observed in any study.

In developmental toxicity studies, maternal toxicity was evident in rats as a dose-related increase in mortality. A dose-related decrease in fetal body weight was observed in rats. The high incidence of maternal deaths and fetotoxicity noted at all dose levels tested did not allow for an establishment of a NOAEL (LOAEL = 1200 mg/kg/day; LDT). No maternal or developmental toxicity was observed in mice treated up to 2,100 mg/kg/day. No treatment-related external, visceral, or skeletal abnormalities were found in either species. Historically, the requirement for a rabbit prenatal developmental toxicity study has been waived. Given the data available on the toxicity of oxytetracyclines in rats, mice and humans and the lack of reported adverse effects to children and infants, further studies will not provide additional information for risk assessment.

In a study citation that was reported by a Joint FAO/WHO committee in 2000, reproductive parameters such as litter size, litter and pup weight, and the number and percent of live or dead fetuses did not show significant differences in the first or second generations. Additionally, growth rate was not significantly affected. The NOAEL in this study was 18 mg/kg/day (note that only 1 dose was tested). Historically, the data requirement for the 2-generation reproductive study was waived based on the information available on the effects of oxytetracyclines in humans. A reproductive study is unlikely to result in a more sensitive endpoint than the one already being used for risk assessment.

Although benign tumors were observed in rats, HED has no carcinogenicity concerns for this chemical. In F344/N rats, histological examination showed a dose related increase in the incidence of benign phaeochromcytomas in the adrenal gland of male rats fed 2,500

mg/kg/day. In females an increase in the incidence of adenomas of the pituitary gland was found in the highest dose group (1,875 mg/kg/day). Mice fed up to 1,875 mg/kg/day exhibited no evidence of carcinogenicity. The bacterial reverse mutation test, chromosome aberration study, and sister chromatid exchange assays were all negative, with and without metabolic activation. The mouse lymphoma forward mutation assay revealed that oxytetracycline was mutagenic only with metabolic activation, however, the dose levels were close to toxic concentrations and the positive effect in the in vivo micronucleus assay in mice was not dose related.

Subchronic Mouse Feeding Study

In a range finding study groups of B6C3F1 mice (10/sex/group) were fed diets containing 0, 3100, 6300, 12500, 25000 or 50000 ppm OTC-HCl for 13 weeks. These dose levels are approximately equal to an intake of 0, 465, 945, 1875, 3750, or 7500 mg/kg/day. No dose related effects were observed on mortality, food consumption, macroscopy and histology. Body weights were decreased from 3 to 15% at 25000 ppm and at 50000 ppm. OTC concentrations in bone were measurable fluorometrically in high-dosed females (NTP, 1987).

Subchronic Rat Feeding Study

In a range finding study, groups of F344/N rats (10/sex/group) were fed diets containing 0, 3100, 6300, 12500, 25000 or 50000 ppm OTC-HCl for 13 weeks. These dose levels were approximately equal to intakes of 0, 1200, 1350 or 1500 mg/kg/day. No dose related effects were observed on mortality, food consumption, body weight or macroscopy. Minimal periacinar fatty metamorphosis in the liver of male rats was observed at all dose levels (no dose relation, control values not given). Measurable OTC concentrations in bones were detected in both sexes and increased with the dose. The OTC concentration in bone was significantly increased in females from 12500 ppm and up and in males at 50000 ppm only (NTP, 1987).

Chronic Rat Feeding Study

Groups of Osborne-Mendel male rats were fed diets containing 0 (180 rats), 100 (100 rats), 1000 (130 rats) or 3000 ppm (100 rats) OTC-HCl for 24 months. Observations included clinical signs, mortality, food consumption, body weight, haematology, macroscopy, and histopathology. After 24 months the mortality rates were 43, 23, 23 and 13% for the control and experimental groups, respectively. Treated rats gained weight more rapidly than controls. Body weight and haematology were not affected. At macroscopy pale kidneys were observed in 4, 7, 16 and 16% in the control and treated groups, respectively. A slight to moderate brownish pigmentation of the thyroid gland was seen in treated rats, but it was not dose-related. Tumor incidences were not enhanced. The NOAEL in this study was 3000 ppm (highest dose tested), equivalent to 150 mg/kg b.w. (Diechmann et al., 1964).

In a second study, groups of Sprague-Dawley rats were fed diets containing 0, 100, or 1,000pm (approximately 0, 5, or 50 mg/kg/day) hydroxytetracycline monohydrochlorate. Observations included clinical signs, mortality, body weight, food consumption,

haematology, organ weights, macroscopy and histopathology. No dose related effects were observed. The NOAEL was 50 mg/kg/day, the highest dose tested.

Chronic Dog Feeding Studies

Groups of mongrel dogs (2/sex/group) were fed diets containing 0, 5000 or 10000 ppm OTC-HCl for 12 months. Observations included clinical signs, mortality, body weight, food consumption, haematology, organ weights, macroscopy and histopathology. No dose related effects were observed except for a degenerating germinal epithelium in the testicular tubules in high-dosed male dogs. The NOAEL in this study was 5000 ppm in the diet, equivalent to 125 mg/kg/day.

In a second study, groups of 8 male dogs, four beagle dogs and four mongrel dogs per group, were fed diets containing 0, 1000, 3000 or 10000 ppm OTC-HCl for 24 months. An interim sacrifice of 1 beagle and 1 mongrel dog/group was performed after 12 months. Observations included clinical signs, mortality, body weight, food consumption, haematology, alkaline phosphatase (ALP), bromosulphophthalein (BSP) clearance, urea nitrogen determinations, organ weight macroscopy, histopathology and semen examination. Two dogs died after 12 and 24 months, respectively (1 because of filaria and 1 because of gastroenteritis). No dose- related effects were observed. Atrophy of testes and epididymus occurred more frequently in control dogs than in treated ones. The NOAEL was 10000 ppm in the diet (the highest dose tested), equivalent to 250 mg/kg b.w. (Deichmann et al., 1964).

Combined Chronic Toxicity/Carcinogencity (Rats)

Groups of F344/N rats (50/sex/group) were fed diets containing 0, 25000, or 50000 ppm OTC-HCl (purity 98.8%) for 103 weeks. Observations included clinical signs, mortality, body weight, food consumption, macroscopy and histopathology. Mean male body weights were 5-8% lower during the first year of the study at 50000 ppm. Histological examination showed a dose related increase in the incidence of benign phaeochromocytomas in the adrenal gland of male rats. In females an increase in the incidence of adenomas of the pituitary gland was found in the highest dose group (NTP, 1987).

Combined Chronic Toxicity/Carcinogencity (Mice)

Groups of B6C3F1 mice (50/sex/group) were fed diets containing 0, 6300 or 12500 ppm OTC-HCl (purity 98.8%) for 103 weeks. Observations included clinical signs, mortality, body weight, food consumption, macroscopy and histopathology. Mean body weights of high dosed mice were 5-9% lower than those in the control group only after the first half year of the study. The tumor incidence was not significantly increased in either sex. The NOAEL in this study was 12500 ppm in the diet (the highest dose tested), equal to 1372 mg/kg b.w. (NTP, 1987).

Metabolism (Mice)

After oral administration of 47.6 mg ^{14}C-labelled OTC-HCl/kg b.w. to mice, 72% of the applied dose was found in the large intestine after 2 hours; only 5% was absorbed, of which the major portion (3.6%) was excreted in the urine. In the liver 1.9% and 1.1% of the dose applied was recovered after 1 and 2 hours, respectively (Snell et al., 1957).

The microbiological effects of oxytetracycline were investigated by studies examining the induction of drug- resistant organisms in dogs. In a 6-week study in dogs, there was no increase in the level of resistant fecal coliforms at 2 ppm in the diet (equivalent to 0 .05 mg/kg/day). Dogs receiving 10 ppm (equivalent to 0.25 mg/kg/day) displayed an increase in a multiple antibiotic-resistant population of enteric lactose-fermenting organisms.

The data requirement for a metabolism study in animals has been historically waived by the agency based on the availability of human data (see human data section below). This was due to the widespread use of oxytetracycline as a drug and no animal feed items involved for pears or peaches (1993 Registration Eligibility Document). However, there is a relevant study on mice in the open literature. After oral administration of 47.6 mg ^{14}C-labeled hydroxyoxtetracycline monohydrochloride/kg b.w. to mice, 72% of the applied dose was found in the large intestine after 2 hours; only 5% was absorbed, of which the major portion (3.6%) was excreted in the urine. In the liver 1.9% and 1.1% of the dose applied was recovered after 1 and 2 hours, respectively.

Mode of Action and Data from Human Drug Use

In additional to the available animal studies and reports, there is extensive data on the toxicity of oxytetracyclines in humans. In humans, oxytetracycline is administered orally and intravenously to treat infectious diseases caused by a wide variety of microorganisms such as chlamydia, rickettsial, mycoplasma pneumonia, spirochetes, gram-negative bacteria (*Bartonella bacilliformis, Pasteurella pestis, Brucella sp.*), and gram-positive bacteria (*Streptococcus sp., Staphylococcus aureus, Neisseria gonorrhoeae*). Tetracyclines exert their activity in bacteria by inhibiting protein synthesis. Inhibition occurs when oxytetracycline binds to the 30S ribosomes, preventing aninoacyl tRNA from reading the mRNA ribosome complex, thereby preventing polypeptide chain elongation. High concentrations of tetracyclines also impair protein synthesis in mammalian cells. However, the active transport system found in bacteria is absent in these cells and there are differences in sensitivity at the ribosomal level. These differences are likely to be important determinants in the selective action of tetracyclines. Both the oral and intravenous dose for adults ranges from 1 to 2 grams per day. The daily oral dose for children is 25 to 50 mg/kg daily in two to four divided doses.

The antibiotic may cause gastrointestinal irritation, mostly after oral administration, in some but not in all individuals. Epigastric burning and distress, abdominal discomfort, nausea, vomiting and diarrhea may occur which may be lessened by administrating oxytetracycline with a meal and/or at more frequent intervals and smaller doses.

