Hydrogen Peroxide

Crops

Identification of Petitioned Substance

Chemical Names:
Hydrogen Peroxide

Other Name:
Dihydrogen Dioxide

Trade Names:
OxiDate®, SaniDate®

CAS Numbers:
7722-84-1

Other Codes:
231-765-0 (EINECS No.)

Summary of Petitioned Use

The National Organic Program (NOP) final rule currently allows the use of hydrogen peroxide in organic crop production under 7 CFR §205.601(a)(4) as an algicide, disinfectant, and sanitizer, as well as 7 CFR §205.601(i)(5) for plant disease control as a fungicide. This report provides targeted technical information and augments the 1995 Technical Advisory Panel Report on hydrogen peroxide for the National Organic Standards Board's sunset review of the substance.

Characterization of Petitioned Substance

Composition of the Substance:

Hydrogen peroxide is a small inorganic molecule comprised of two hydrogen atoms and two oxygen atoms with a molecular formula of H_2O_2. As a peroxy compound, hydrogen peroxide contains a highly reactive oxygen-oxygen single bond (Figure 1). Although modern manufacturing practices allow the production of pure hydrogen peroxide, the substance is sold for most agricultural, industrial and residential uses as a solution in water. Hydrogen peroxide fungicides are typically formulated as concentrates (approximately 30% H_2O_2) and diluted with water to generate working solutions of 0.01–0.3% H_2O_2 (US EPA, 2014).

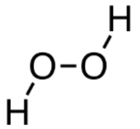


Figure 1. Hydrogen Peroxide Structural Formula

Source or Origin of the Substance:

Commercially available hydrogen peroxide is industrially produced using the anthraquinone autoxidation (AO) process. The AO method involves initial catalytic reduction of an alkyl anthraquinone with hydrogen to form the corresponding hydroquinone. Subsequent autoxidation of the hydroquinone intermediate in air regenerates the anthraquinone with concomitant liberation of hydrogen peroxide (Goor, 2007). As shown in equation 1, the simplified overall reaction involves direct combination of gaseous hydrogen (H_2) and oxygen (O_2). See Evaluation Question #2 for details regarding the anthraquinone AO process, older production methods, and developing technologies for hydrogen peroxide synthesis.

$$H_2 + O_2 \rightarrow H_2O_2 \qquad \text{(equation 1)}$$

Properties of the Substance:

Hydrogen peroxide is a weakly acidic, nearly colorless and clear liquid with solubility in water at all proportions. The hydrogen and oxygen atoms within the hydrogen peroxide molecule are covalently bound in a nonpolar H–O–O–H structure having association (hydrogen bonding) somewhat less than that found in water. Table 1 below summarizes the chemical and physical properties for hydrogen peroxide.

Table 1. Physical and Chemical Properties for Hydrogen Peroxide.

Property	Description
Molecular formula	H_2O_2
Molecular weight (g/mol)	34.01
Color/Form	Colorless liquid
Odor	Odorless, or having an odor resembling that of ozone
Melting point (°C)	–0.43
Boiling point (°C)	150–152
Dissociation Constant (pKa)	11.75
Relative density of pure H_2O_2 at 20 °C (g/mL)	1.45
Relative density of 50% H_2O_2 in water at 20 °C (g/mL)	1.20
Water Solubility at 25°C (g/L)	1,000
Organic Solubility	Soluble in ether and alcohol (i.e., ethanol), insoluble in petroleum ether
Octanol-water partition coefficient (K_{ow})	0.032
Soil organic carbon-water partition coefficient (K_{oc}) (calculated from K_{ow}; dimensionless)	0.2
Photoreactivity and Thermal Stability	Stable up to relatively high temperature, not stable to sunlight
Oxidation/Reduction	H_2O_2 is capable of oxidizing metals, metal ions, organic and inorganic compounds
Corrosion Characteristics	Corrosive to metals like copper and steel but not to aluminum
Vapor pressure at 25 °C (mm Hg)	1.97
Henry's Law Constant at 25 °C (atm•m³/mol)	7.04×10^{-9}
Viscosity at 25 °C (cP)	1.01

Data Sources: US EPA, 2009a; Goor, 2007; HSDB, 2005; EC, 2003; Eul, 2001
cP = centiPoise, equivalent to millipascals seconds (mPa•s)

Specific Uses of the Substance:

Hydrogen peroxide and other biopesticidal peroxy compounds are used as algicides and fungicides in greenhouses and horticultural settings, applied to greenhouse structures and surfaces as well as greenhouse seeds, soils and plants (US EPA, 2009b). The substance is also used in some turf and orchard settings. As a broad-spectrum fungicide, hydrogen peroxide pesticide products are applied for the prevention and control of plant pathogenic diseases. Hydrogen peroxide products may be used as a pre-plant dip treatment for root disease and stem rot disease caused by *Pythium*, *Phytophthora*, *Rhizoctonia*, *Fusarium* or *Thielaviopsis* on seeds, seedlings, bulbs or cuttings; soil drench for the control of soil-borne plant at the time of seeding or transplanting, as well as a preventative treatment throughout the plant's life; and a foliar treatment for field grown crops, crops grown in commercial greenhouses or crops grown in other similar sites (BioSafe, 2010).