Intravenous administration may produce thrombophlebitis. Oxytetracycline appears to be one of the least hepatoxic among the tetracyclines. Most hepatic toxicity develops in humans receiving 2000 mg or more of drug per day parenterally. This effect may occur when large quantities are administered orally. Pregnant women appear to be susceptible to severe tetracycline-induced hepatic damage. Children under 7 years of age may develop a brown discoloration of the teeth. Treatment of pregnant women may also produce discoloration of the teeth of infants. Oxytetracycline is deposited in the skeleton of fetuses and children which can produce depression of bone growth. However, this is readily reversible if the period of exposure to the drug is short.

Additionally, various skin reactions such as morbiliform rashes, urticaria, and generalized dermatitis may occur following exposure to oxytetracyclines in humans, but they are rare. Angioedema and anaphylaxis may develop. Other effects such as burning sensation of the eyes, cheilosis, brown or black coating of the tongue, atrophic or hypertrophic glossitis, pruritus ani or vulvae or vaginitis, fever and eosinophilia may persist for weeks after cessation of therapy. Administration of oxytetracycline to undernourished adults results in weight loss, increased urinary but not fecal nitrogen excretion, negative nitrogen balance, and elevated serum non-protein nitrogen concentrations. Administration of oxytetracycline may lead to development of superinfections by strains of bacteria or yeasts resistant to the agent (see antimicrobial resistance section).

A microbiological study was conducted in humans. In humans receiving oral treatment with oxytetracycline at 2, 20, or 2000 mg per day for 7 consecutive days, there was no evidence of resistant bacteria of the family enterobacteriaceae in the feces at 2mg/day (equivalent to 0.03 mg/kg/day based on a 60-kg person). Humans receiving 20 and 2000 mg per day (equivalent to 0.33 and 3.3 mg/kg/day, respectively) had a decrease in the number of susceptible enterobacteriaceae and an increase in the number of resistant strains in intestinal flora.

Tetracyclines as a class are incompletely absorbed from the gastrointestinal tract. The percentage of an oral dose of oxytetracycline absorbed by the gastrointestinal tract is between 60 to 80%. Most absorption takes place in the stomach and upper small intestine. Absorption of tetracyclines is impaired by chelation of divalent or trivalent cations. Therefore, the absorption of oxytetracycline is compromised by the concurrent ingestion of diary products, aluminum hydroxide gels, calcium, magnesium, iron and zinc salts, and bismuth subsalicylates. Tetracyclines are widely distributed through the body and into tissues and secretions, particularly in the liver, kidney, bones and teeth. Tetracyclines are eliminated primarily by the kidney, although they are also concentrated in the liver and excreted by way of the bile into the intestines. Renal clearance of tetracyclines is by glomerular filtration. From 10-35% of the dose of oxytetracycline is excreted in active form in the urine as the parent drug.

Qualitative Assessment of Antimicrobial Resistance

The overall risk of the development of antibiotic resistance to oxytetracycline in human health and the environment is medium to high. There are documented cases of resistance

to oxytetracycline in the orchards and this poses the potential of horizontal transfer of resistant plasmids and transposons. There is a medium- to high-chance that resistant bacteria will be ingested but it is a highly- to critically-important risk that an adverse health consequence would occur from human exposure to resistant bacteria. The overall risk assessment rank is medium to high. Therefore, in addition to this qualitative assessment, the cRfD was selected using an animal resistance endpoint in mature beagle dogs. This endpoint is the lowest in the available toxicity database and allows the risk assessment team to estimate risk based on the most protective toxicity endpoint available.

Endpoints used in the assessment are provided in Table 5.

Table 5. Endpoint Used for Oxytetracycline Risk Assessment

Dietary	NOAEL mg/kg/day	RfD mg/kg/day	PAD mg/kg/day
chronic - all populations	0.05	0.005 (UF=10; FQPA = 1)	0.005

Exposure Assessment

Analysis of dietary and drinking water exposure pathways were included in the oxytetracycline risk assessment. Sources of dietary exposure include food from treated crops of apple, peach, nectarine, and pears; as well as from drinking water. The dietary exposure to oxytetracycline is expected to be low due to the long PHIs and the limited number of crop uses. Drinking water exposure may occur due to run-off from the agricultural uses of oxytetracycline in orchards. Occupational exposures are not assessed for TREDs. Residential exposures were not assessed because no residential exposures are anticipated.

The use of oxytetracycline as a drug in food animals is regulated by the FDA according to 21 CFR 556.500. The FDA has established the following tolerances for the sum of residues of the tetracyclines including chlortetracycline, oxytetracycline, and tetracycline: 2 ppm in muscle (meat) of cattle, swine, sheep, poultry, fish and lobsters; 6 ppm in liver, 12 ppm in fat and kidney, and 0.3 ppm in milk. HED notes that the drug uses of oxytetracycline in livestock and humans result in considerably higher exposure levels to oxytetracycline residues than the agricultural uses, and emphasizes that the present risk assessment only included the agricultural uses.

Risk Assessment and Risk Characterization

Risk assessments were conducted for dietary and drinking water exposure pathways together as an aggregate assessment of risk from the combined food and drinking water pathways. A cumulative risk assessment considering risks from other pesticides or chemical compounds having a common mechanism of toxicity has not been conducted for this TRED. HED has not yet determined if there are any other chemical substances that have a mechanism of toxicity in common with that of oxytetracycline.

Aggregate Exposures and Risks

Since there is potential for concurrent exposure via food and water, the combined exposures are estimated for the aggregate assessment. To assess aggregate risk, drinking water model-based EDWCs determined by EFED are included in the dietary exposure assessment along with potential residue levels in foods.

HED conducted partially refined chronic dietary exposure analyses using the Dietary Exposure Evaluation Model with the Food Commodity Intake Database (DEEM-FCID™). The chronic dietary analyses were conducted for the general U.S. population and all population subgroups.

Chronic aggregate risks are expressed as a percentage of the chronic Population Adjusted Dose (cPAD). An aggregate risk of 100% of the PAD is the level of exposure that should not be exceeded, (i.e., estimated risk less than 100% of PAD is not of concern). The PAD is the chronic reference dose (cRfD) modified by the special FQPA Safety Factor. The special FQPA safety factor for sensitivity in infants and children for the chronic dietary assessment is 1X. **Based on these analyses, chronic aggregate risk from existing and proposed uses of oxytetracycline are below HED's level of concern for the general US population and all population subgroups**. Chronic aggregate exposure estimates were <100% of the cPAD, with the highest chronic aggregate exposure (0.000598 mg/kg/day) occurring in All infants <1 year old (12% cPAD).

An MSDS is included in the Appendix.

Environmental Fate

All requirements for fate data on oxytetracycline were waived during the reregistration process since oxytetracycline had a limited use pattern and because it was expected to pose low risk (Office of Pesticide Programs, 1993). Product chemistry studies offer data on water solubility (MRID 44219401, 46109401, 43262301, and 41602001). A peer-reviewed study from the open literature on the soil to water partition coefficients of oxytetracycline in 30 soils of the eastern United States provides the information on mobility that is used in this assessment (Jones *et al.*, 2004). .

Oxytetracycline has uses regulated by the FDA that may lead to environmental and irrigation reservoir exposure, such as concentrated animal feeding operations (CAFO), concentrated aquatic animal production facilities (CAAPF), aquaculture, and silviculture operations. These uses require an NPDES permit to discharge pollutants; although oxytetracycline has not been found to be a listed pollutant [40 CFR 122 (2004)]. Studies have shown that antibiotics mixed in aquaculture feed tend to accumulate in and persist in the sediment below, where wild fish and invertebrates can uptake them into their tissues to levels unacceptable for human consumption (Milewski, 2001; Capone *et al.*, 1996). .

The following are fate and transport data from product chemistry studies and the open literature.

Solubility

Product chemistry studies indicate that the water solubility of hydrochloride salt is 1g in 2 mL (500,000 mg L^{-1}) and that oxytetracycline base and calcium salt are slightly soluble (MRID 41602001, 46109401, 43262301, 44219401). They also report that the 0.1% solution pH of the calcium salt is 7.5 to 10.0, which implies that the water solubility is somewhat near 10 g L^{-1} (10,000 mg L^{-1}; MRID 44219401). Therefore, these compounds are soluble enough to dissolve in surface water and groundwater. However, their exact water solubilities are not well defined.

Mobility

Soil to water partition coefficients (K_d) for oxytetracycline in 30 eastern U.S. soils representing five soil orders and 28 soil series have been published in a peer-reviewed study (Jones *et al.*, 2005). The study concluded that soil texture, cation exchange capacity, and iron oxide content appeared to most influence oxytetracycline sorption in soils with organic carbon content of 0 to 4%. Soil organic carbon content negatively correlated with compound sorption in those soils, but not with a single soil of 9% organic carbon. K_d values ranged from 486 L kg^{-1} to 12,047 L kg^{-1} (pH 5.5). Data from this study were used to generate EDWCs for this assessment.

Degradation

The following studies from open literature may offer insight regarding the degradation of oxytetracycline. The USGS Kansas Water Science Center (http://ks.water.usgs.gov) published a study on the chemical degradation of antibiotics in anaerobic swine lagoons, which found that oxytetracycline hydrolysis rates generally increase as pH deviates from 7 and as temperature increases in synthetic systems (Loftin *et al.*, 2004). A kinetics study of oxytetracycline found that high temperatures, light exposure, alkaline conditions, the presence of a substrate, and the presence of organic matter each led to decreased concentrations of the compound in deionized water as compared to contrasting conditions (Doi and Stoskopf, 2000).

Monitoring studies of oxytetracycline were not found in a brief literature search. Oxytetracycline and related tetracyclines are not analytes listed in the U. S. Geological Service (USGS) National Water Quality Assessment (NAWQA) database[2], National Stream Quality Accounting Network (NASQAN) database (http://water.usgs.gov/nasqan), or the California Department of Pesticide Regulation (DPR) Surface Water Database (http://www.cdpr.ca.gov/docs/sw/surfdata.htm).

States and federal agencies have no oxytetracycline monitoring data reporting requirements specified by statute, regulation, or guidance. Consequently, oxytetracycline is not listed in the EPA Safe Drinking Water Information System (SDWIS) database (http://www.epa.gov/safewater/data/getdata.html), nor is it found in EPA Unregulated

Contaminants Monitoring Regulation (UCMR) chemical monitoring databases (http://www.epa.gov/safewater/data/ucmrgetdata.html). Groundwater monitoring studies from 1971 to 1991 listed in the EPA Pesticides in Ground Water Database (USEPA, 1992) did not include oxytetracycline as an analyte.

Based on the soil to water partitioning data (Jones *et al.*, 2005), carbon filtering may reduce oxytetracycline concentrations, as other chemicals with high soil to water or octanol to water partition coefficients tend to be hydrophobic and are removed well with activated carbon filtering. Flocculation and sedimentation removal may be effective at reducing oxytetracycline concentrations as well. These processes use the affinity of the compound to organic matter to collect and remove it from water. However, the mobility study by Jones *et al.* (2005) referenced above found that oxytetracycline sorption to soils negatively correlated with soil organic carbon content in soils with 0 to 4% organic carbon. Consequently, the chemical complexity of oxytetracycline may render treatment processes such as carbon filtering, flocculation, and sedimentation ineffective.

Hydrolysis rates for oxytetracycline may increase as pH deviates from 7 (Loftin et al., 2004). Therefore, softening may substantially reduce oxytetracycline concentrations (via alkaline hydrolysis), as softening raises the pH of the water as high as 11.

An avian acute oral toxicity test on bobwhite quail (Colinus virginianus) revealed that calcium oxytetracycline has an $LD_{50} > 2{,}000$ mg/kg and is practically non-toxic. In dietary studies performed on the bobwhite quail (Colinus virginianus) and the mallard duck (Anas platyrhynchos), calcium oxytetracycline was found to be practically non-toxic with $LC_{50} >$ 5,620 ppm ai.

Freshwater fish toxicity test revealed that oxytetracycline hydrochloride has a $LC_{50} > 116$ ppm for the rainbow trout) Oncorhynchus mykiss) and a $LC_{50} > 95$ ppm for bluegill sunfish (Lepomis macrochirus). These LC_{50} values are classified as practically non-toxic.

In Europe, furunculosis, a major disease of salmonid fish caused by Aeromonas salmonicida, is treated with the use of oxytetracycline.

A 48-hour Daphnia magna toxicity test showed a 48-hour $EC_{50} > 102$ ppm and this is classified oxytetracycline hydrochloride as practically non-toxic.

An acute contact honey bee study showed that the $LD_{50\ for}$ worker honeybees exposed to calcium oxytetracycline is >> 100 ug/bee and therefore practically non-toxic.

11. Research information about the substance which included comprehensive substance reviews and research.

These items are covered in the EPA, recent reviews oxytetracycline hydrochloride which is cover in other sections. The entire EPA review maybe found on a docket for this action under docket identification (ID) number EPA-HQ-OPP-2005-0492. Publicly available docket materials are available either in the electronic docket at <A

HREF="http://www.regulations.gov">http://www.regulations.gov</A>, or, if only available in hard copy, at the Office of Pesticide Programs (OPP) Regulatory Public Docket in Rm. S-4400, One Potomac Yard (South Building), 2777 S. Crystal Drive Arlington, VA.

12 Petition Justification Statements

Bacterial diseases of tree fruit can lead to not only loss of current year production, but also future years and potentially the survival of the tree itself. Available biological options and cultural management practices do not provide effective tools to manage bacterial diseases. Additional substances are needed by organic growers when conditions favorable for bacterial infection arise. Oxytetracycline hydrochloride is a microbiologically derived synthetic substance that will aid organic growers in managing their orchards by providing a supplemental product to meet pome fruit grower demand as well as a new and effective product for stone fruit growers.

Fire blight is an extremely devastating disease of pome fruit trees, which can wipe out an entire orchard within several years if left unchecked. Infection occurs at bloom during periods of warm temperatures and high humidity. Increased planting of susceptible pome fruit varieties, particularly in the Pacific Northwest, has increased the potential for significant outbreaks of the disease.

Bacterial spot of stone fruit is an equally serious disease that typically develops during periods of high rainfall after petal fall. Infection impacts both fruit and leaves and occurs immediately after flowering. Susceptible varieties can be completely defoliated. Under heavy disease pressure, even tolerant varieties can be infected (http://newsletters.caes.uga.edu/srpn/5-2/2005%20South%20Carolina%20Bacterial%20Spot%20Memo.pdf). Effective disease management is necessary, particularly in susceptible varieties, to limit buildup of disease inoculum in the trees. Repeated infection over several years can lead to death of trees.

Non-synthetic and Cultural Options:

Biological options for fire blight and bacterial spot control are very limited. BlightBan (*Pseudomonas fluorescens* strain A506) is a live bacteria, which must colonize floral surfaces to prevent infection by *Erwinina amylovora* (causal agent of fire blight). Washington State University extension reports that BlightBan has achieved, at best, a 50% reduction of fire blight in field tests (http://www.ncw.wsu.edu/treefruit/fireblight/principles.htm). This level of control is inadequate and unacceptable, particularly under moderate to severe fire blight outbreaks. BlightBan is not labeled for control of bacterial spot in stone fruit. Other biologicals and chemicals have proven even less effective.

Cultural methods utilized for fire blight and bacterial spot management such as sanitation of disease strikes to reduce inoculum, nutrition timing, growing tolerant varieties, and disease modeling are practiced by growers but are not sufficient for controlling fire blight

and bacterial spot when favorable conditions for development of the disease arise. Thus, cultural practices can't be used successfully in lieu of the petitioned substance to manage these bacterial diseases.

Synthetic products include:

Copper – Copper products can provide some limited fire blight and bacterial spot suppression if applied frequently, but if applied during poor drying conditions during blossoming or after petal fall, copper is phytotoxic to both apples and stone fruit, resulting in significant economic loss.

Fosetyl-Al – The fungicide Alliette containing fosetyl-Al is labeled for control of fire blight, but Washington State University Extension reports neither research nor grower use has demonstrated any effective fire blight control. Alliette is not labeled for control of bacterial spot in stone fruit.

Streptomycin – The microbiologically derived antibiotic, streptomycin, provides effective fire blight control. However, there is significant resistance to streptomycin in *Erwinia amylovora* in the pome fruit producing area of the Pacific Northwest, Michigan, California, and other areas. Washington State University extension does not recommend streptomycin for fire blight control anywhere in the state. Streptomycin is not labeled for use against bacterial spot in stone fruit.

Oxytetracycline – Oxytetracycline, a microbiologically derived antibiotic, provides effective fire blight and bacterial spot control when applied within 24 hours prior to infection or when models indicate conditions favorable to infection are present. Washington State University extension considers oxytetracycline the only effective fire blight control product available to growers in the Pacific Northwest due to streptomycin resistance. After petal fall, Clemson University Extension recommends weekly oxytetracycline treatments in stone fruit for two to three weeks when conditions favor bacterial spot infection (http://www.clemson.edu/scg/fruit/diseasemgt.htm). Emergency exemptions for use in apples of oxytetracycline-based products against resistant strains of fire blight disease have also been granted in Pacific Northwest, California, Michigan and other states, as well.

Benefits of Oxytetracycline Hydrochloride

Without effective bacterial disease management, bacterial disease inoculum may build up over time in trees and provide a reservoir of bacteria for future infection. The limited number and lack of effectiveness of non-synthetic control options means organic orchards are extremely susceptible to disease buildup, repeated infection, and potentially tree death. Without adequate availability of microbiologically derived synthetic substances, the production life of organic orchards may be cut short.

Severity of these diseases and resulting product demand varies significantly from year to year and region to region, making product inventory forecasting a serious challenge for

manufacturers and distributors. Thus, adequate supply of fire blight and bacterial spot control products is challenging during years of widespread, severe outbreaks. Oxytetracycline applications must be made to all susceptible orchards when disease models indicate infection is imminent within 24 hours. This short lead-time does not allow distributors to obtain additional product quickly enough to respond to the grower needs. This has resulted in shortages of product during severe outbreaks leading to significant losses of fruit as well as damage to and loss of trees. A severe outbreak in southwest Michigan apples in 2000 led to a product shortage and killed over 250,000 trees. Michigan State University Extension estimated the region's total economic loss from this outbreak at $42 million (http://www.canr.msu.edu/vanburen/fb2000.htm). Similarly, in 2005, the southeast peach market experienced a severe outbreak of bacterial spot, which resulted in significant damage.

Currently, the only oxytetracycline based technical grade active ingredient on the NOP list is oxytetracycline calcium, which is only commercially available in one end use product. The US EPA has registered the technical grade active ingredients oxytetracycline calcium and oxytetracycline hydrochloride for bacterial disease control in pome and stone fruit. EPA considers oxytetracycline hydrochloride and oxytetracycline calcium technical grade active ingredients to be equivalent for all regulatory purposes and data generated on one compound can be used to assess risks of the other.

There is one end use product based on each of the oxytetracycline technical grade active ingredients registered by the EPA. The oxytetracycline calcium end use product has a WARNING signal word on the label and is NOP listed. The oxytetracycline hydrochloride end use product has a CAUTION signal word on the label, indicating lower risk to the user, but is not NOP listed. The addition of oxytetracycline hydrochloride to the NOP list would provide a second product for bacterial disease control in areas with streptomycin resistance and would help to reduce the risk of oxytetracycline-based product shortages during severe outbreaks of these devastating diseases.

The NOP list currently does not allow use of any microbiologically derived synthetic substance for bacterial spot in stone fruit. As reviewed above, bacterial spot control options for organic growers are extremely limited. Oxytetracycline hydrochloride would be the first petitioned substance registered for control of bacterial spot in stone fruit.

Section 2119 OFPA U.S.C. 65189(m) (1-7) Criteria

1. The potential of such substances for detrimental chemical interactions with other materials used in organic farming systems.

As a pesticide product, this material has been used extensively in agricultural environments since 1974. If detrimental chemical interactions with other materials used in agriculture practices were identified, these would normally appear as advisory or prohibition statements on the label. There are always concerns of potential phytotoxicity with pesticides to new sensitive cultivars of plants so a general precautionary statement appears on the end use label. This is standard label language. Other than this, no other detrimental interactions have been raised in the past.

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.

All requirements for fate data on oxytetracycline were waived during the reregistration process since oxytetracycline had a limited use pattern and because it was expected to pose low risk (Office of Pesticide Programs, 1993). Product chemistry studies offer data on water solubility (MRID 44219401, 46109401, 43262301, and 41602001). A peer-reviewed study from the open literature on the soil to water partition coefficients of oxytetracycline in 30 soils of the eastern United States provides the information on mobility that is used in this assessment (Jones *et al.*, 2004). .

Oxytetracycline has uses regulated by the FDA that may lead to environmental and irrigation reservoir exposure, such as concentrated animal feeding operations (CAFO), concentrated aquatic animal production facilities (CAAPF), aquaculture, and silviculture operations. These uses require an NPDES permit to discharge pollutants; although oxytetracycline has not been found to be a listed pollutant [40 CFR 122 (2004)]. Studies have shown that antibiotics mixed in aquaculture feed tend to accumulate in and persist in the sediment below, where wild fish and invertebrates can uptake them into their tissues to levels unacceptable for human consumption (Milewski, 2001; Capone *et al.*, 1996). .

3. The probability of environmental contamination during manufacturing use, misuse or disposal of such substance.

There are minimal concerns in this area. As a pharmaceutical and pesticide, the manufacturing use and disposal of this product is highly regulated. The pesticide manufacturing use is regulated in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit.

4. The effects of the substance on human health.

The toxicity to humans is well defined for this product since it also has drug applications. EPA estimates that the pharmaceutical oxytetracycline exposure a user is expected to receive from a typical therapeutic dose (25 mg/kg/day for children) is 50,000 to 200,000

times greater than the estimated dietary exposure from the pesticidal sources of oxytetracycline (0.000121 mg/kg/day to 0.000473 mg/kg/day). Therefore, because the pesticide exposure has no more than a minimal impact on the total dose to a pharmaceutical user, EPA believes that there is a reasonable certainty that the potential dietary pesticide exposure will result in no harm to a user being treated therapeutically with oxytetracycline. FDA is aware of EPA's conclusions regarding pesticide exposure in users receiving treatment with a pharmaceutical oxytetracycline drug product and FDA's June 7, 2006 response to EPA is available the public docket (EPA-HQ-OPP-2005-0492).

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

Solubility

Product chemistry studies indicate that the water solubility of hydrochloride salt is 1g in 2 mL (500,000 mg L^{-1}) and that oxytetracycline base and calcium salt are slightly soluble (MRID 41602001, 46109401, 43262301, 44219401). They also report that the 0.1% solution pH of the calcium salt is 7.5 to 10.0, which implies that the water solubility is somewhat near 10 g L^{-1} (10,000 mg L^{-1}; MRID 44219401). Therefore, these compounds are soluble enough to dissolve in surface water and groundwater. However, their exact water solubilities are not well defined.

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The following studies from open literature may offer insight regarding the degradation of oxytetracycline. The USGS Kansas Water Science Center (http://ks.water.usgs.gov) published a study on the chemical degradation of antibiotics in anaerobic swine lagoons, which found that oxytetracycline hydrolysis rates generally increase as pH deviates from 7 and as temperature increases in synthetic systems (Loftin *et al.*, 2004). A kinetics study of oxytetracycline found that high temperatures, light exposure, alkaline conditions, the presence of a substrate, and the presence of organic matter each led to decreased concentrations of the compound in deionized water as compared to contrasting conditions (Doi and Stoskopf, 2000).

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States and federal agencies have no oxytetracycline monitoring data reporting requirements specified by statute, regulation, or guidance. Consequently, oxytetracycline is not listed in the EPA Safe Drinking Water Information System (SDWIS) database (http://www.epa.gov/safewater/data/getdata.html), nor is it found in EPA Unregulated Contaminants Monitoring Regulation (UCMR) chemical monitoring databases (http://www.epa.gov/safewater/data/ucmrgetdata.html). Groundwater monitoring studies from 1971 to 1991 listed in the EPA Pesticides in Ground Water Database (USEPA, 1992) did not include oxytetracycline as an analyte.

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Hydrolysis rates for oxytetracycline may increase as pH deviates from 7 (Loftin et al., 2004). Therefore, softening may substantially reduce oxytetracycline concentrations (via alkaline hydrolysis), as softening raises the pH of the water as high as 11.

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An acute contact honey bee study showed that the $LD_{50\ for}$ worker honeybees exposed to calcium oxytetracycline is >> 100 ug/bee and therefore practically non-toxic.

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

Oxytetracycline is one of few tools available to combat fire blight, a potentially devastating disease in fruit trees. Non-antibiotic alternatives include copper, prohexadione, biological controls, fosetyl-Al, pruning, and planting resistant cultivars. Antibiotic alternatives include streptomycin.

Copper: Copper provides reasonable protection against fire blight disease if applied as preventive sprays in combination with use of disease forecasting models. Copper is effective in reducing the percent of infected blossom cluster infections on apples. The efficacy of copper is dependent upon many factors such as disease pressure, application timing, and its persistence on plant surfaces. The persistence is dependent upon weather conditions. In current disease management, copper plays an important part in a fire blight management program, but can only be safely applied in the early spring or autumn when the trees are dormant.

Prohexadione: Prohexadione® has no pesticidal properties. It reduces linear growth of branches resulting in reduced tree canopy volume. Prohexadione treatment of trees reduces their susceptibility to fire blight. It may be an additional tool in the management of fire blight.

Biological Control Agent: BlightBan® (a.i. *Pseudomonas fluorescens* strain A506) is used to complement streptomycin (see below); it is not a replacement for streptomycin and other antibiotics. Commercial use of Blightban is limited due to poor efficacy and high cost.

Fosetyl-Al: Aliette®, a fungicide, is also registered for fire blight control, but data supporting this use are not convincing of its efficacy against fire blight. No practical control activity was observed in experimental trials in Michigan. Fosetyl-Al is not used commercially for the control of fire blight because it does not appear to be efficacious.

Pruning: The branches and tree limbs that show fire blight disease symptoms in the late season are removed from the trees and destroyed to prevent the spread of disease and source of inoculums for the next year. This practice is effective in reducing the primary inoculums and tree death.

Resistant Cultivars: Red Delicious variety of apple has some resistance against the fire blight disease but it is not grown widely because most consumers prefer other varieties. All other commercially grown varieties are susceptible.

Streptomycin: Streptomycin is a registered antibiotic for the control of fire blight, but in some areas the pathogen has developed resistance to the antibiotic.

7. Its compatibility with a system of sustainable agriculture.

One key element of sustainable agriculture is the utilization of Integrated Pest Management (IPM) programs. Tetracycline (oxytetracycline hydrochloride complex) has been used in agriculture since 1974 for the control of bacterial diseases of apples and peaches. It is a main weapon in the arsenal to combat fire blight. As an antibiotic it can generally be used throughout the growing season. Since disease problems occur under specific set of climatic conditions, e.g. temperature and humidity, this antibiotic is generally applied when needed based upon disease risk management computer models such as Cougarblight™ and Maryblyt™, as part of an integrated pest management program. It also has a broad window of application versus the copper based fungicides which present greater risk if applied when bloom or fruit is present. It also controls its targeted diseases where the new biological products entering the market place only suppress the disease pressure rather than control it.

APPENDICES

MSDS for AgroSource Oxytetracycline Technical Fungicide/Bactericide Agricultural Oxytetracycline,

Label for AgroSource Oxytetracycline Technical Fungicide/Bactericide Agricultural Oxytetracycline, EPA Reg. No. 80990-2

Label for Fireline™ 17 WP Fungicide/Bactericide Agricultural Oxytetracycline, EPA Reg. No. 80990-1

Label for FlameOut™ Fungicide/Bactericide Agricultural Oxytetracycline, EPA Reg. No. 80990-1-82695

Label for FlameOut™ Fungicide/Bactericide Agricultural Oxytetracycline, EPA Reg. No. 80990-1-4581

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#1

AGROSOURCE, INC.

MATERIAL SAFETY DATA SHEET

AgroSource Oxytetracycline Technical Fungicide/Bactericide
Agricultural Oxytetracycline

This document has been prepared to meet the requirements of U. S. OSHA Hazard Communication Standard, 29, CFR 1910.1200. The information contained herein is for the concentrate as packaged unless otherwise indicated.

SECTION 1- PRODUCT & COMPANY IDENTIFICATION

Trade Name: AgroSource Oxytetracycline Technical Fungicide/Bactericide Agricultural Oxytetracycline
Product Number: 1002
EPA Registration Number: 80990-2
Active Ingredient: Oxytetracycline Hydrochloride
CAS Number: 2058-46-0
Chemical Name: 2-naphthacenecarboxamide, 4-(dimethylamino)-1, 4, 4a, 5, 5a, 6, 11, 12a-octahydro-3, 6, 10, 12 dioxo-monohydrochloride, 12a pentahydroxy-6-methyl-1, 11-dioxo-monohydrochloride
ANSI Common Name: Oxytetracycline
Molecular Formula: $C_{22}H_{24}N_2O_9HCl$ (oxytetracyline hydrochloride)
Chemical Classification: Antibiotic
Use: Control of bacterial diseases on agricultural crops.

Manufacturer:
AgroSource, Inc.
P. O. Box 1341
Mountainside, New Jersey 07092-0341
U. S. A.
General Information: (908) 931-9001

Emergency Telephone Numbers:
IN CASE OF EMERGENCY CALL INFO TRAC
(800) 535-5053 or (352) 323-3500

SECTION 2- COMPOSITION, INFORMATION ON INGREDIENTS

Component	% w/w	CAS Number	OSHA PEL**	ACGIH TLV**
Oxytetracycline (hydrochloride)	98.3	2058-46-0	Not Established	Not Established

** Permissible Exposure Limits (PEL) & Threshold Limit Value (TLV) are 8-hour time weighted average (TWA)

SECTION 3- HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

IMMEDIATE CONCERNS:

- Pale yellow to tan crystalline powder
- Thermal decomposition and burning may form toxic by-products
- For large exposures or fires, wear personal protective equipment

POTENTIAL HEALTH EFFECTS: Effects from over exposure may result from either swallowing, inhaling or coming into contact with skin or eyes. Symptoms of oxytetracycline hydrochloride exposure include gastrointestinal irritation, nausea and vomiting. Exposure may cause allergic reaction and anaphylaxis to occur in sensitive individuals. Eye contact may cause moderate eye irritation. As with other antibiotics, it has the potential to change the micro flora of the intestine and allow overgrowth of non-susceptible organisms.

MEDICAL CONDITIONS AGGRAVATED: Excessive exposure to any dust may aggravate pre-existing respiratory conditions. May cause allergic reaction and anaphylaxis to occur in individuals with allergic history or pre-existing dermatitis.

SECTION 4- FIRST AID MEASURES

Eye Contact: If in eyes, hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.

Skin Contact: If on skin or clothing, take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes.

Inhalation: If inhaled, remove to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. Call a poison control center or doctor immediately for further treatment advice.

Ingestion: If swallowed, call a poison control center or doctor immediately for treatment advice. Have the person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by a poison control center or doctor. Do not give anything by mouth to an unconscious person.

Notes to Physician: Treat symptomatically. There is no specific antidote. Emesis may be indicated in recent substantial ingestion unless the patient is or could rapidly become obtunded, comatose or convulsing. Is most effective if initiated within 30 minutes. Plasma tetracycline levels are not clinically useful. No specific lab work (CBC, electrolyte, urinalysis) is needed unless otherwise indicated. Anaphylaxis may be managed with appropriate supportive measures including securing an adequate airway, epinephrine and diphenhydramine.

SECTION 5- FIREFIGHTING MEASURES

Extinguishing Media: In case of fire use water spray, dry chemical, foam or CO_2 extinguishing media.

Fire Fighting Equipment and Procedures: Wear full protective clothing and self-contained breathing apparatus. Evacuate non-essential personnel from the area to prevent exposure to fire, smoke, fumes or products of combustion. Prevent use of contaminated buildings, area and equipment until decontaminated.

Fire and Explosion Hazards: None known. As with all dry powders, it is advisable to ground material equipment in contact with dry material to dissipate the potential buildup of static electricity.

Flash Point: Not applicable.

Auto ignition Temperature: Not Available

Flammability: Not Available; Limits- Not Applicable

Hazardous Combustion or Decomposition Products Associated with Fire: May emit carbon monoxide, carbon dioxide, nitrogen oxides, hydrogen chloride gas.

SECTION 6- ACCIDENTAL RELEASE

Spill and Disposal Procedures: Control the spill at its source and prevent it from spreading, contaminating soil, or entering sewage or drainage systems or bodies of water. Clean up spills immediately and use suitable protective equipment (Section 8). Keep unnecessary persons away. If emergency response personnel are unavailable or unwarranted, clean up a solid spill by carefully sweeping up the material (avoid creating dust) and using a proper tool to place it into an appropriate disposal container. If liquid, cover the spill with an absorbing material and follow the same procedure used for a solid spill. Scrub the area with a hard water detergent. Pick up liquid with absorbent material and follow the same procedure used for a solid spill. Dispose of or treat all spill residues according to applicable local, state and federal regulations (Section 13). Use suitable protective equipment (Section 8). Follow fire prevention procedures (Section 5).

SECTION 7- HANDLING AND STORAGE

Engineering Controls: Local exhaust ventilation sufficient to control dust is recommended.

Handling Procedures and Equipment: Avoid generating dust. Use respiratory protection in the absence of adequate ventilation controls (Section 8). Wash skin thoroughly after shift exposure. Keep containers closed when not in use. Clean up spills promptly (Section 6).

Handling and Storage: Store in a cool, dry place and protect from moisture. Avoid contact with skin or eyes. Do not breathe dust or spray. Do not ingest. Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet. Do not store food, beverages or tobacco products in the storage area. Protect containers from damage. Use entire contents of packages, do not store open packages. Keep out of reach of children and domestic animals. Only for formulating into anti-bacterial pesticide uses on agricultural crops listed on the label.

SECTION 8- EXPOSURE CONTROLS, PERSONAL PROTECTION

Note: The following recommendations for exposure controls and personal protection are for the manufacturing, formulating or packaging this product.

Inhalation: Use MSHA/NIOSH approved dust/mist respirator with any R, P, or HE filter. Do not breathe dust or spray.

Skin Contact: Wear chemical resistant (e. g. nitrile or butyl) gloves, coveralls, socks and chemical resistant footwear. For overhead exposure, wear chemical resistant headgear.

Eye Contact: Safety glasses required. Use chemical splash goggles if potential exists for direct exposure to dust, splashes or sprays. Facilities storing or utilizing this material should be equipped with an eyewash facility and a safety shower.

Ingestion: Prevent eating, drinking, tobacco usage and cosmetic application in areas where there is potential for exposure. Wash thoroughly with soap and water after handling.

SECTION 9- PHYSICAL AND CHEMICAL PROPERTIES

Appearance: . Pale yellow to tan crystalline powder.

Odor: Odorless to faint odor.

Molecular Weight: 496.9 (Oxytetracycline hydrochloride)

Solubility in Water: Oxytetracycline hydrochloride is soluble in water.

pH: 2.3-2.9

Volatile Components (% w/w): < 8% (water)

Density (lb./cu ft): Not available.

Boiling Point (degrees C/degrees F): Not applicable.

Freezing Point (degrees C/degrees F): Not applicable.

Melting Range (degrees C/degrees F): Not available.

Vapor Pressure (mm Hg @ degrees C/degrees F): Not available.

SECTION 10- STABILITY AND REACTIVITY

Stability: Stable under normal storage and use conditions. Hygroscopic; moisture can cause decomposition.

Hazardous Polymerization: Should not occur.

Hazardous Decomposition: None known.

Incompatibilities: Decomposed by strong acids and alkalis.

Storage Conditions: Hygroscopic, protect from moisture. Sensitive to air, light, heat and bases so protect from exposure. Keep containers sealed and avoid damage.

SECTION 11- TOXICOLOGICAL INFORMATION

Oxytetracycline

Test	Species	Result
Oral LD_{50}	Mouse	6,646 mg/kg, Practically Non-Toxic
Dermal LD_{50}	Rabbit	>2,000 mg/kg, Slightly Toxic
Eye	Rabbit	Moderately Toxic
Skin	Rabbit	Non-Irritating
Skin	Guinea Pig	Sensitizing

Mutagenic Potential: None observed.

Reproductive Hazard Potential: Possible risk of congenital malformation in the fetus.

Chronic/Sub-chronic Toxicity: Gastrointestinal irritation with nausea, epigastric pain and burning, vomiting, abdominal pain, transitory yellowish-brown discoloration of the tongue, anorexia and diarrhea have been reported following oral administration. Blood disorders (delay in coagulation) have been reported. Possible hypersensitization and super-infections due to overgrowth of organisms not affected by the antibiotic agent. Three types of renal disease is associated with over exposure: Acute Non-Oliguric Renal Failure (individuals with pre-existing pancreatitis or fatty liver), Uremia (individuals with pre-existing impaired renal function), and Reversible Nephrotoxicity (due to out-dated or degraded tetracyclines).

Carcinogenic Potential: Not classifiable based on its IARC, ACGIH, OSHA, NTP or EPA.

SECTION 12- ECOLOGICAL INFORMATION

Environmental Fate: Oxytetracycline is unstable to light and heat. it should not accumulate in the soil.

Other: This product is a pesticide. Avoid contact of spilled materials and runoff with soil and surface waterways.

SECTION 13- DISPOSAL CONSIDERATION

Disposal: Do not reuse product containers. Dispose of product containers, waste containers and residues according to local, state and federal health and environmental regulations.

Characteristic Waste: Not Applicable

Listed Waste: Not Applicable

SECTION 14- TRANSPORT INFORMATION

U.S. DOT (Department of Transportation Classification: Not regulated by DOT

Reportable Quantity (RQ); None

Shipping Freight Description: Insecticides or Fungicides, Agricultural, N. O. S.

ICAO/IATA Classification: Not available.

IMDG Classification: Not available.

SECTION 15- REGULATORY INFORMATION

Toxic Substances Control Act (TSCA) Classification: Exempt. Oxytetracycline is a non-hazardous, non-restricted substance. It is listed in the TSCA inventory but is not regulated. Subject to FIFRA.

RCRA Hazardous Waste Classification (40 CFR 261): Not applicable.

CERCLA/SARA 302 Reportable Quantity (RQ): None

EPCRA SARA Title III Classification:
Section 311/312: Acute Health Hazard/Chronic Health Hazard.
Section 313: Toxic Chemicals: Not applicable

SECTION 16- OTHER INFORMATION

NFPA Hazard Ratings: Health 1, Flammability 0, Instability 0 (0-Minimal, 1-Slight, 2-Moderate, 3-Serious, 4-Extreme)

HMIS Hazard Ratings: Health N/A, Flammability N/A, Reactivity N/A (0-Minimal, 1-Slight, 2-Moderate, 3-Serious, 4- Severe)

Important: While the descriptions, data and information contained in the Material Safety Data Sheet are presented in good faith and are believed to be accurate as of the date indicated, AgroSource, Inc. makes no warranty with respect hereto and disclaims all liability from reliance thereon. The Material Safety Data Sheet is provided for guidance only. Many factors may affect the product during processing, application or use. Therefore, it is recommended that packagers, handlers and users test to determine suitability under their specific conditions.

 Original Issued Date: 02/08/05; Revision Date: ----; Replaces: ----

#2

AgroSource Oxytetracycline Technical
Fungicide/Bactericide
Agricultural Oxytetracycline

This material is a non-sterile, non-pharmaceutical grade, technical antibiotic product intended for formulation into EPA-registered end-use pesticide products.

Not for Resale Under This Label

Active Ingredient:

Oxytetracycline Hydrochloride*	98.30%
Related Compounds	0.92%
Other Ingredients:	0.78%
	100.00%

* minimum 83.5% oxytetracycline

EPA Reg. No. 80990-2
EPA Est. No. 80990-CHN-001

KEEP OUT OF THE REACH OF CHILDREN

DANGER

FIRST AID	
Call a poison control center or doctor immediately for treatment advice.	
If In Eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.
If On Skin or Clothing:	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes.
HOT LINE NUMBER	
Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact InfoTrac at 1-800-535-5053 for emergency medical treatment information.	

See Side Panel for Additional Precautions

NOTICE: Read the entire Directions for Use and Conditions of Sale and Limitation of Warranty and Liability before buying or using this product.

AgroSource, Inc.
P. O. Box 1341
Mountainside, NJ 07092-0341

NET CONTENTS: 25 KG

PRECAUTIONARY STATEMENTS
Hazards To Humans & Domestic Animals

DANGER: Corrosive. Causes irreversible eye damage. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield or safety glasses). May cause allergic skin reactions. Do not breathe dust. Wear dust mask and rubber gloves. Wash thoroughly with soap and water after handling and before eating drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse. This material is not to be used for medical, veterinary or human purposes.

Environmental Hazards

Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

This manufacturing use product is intended to be formulated as an active ingredient into end-use pesticide products. The manufacturer of such products shall be responsible for registering its product with EPA as a pesticide for acceptable use patterns.

Only for formulation into an anti-bacterial pesticide for the following uses:

Terrestrial Foods – Nectarine, Peach, Pear

Terrestrial Non-Food & Domestic Outdoor

Storage & Disposal

Do not contaminate water, food or feed by storage or disposal.

Storage: Keep container tightly closed and sealed. Product is moisture, temperature and light sensitive. Product is hygroscopic so protect from moisture. Store in a cool (<77°F, 25°C), dry place away from heat and open flames with minimum exposure to the atmosphere. Avoid extremes in temperature.

Pesticide Disposal: Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.

Container Disposal: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into process equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by state and local authorities. If the drum cannot be reused, dispose of in the same manner.

Conditions of Sale and Limitation of Warranty and Liability

The Directions for Use of this product should be followed carefully. It is impossible to eliminate all risks inherently associated with the use of this product. Crop injury, ineffectiveness or other unintended consequences may result because of such factors as manner of use or application, weather or crop conditions, presence of other materials, resistant strains or other influencing factors in the use of the product, which are beyond the control of AgroSource, Inc. or Seller. All such risks shall be assumed by Buyer and User, and Buyer and User agree to hold AgroSource, Inc. and Seller harmless for any claims relating to such factors.

AgroSource, Inc. warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes stated in the Directions for Use, subject to the inherent risks referred to above, when used in accordance with directions under normal use conditions. This warranty does not extend to the use of the product contrary to label instructions, or under abnormal conditions or under conditions not reasonably foreseeable to or beyond the control of Seller or AgroSource, Inc., and Buyer and User assume the risk of any such use. AGROSOURCE, INC. MAKES NO WARRANTIES OF MERCHANTABILITY OR OF FITNESS FOR A PARTICULAR PURPOSE NOR ANY OTHER EXPRESS OR IMPLIED WARRANTY EXCEPT AS STATED ABOVE.

In no event shall AgroSource, Inc. or Seller be liable for any incidental, consequential or special damages resulting from the use or handling of this product. THE EXCLUSIVE REMEDY OF THE USER OR BUYER, AND THE EXCLUSIVE LIABILITY OF AGROSOURCE, INC. AND SELLER FOR ANY AND ALL CLAIMS, LOSSES, INJURIES OR DAMAGES (INCLUDING CLAIMS BASED ON BREACH OF WARRANTY, CONTRACT, NEGLIGENCE, TORT, STRICT LIABILITY OR OTHERWISE) RESULTING FROM THE USE OR HANDLING OF THIS PRODUCT, SHALL BE THE RETURN OF THE PURCHASE PRICE OF THE PRODUCT OR, AT THE ELECTION OF AGROSOURCE, INC. OR SELLER, THE REPLACEMENT OF THE PRODUCT.

AgroSource, Inc. and Seller offer this product, and Buyer and User accept it, subject to the foregoing conditions of sale and limitations of warranty and of liability, which may not be modified except by written agreement signed by a duly authorized representative of AgroSource, Inc.

Made in China

#3

FIRELINE™ 17 WP

Fungicide/Bactericide
Agricultural Oxytetracycline

GROUP	18	FUNGICIDE

- **For control of fire blight on pear and bacterial spot on peach and nectarine**

Active Ingredient:

Oxytetracycline Hydrochloride*	18.30%
Related Compounds	0.17%
Other Ingredients:	81.53%
	100.00%

* Equivalent to 17% oxytetracycline

ACCEPTED
JAN 6 2006
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 80990-1

KEEP OUT OF THE REACH OF CHILDREN

CAUTION

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

See Side/Back Panel for Additional Precautionary Statements, First Aid and Directions for Use

EPA Reg. No. 80990-1
EPA Est. No. 39578-TX-1

Product Number 1001

AgroSource, Inc.
P. O. Box 1341
Mountainside, New Jersey 07092-0341

NOTICE: Read the entire Directions for Use and Conditions of Sale and Limitation of Warranty and Liability before buying or using this product. If the terms are not acceptable, return the product at once, unopened and undamaged, and the purchase price will be refunded.

NET CONTENTS: 2 pounds

FIRST AID	
Call a poison control center or doctor immediately for treatment advice.	
If In Eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.
If On Skin or Clothing:	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes.
HOT LINE NUMBER	
Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact InfoTrac at 1-800-535-5053 for emergency medical treatment information.	

PRECAUTIONARY STATEMENTS
Hazards To Humans & Domestic Animals

CAUTION: Causes moderate eye irritation. Harmful if absorbed through skin. Avoid contact with eyes or clothing. Do not breathe spray mist. Prolonged or frequently repeated exposure may cause allergic reactions in some individuals. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum or using tobacco. Remove and wash contaminated clothing before reuse. This material is not to be used for medical, veterinary or human purposes.

Personal Protective Equipment (PPE):

Some materials that are chemical resistant to this product are listed below. If you want more options, follow the instructions for Category A on an EPA chemical resistant category selection chart.

Applicators and other handlers must wear:

- long-sleeved shirt
- long pants
- chemical-resistant gloves made of any waterproof material
- shoes plus socks
- NIOSH approved respirator with any N, R, P or HE filter

Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

Engineering Control Statements:

When handlers use closed systems or enclosed cabs in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240(d)(4-6)], the handler PPE requirements may be reduced or modified as specified in the WPS.

User Safety Recommendations:

Users should:

- Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.
- Remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.

Environmental Hazards

Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment washwater.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirements specific to your State or Tribe, consult the agency responsible for pesticide regulation.

AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR part 170. This Standard contains requirements for the protection of agricultural workers on farms, forests, nurseries and greenhouses, and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE) and restricted entry interval. The requirements in this box apply to uses that are covered by the Worker Protection Standard.

Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours.

For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water, wear:

- Coveralls over long-sleeved shirt and long pants
- Chemical-resistant gloves made of any waterproof material
- Shoes plus socks
- Protective eyewear

Do not apply this product through any type of irrigation system.

Resistance Management Statements FIRELINE™ 17 WP fungicide/bactericide contains a Group 18 (fungicide/bactericide). Fungal isolates/bacterial strains with acquired resistance to Group 18 may eventually dominate the fungal/bacterial population if Group 18 fungicides/bactericides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by **FIRELINE ™ 17 WP** fungicide/bactericide or other Group 18 products.

To delay fungicide/bactericide resistance consider:

- Avoiding the consecutive use of **FIRELINE ™ 17 WP** fungicide/bactericide or other target site of action Group 18 fungicides/bactericides that have a similar target site of action, on the same pathogens.
- Using tank-mixtures or premixes with fungicide/bactericides from different target site of action Groups as long as the involved products are all registered for the same use and are both effective at the tank mix or prepack rate on the pathogen(s) of concern. Do not use any product that has a prohibition on tank mixing and follow the more restrictive use directions.
- Basing fungicide/bactericide use on a comprehensive IPM program.
- Monitoring treated fungal/bacterial populations for loss of field efficacy.
- Contacting your local extension specialist, certified crop advisors, and/or manufacturer for fungicide/bactericide resistance management and/or IPM recommendations for specific crops and resistant pathogens.

Treatment of Pears, Peaches & Nectarines:

MIXING: To avoid possible pesticide contamination, use only clean metal or plastic containers in preparing all solutions.

MIXING INSTRUCTIONS			
Concentrate Desired	**Quantity FIRELINE™ 17 WP Per Volume of Water**		
ppm*	**50 gals.**	**100 gals.**	**500 gals.**
150	6.0 oz.	12.0 oz.	3 ¾ lbs.
200	8.0 oz.	16.0 oz.	5 lbs.

*ppm = parts per million

Crop	Disease	Recommended Concentration or Rate	Use Directions
Pears	Fire Blight	200 ppm	Begin spray application at 10% bloom at a rate of 50-100 gals. of solution per acre. Repeat applications at 4 to 6 day intervals. This may involve up to 8-10 applications. Do not apply within 60 days of harvest. Use of **FIRELINE™ 17 WP** may cause phytotoxicity to the fruit and/or foliage of sensitive varieties of pears, especially Asian varieties.
Peaches & Nectarines	Bacterial Spot	150 ppm	Begin application with shuck split using a rate of 3 gallons per tree (240 gals. spray solution per acre based on 80 trees per acre). Apply spray solution to point of runoff. Gallons of spray per acre may be increased for larger trees. Do not exceed 500 gals. of spray solution per acre. Use pressure sprayer capable of delivering the spray at least 250 lbs pressure per square inch through a hand-held single nozzle gun, or 150 lbs. pressure per square inch using a wind-blast sprayer. For best results with air-blast sprayer, do not exceed 3 miles per hour ground speed or 100 miles per hour spray velocity. **Note:** The spray application schedules are based on a definite biological growth period for peaches, the shuck split. Shuck split stage for peaches varies North to South by state. in individual states and by varieties. Applications are weekly after shuck split stage. This may involve up to 8 or 9 applications. Do not apply within 3 weeks of harvest.

Additional information regarding use of **FIRELINE™ 17 WP** fungicide/bactericide may be obtained from your local Agricultural Extension Agent or State Experimental Station.

Use of **FIRELINE ™ 17 WP** fungicide/bactericide may cause phytotoxicity to the fruit and/or foliage of sensitive varieties of pears and peaches.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Keep tightly closed and sealed. Product is moisture, temperature and light sensitive. Product is hygroscopic so protect from moisture. Store in a cool (<77°F, 25°C), dry place away from heat and open flames with minimum exposure to the atmosphere. Avoid extremes in temperature.

Pesticide Disposal: Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.

Container Disposal: Completely empty bag into application equipment. Then dispose of bag in a sanitary landfill, by incineration, or if allowed by State and local authorities, by burning. If burned, stay out of smoke.

Conditions of Sale and Limitation of Warranty and Liability

The Directions for Use of this product should be followed carefully. It is impossible to eliminate all risks inherently associated with the use of this product. Crop injury, ineffectiveness or other unintended consequences may result because of such factors as manner of use or application, weather or crop conditions, presence of other materials, resistant strains or other influencing factors in the use of the product, which are beyond the control of AgroSource, Inc. or Seller. All such risks shall be assumed by Buyer and User, and Buyer and User agree to hold AgroSource, Inc. and Seller harmless for any claims relating to such factors.

AgroSource, Inc. warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes stated in the Directions for Use, subject to the inherent risks referred to above, when used in accordance with directions under normal use conditions. This warranty does not extend to the use of the product contrary to label instructions, or under abnormal conditions or under conditions not reasonably foreseeable to or beyond the control of Seller or AgroSource, Inc., and Buyer and User assume the risk of any such use. AGROSOURCE, INC. MAKES NO WARRANTIES OF MERCHANTABILITY OR OF FITNESS FOR A PARTICULAR PURPOSE NOR ANY OTHER EXPRESS OR IMPLIED WARRANTY EXCEPT AS STATED ABOVE.

To the extent allowable under State law, AgroSource, Inc. or Seller shall not be liable for any incidental, consequential or special damages resulting from the use or handling of this product. THE EXCLUSIVE REMEDY OF THE USER OR BUYER, AND THE EXCLUSIVE LIABILITY OF AGROSOURCE, INC. AND SELLER FOR ANY AND ALL CLAIMS, LOSSES, INJURIES OR DAMAGES (INCLUDING CLAIMS BASED ON BREACH OF WARRANTY, CONTRACT, NEGLIGENCE, TORT, STRICT LIABILITY OR OTHERWISE) RESULTING FROM THE USE OR HANDLING OF THIS PRODUCT, SHALL BE THE RETURN OF THE PURCHASE PRICE OF THE PRODUCT OR, AT THE ELECTION OF AGROSOURCE, INC. OR SELLER, THE REPLACEMENT OF THE PRODUCT.

AgroSource, Inc. and Seller offer this product, and Buyer and User accept it, subject to the foregoing conditions of sale and limitations of warranty and of liability, which may not be modified except by written agreement signed by a duly authorized representative of AgroSource, Inc.

Fireline is trademark of AgroSource, Inc.

#4

FlameOut™

Fungicide/Bactericide
Agricultural Terramycin

GROUP	18	FUNGICIDE

For control of Fire Blight on pear and Bacterial Spot on peach and nectarine

Active Ingredient:	
Oxytetracycline Hydrochloride*	18.30%
Related Compounds	0.17%
Other Ingredients:	81.53%
	100.00%

*Equivalent to 17% oxytetracycline

KEEP OUT OF THE REACH OF CHILDREN
WARNING/AVISO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

FIRST AID

Call a poison control center or doctor immediately for treatment advice.

If In Eyes:

- Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.

If On Skin or Clothing:

- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact Rocky Mountain Poison Control Center (303) 623-5716 for emergency medical treatment information.

EPA Reg. No. 80990-1-4581 **EPA Est. No. 39578-TX-1**

NOTICE: Read the entire Directions for Use and Conditions of Sale and Limitation of Warranty and Liability before buying or using this product. If the terms are not acceptable, return the product at once, unopened and undamaged, and the purchase price will be refunded.

Distributed by:
Cerexagri, Inc.
630 Freedom Business Center, Suite 402 • King of Prussia, PA 19406
1 800-438-6071 • www.cerexagri.com

Net Contents: _____

Cerexagri

PRECAUTIONARY STATEMENTS
Hazards To Humans & Domestic Animals

WARNING: Causes substantial but temporary eye injury. Harmful if absorbed through skin. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield or safety glasses). Do not breathe dust or spray mist. May cause allergic skin reactions. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum or using tobacco. Remove and wash contaminated clothing before reuse. This material is not to be used for medical, veterinary or human purposes.

Personal Protective Equipment (PPE):

Some materials that are chemical resistant to this product are listed below. If you want more options, follow the instructions for Category A on an EPA chemical resistant category selection chart.

Applicators and other handlers must wear:

- long-sleeved shirt
- long pants
- chemical-resistant gloves made of any waterproof material
- shoes plus socks
- protective eyewear
- NIOSH approved respirator with any N, R, P or HE filter

Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

Engineering Control Statements:

When handlers use closed systems or enclosed cabs in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240(d)(4-6)], the handler PPE requirements may be reduced or modified as specified in the WPS.

User Safety Recommendations:

Users should:

- Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.
- Remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.

Environmental Hazards

Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment washwater.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Do not apply this product through any type of irrigation system. Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirements specific to your State or Tribe, consult the agency responsible for pesticide regulation.

AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR part 170. This Standard contains requirements for the protection of agricultural workers on farms, forests, nurseries and greenhouses, and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE) and restricted entry interval. The requirements in this box apply to uses that are covered by the Worker Protection Standard.

Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours.

For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water, wear:

- Coveralls over long-sleeved shirt and long pants
- Chemical-resistant gloves made of any waterproof material
- Shoes plus socks
- Protective eyewear

Resistance Management Statements: FLAMEOUT™ fungicide/bactericide contains a Group 18 (fungicide/bactericide). Fungal isolates/bacterial strains with acquired resistance to Group 18 may eventually dominate the fungal/bacterial population if Group 18 fungicides/bactericides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by **FLAMEOUT™** fungicide/bactericide or other Group 18 products.

To delay fungicide/bactericide resistance consider:

- Avoiding the consecutive use of **FLAMEOUT™** fungicide/bactericide or other target site of action Group 18 fungicides/bactericides that have a similar target site of action, on the same pathogens.
- Using tank-mixtures or premixes with fungicide/bactericides from different target site of action Groups as long as the involved products are all registered for the same use and are both effective at the tank mix or prepack rate on the pathogen(s) of concern.
- Basing fungicide/bactericide use on a comprehensive IPM program.
- Monitoring treated fungal/bacterial populations for loss of field efficacy.
- Contacting your local extension specialist, certified crop advisors, and/or manufacturer for fungicide/bactericide resistance management and/or IPM recommendations for specific crops and resistant pathogens.

Treatment of Pears, Peaches & Nectarines:

MIXING: To avoid possible pesticide contamination, use only clean metal or plastic containers in preparing all solutions.

MIXING INSTRUCTIONS

Concentrate Desired	Quantity FLAMEOUT™ Per Volume of Water		
ppm*	50 gals.	100 gals.	500 gals.
150	6.0 oz.	12.0 oz.	3 ¾ lbs.
200	8.0 oz.	16.0 oz.	5 lbs.

*ppm = parts per million

Crop	Disease	Recommended Concentration or Rate	Use Directions
Pears	Fire Blight	200 ppm	Begin spray application at 10% bloom at a rate of 50-100 gals. of solution per acre. Repeat applications at 4 to 6 day intervals. This may involve up to 8-10 applications. Do not apply within 60 days of harvest. Use of **FLAMEOUT™** may cause phytotoxicity to the fruit and/or foliage of sensitive varieties of pears, especially Asian varieties.
Peaches & Nectarines	Bacterial Spot	150 ppm	Begin application with shuck split using a rate of 3 gallons per tree (240 gals. spray solution per acre based on 80 trees per acre). Apply spray solution to point of runoff. Gallons of spray per acre may be increased for larger trees. Do not exceed 500 gals. per acre. Use pressure sprayer capable of delivering the spray at least 250 lbs pressure per square inch through a hand-held single nozzle gun, or 150 lbs. pressure per square inch using a wind-blast sprayer. For best results with air-blast sprayer, do not exceed 3 miles per hour ground speed or 100 miles per hour spray velocity. **Note:** The spray application schedules are based on a definite biological growth period for peaches, the shuck split. Shuck split stage for peaches varies North to South by state, in individual states and by varieties. Applications are weekly after shuck split stage. This may involve up to 8 or 9 applications. Do not apply within 3 weeks of harvest.

Additional information regarding use of **FLAMEOUT™** fungicide/bactericide may be obtained from your local Agricultural Extension Agent or State Experimental Station. Use of **FLAMEOUT™** fungicide/bactericide may cause phytotoxicity to the fruit and/or foliage of sensitive varieties of pears and peaches.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Keep tightly closed and sealed. Product is moisture, temperature and light sensitive. Product is hygroscopic so protect from moisture. Store in a cool (<77°F, 25°C), dry place away from heat and open flames with minimum exposure to the atmosphere. Avoid extremes in temperature.

Pesticide Disposal: Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.

Container Disposal: Completely empty bag into application equipment. Then dispose of bag in a sanitary landfill, by incineration, or if allowed by State and local authorities, by burning. If burned, stay out of smoke.

EMERGENCY TELEPHONE NUMBERS:

CHEMTREC: (800) 424-9300

MEDICAL: (303) 623-5716 Rocky Mountain Poison Control Center

Conditions of Sale and Limitation of Warranty and Liability

The Directions for Use of this product should be followed carefully. It is impossible to eliminate all risks inherently associated with the use of this product. Crop injury, ineffectiveness or other unintended consequences may result because of such factors as manner of use or application, weather or crop conditions, presence of other materials, resistant strains or other influencing factors in the use of the product, which are beyond the control of Cerexagri, Inc. or Seller. All such risks shall be assumed by Buyer and User, and Buyer and User agree to hold Cerexagri, Inc. and Seller harmless for any claims relating to such factors.

Cerexagri, Inc. warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes stated in the Directions for Use, subject to the inherent risks referred to above, when used in accordance with directions under normal use conditions. This warranty does not extend to the use of the product contrary to label instructions, or under abnormal conditions or under conditions not reasonably foreseeable to or beyond the control of Seller or Cerexagri, Inc., and Buyer and User assume the risk of any such use. CEREXAGRI, INC. MAKES NO WARRANTIES OF MERCHANTABILITY OR OF FITNESS FOR A PARTICULAR PURPOSE NOR ANY OTHER EXPRESS OR IMPLIED WARRANTY EXCEPT AS STATED ABOVE.

In no event shall Cerexagri, Inc. or Seller be liable for any incidental, consequential or special damages resulting from the use or handling of this product. THE EXCLUSIVE REMEDY OF THE USER OR BUYER, AND THE EXCLUSIVE LIABILITY OF CEREXAGRI, INC. AND SELLER FOR ANY AND ALL CLAIMS, LOSSES, INJURIES OR DAMAGES (INCLUDING CLAIMS BASED ON BREACH OF WARRANTY, CONTRACT, NEGLIGENCE, TORT, STRICT LIABILITY OR OTHERWISE) RESULTING FROM THE USE OR HANDLING OF THIS PRODUCT, SHALL BE THE RETURN OF THE PURCHASE PRICE OF THE PRODUCT OR, AT THE ELECTION OF CEREXAGRI, INC. OR SELLER, THE REPLACEMENT OF THE PRODUCT.

Cerexagri, Inc. and Seller offer this product, and Buyer and User accept it, subject to the foregoing conditions of sale and limitations of warranty and of liability, which may not be modified except by written agreement signed by a duly authorized representative of Cerexagri, Inc.

Cerexagri, Inc. is a wholly-owned subsidiary of Arkema Inc.

FlameOut is a trademark of Cerexagri, Inc.

80990-1-4581(031805-1522)

#5

FlameOut™

Fungicide/Bactericide
Agricultural Oxytetracycline

GROUP	18	FUNGICIDE

For control of Fire Blight on pear and Bacterial Spot on peach and nectarine

Active Ingredient:

Oxytetracycline Hydrochloride*	18.30%
Related Compounds	0.17%
Other Ingredients:	81.53%
	100.00%

*Equivalent to 17% oxytetracycline

KEEP OUT OF THE REACH OF CHILDREN

WARNING/AVISO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

FIRST AID

Call a poison control center or doctor immediately for treatment advice.

If In Eyes:

- Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye.

If On Skin or Clothing:

- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact Rocky Mountain Poison Control Center (303) 623-5716 for emergency medical treatment information.

EPA Reg. No. 80990-1-82695 **EPA Est. No. 39578-TX-1**

NOTICE: Read the entire Directions for Use and Conditions of Sale and Limitation of Warranty and Liability before buying or using this product. If the terms are not acceptable, return the product at once, unopened and undamaged, and the purchase price will be refunded.

Sold by:
Cerexagri-Nisso LLC
630 Freedom Business Center • Suite 402
King of Prussia, PA 19406
1 800-438-6071 • www.cerexagri-nisso.com

Net Contents: _____

Cerexagri-Nisso LLC

PRECAUTIONARY STATEMENTS
Hazards To Humans & Domestic Animals

WARNING: Causes substantial but temporary eye injury. Harmful if absorbed through skin. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield or safety glasses). Do not breathe dust or spray mist. May cause allergic skin reactions. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum or using tobacco. Remove and wash contaminated clothing before reuse. This material is not to be used for medical, veterinary or human purposes.

Personal Protective Equipment (PPE):

Some materials that are chemical resistant to this product are listed below. If you want more options, follow the instructions for Category A on an EPA chemical resistant category selection chart.

Applicators and other handlers must wear:

- long-sleeved shirt
- long pants
- chemical-resistant gloves made of any waterproof material
- shoes plus socks
- protective eyewear
- NIOSH approved respirator with any N, R, P or HE filter

Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

Engineering Control Statements:

When handlers use closed systems or enclosed cabs in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240(d)(4-6)], the handler PPE requirements may be reduced or modified as specified in the WPS.

User Safety Recommendations:

Users should:

- Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.
- Remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.

Environmental Hazards

Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment washwater.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Do not apply this product through any type of irrigation system. Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirements specific to your State or Tribe, consult the agency responsible for pesticide regulation.

AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR part 170. This Standard contains requirements for the protection of agricultural workers on farms, forests, nurseries and greenhouses, and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE) and restricted entry interval. The requirements in this box apply to uses that are covered by the Worker Protection Standard.

Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours.

For early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil or water, wear:

- Coveralls over long-sleeved shirt and long pants
- Chemical-resistant gloves made of any waterproof material
- Shoes plus socks
- Protective eyewear

Resistance Management Statements: **FLAMEOUT™** fungicide/bactericide contains a Group 18 (fungicide/bactericide). Fungal isolates/bacterial strains with acquired resistance to Group 18 may eventually dominate the fungal/bacterial population if Group 18 fungicides/bactericides are used repeatedly in the same field or in successive years as the primary method of control for targeted species. This may result in partial or total loss of control of those species by **FLAMEOUT™** fungicide/bactericide or other Group 18 products.

To delay fungicide/bactericide resistance consider:

- Avoiding the consecutive use of **FLAMEOUT™** fungicide/bactericide or other target site of action Group 18 fungicides/bactericides that have a similar target site of action, on the same pathogens.

  Using tank-mixtures or premixes with fungicide/bactericides from different target site of action Groups as long as the involved products are all registered for the same use and are both effective at the tank mix or prepack rate on the pathogen(s) of concern.
- Basing fungicide/bactericide use on a comprehensive IPM program.
- Monitoring treated fungal/bacterial populations for loss of field efficacy.
- Contacting your local extension specialist, certified crop advisors, and/or manufacturer for fungicide/bactericide resistance management and/or IPM recommendations for specific crops and resistant pathogens.

Treatment of Pears, Peaches & Nectarines:

MIXING: To avoid possible pesticide contamination, use only clean metal or plastic containers in preparing all solutions.

MIXING INSTRUCTIONS

Concentrate Desired	Quantity FLAMEOUT™ Per Volume of Water		
ppm*	50 gals.	100 gals.	500 gals.
150	6.0 oz.	12.0 oz.	3 ¾ lbs.
200	8.0 oz.	16.0 oz.	5 lbs.

*ppm = parts per million

Crop	Disease	Recommended Concentration or Rate	Use Directions
Pears	Fire Blight	200 ppm	Begin spray application at 10% bloom at a rate of 50-100 gals. of solution per acre. Repeat applications at 4 to 6 day intervals. This may involve up to 8-10 applications. Do not apply within 60 days of harvest. Use of **FLAMEOUT™** may cause phytotoxicity to the fruit and/or foliage of sensitive varieties of pears, especially Asian varieties.
Peaches & Nectarines	Bacterial Spot	150 ppm	Begin application with shuck split using a rate of 3 gallons per tree (240 gals. spray solution per acre based on 80 trees per acre). Apply spray solution to point of runoff. Gallons of spray per acre may be increased for larger trees. Do not exceed 500 gals. per acre. Use pressure sprayer capable of delivering the spray at least 250 lbs pressure per square inch through a hand-held single nozzle gun, or 150 lbs. pressure per square inch using a wind-blast sprayer. For best results with air-blast sprayer, do not exceed 3 miles per hour ground speed or 100 miles per hour spray velocity. **Note:** The spray application schedules are based on a definite biological growth period for peaches, the shuck split. Shuck split stage for peaches varies North to South by state, in individual states and by varieties. Applications are weekly after shuck split stage. This may involve up to 8 or 9 applications. Do not apply within 3 weeks of harvest.

Additional information regarding use of **FLAMEOUT™** fungicide/bactericide may be obtained from your local Agricultural Extension Agent or State Experimental Station.

Use of **FLAMEOUT™** fungicide/bactericide may cause phytotoxicity to the fruit and/or foliage of sensitive varieties of pears and peaches.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Keep tightly closed and sealed. Product is moisture, temperature and light sensitive. Product is hygroscopic so protect from moisture. Store in a cool (<77°F, 25°C), dry place away from heat and open flames with minimum exposure to the atmosphere. Avoid extremes in temperature.

Pesticide Disposal: Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.

Container Disposal: Completely empty bag into application equipment. Then dispose of bag in a sanitary landfill, by incineration, or if allowed by State and local authorities, by burning. If burned, stay out of smoke.

EMERGENCY TELEPHONE NUMBERS:

CHEMTREC: (800) 424-9300

MEDICAL: (303) 623-5716 Rocky Mountain Poison Control Center

Conditions of Sale and Limitation of Warranty and Liability

The Directions for Use of this product should be followed carefully. It is impossible to eliminate all risks inherently associated with the use of this product. Crop injury, ineffectiveness or other unintended consequences may result because of such factors as manner of use or application, weather or crop conditions, presence of other materials, resistant strains or other influencing factors in the use of the product, which are beyond the control of Cerexagri-Nisso LLC, Manufacturer or Seller. All such risks shall be assumed by Buyer and User, and Buyer and User agree to hold Cerexagri-Nisso LLC, Manufacturer and Seller harmless for any claims relating to such factors. Cerexagri-Nisso LLC warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes stated in the Directions for Use, subject to the inherent risks referred to above, when used in accordance with directions under normal use conditions. This warranty does not extend to the use of the product contrary to label instructions, or under abnormal conditions or under conditions not reasonably foreseeable to or beyond the control of the Seller, Manufacturer or Cerexagri-Nisso LLC, and Buyer and User assume the risk of any such use. CEREXAGRI-NISSO LLC AND MANUFACTURER MAKE NO WARRANTIES OF MERCHANTABILITY OR OF FITNESS FOR PARTICULAR PURPOSE NOR ANY OTHER EXPRESS OR IMPLIED WARRANTY EXCEPT AS STATED ABOVE.

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