The OxiDate® product label and agricultural extension resources indicate that hydrogen peroxide treatments may be effective in preventing or controlling late-season outbreaks of grape diseases, such as powdery mildew, downy mildew and bunch rot (BioSafe, 2010; Schilder, 2011). Indeed, hydrogen peroxide is particularly effective against fungal diseases on plant surfaces, including powdery mildew, because the substance only contacts the surface of infected plants and not deeper into infected plant tissues. Hydrogen peroxide has also been employed in organic apple production to combat the fungus *Venturia inaequalis*, the pathogen responsible for apple scab disease (Phillips, 2005). Likewise, hydrogen peroxide has been included in lists of alternative substances for downy mildew control in cucurbits (Kuepper, 2003). In addition to field and greenhouse applications, hydrogen peroxide provides control of postharvest diseases of strawberries and oranges, such as *Botrytis cinerea*, *Rhizopus stolonifer*, *Penicillium digitatum*, and *Penicillium italicum* (El-Mougy, 2008), as well as pink rot of potato fungus, *Phytophthora erythroseptica* (Al-Mughrabi, 2006). Some greenhouse managers also use hydrogen peroxide in irrigation water recirculation systems to prevent the spread of soil borne disease organisms (Newman, 2004).

Hydrogen peroxide is also found in numerous health care and consumer products. According to the Centers for Disease Control and Prevention, "commercially available 3% hydrogen peroxide is a stable and effective disinfectant when used on inanimate surfaces," and is used at concentrations of 3–6% for spot-disinfecting ventilators, endoscopes and fabrics in patients' rooms (CDC, 2008). The substance is also used as a topical disinfectant and antimycotic to sterilize contact lenses. Small amounts of hydrogen peroxide are used in cosmetic preparations such as hair colorations and bleaching formulations. Indeed, hydrogen peroxide is the active ingredient in color-safe household bleaches and carpet and hard-surface cleaners. Hydrogen peroxide and other inorganic peroxo compounds are commonly employed as peroxide sources in oral hygiene and teeth whitening products. Topical solutions containing 3% hydrogen peroxide are sold as over-the-counter drugs for antisepsis and disinfection in the United States (Eul, 2001).

Beyond agriculture, disinfection and residential use, hydrogen peroxide is also used in a variety of industrial processes. Hydrogen peroxide is used in the textile industry for bleaching cotton, linen, bast fiber (soft, woody fiber obtained from plant stems), wool, silk, polyester fiber and polyurethane fiber. Likewise, the substance is used to bleach sulfate and sulfite cellulose, wood pulp, and wastepaper, and to brighten wood veneers and wooden structures in the pulp and paper industry. The chemical industry employs hydrogen peroxide for the production of peroxy compounds, such as sodium perborate, sodium percarbonate, metallic peroxides, or percarboxylic acids. In organic chemistry, hydrogen peroxide is used for epoxidation and hydroxylation (manufacture of plasticizers and stablizers for the plastics industry), oxidation (manufacture of amine oxides as surfactants for detergents), oxohalogenation, and initiation of polymerization. BASF and Dow Chemical Company recently developed a process for the production of propylene oxide (C_3H_6O) using hydrogen peroxide. Lastly, hydrogen peroxide is used to polish copper, brass and other copper alloys; for etching and cleaning printed circuit boards; to clean silicon wafers used in the manufacture of silicon semiconductors; for *in situ* leaching in underground uranium mining; and for environmental protection applications (i.e., to detoxify mining wastewater effluents and deodorize sulfur-containing effluents) (Eul, 2001; Goor, 2007).

Approved Legal Uses of the Substance:

The US Environmental Protection Agency (US EPA) first registered pesticidal hydrogen peroxide products for use in the United States in 1977 (US EPA, 2009b). Based on a recent search of the Pesticide Product Information System (PPIS), there are currently 164 registered formulations containing hydrogen peroxide as an active ingredient (US EPA, 2014). In agriculture, hydrogen peroxide pesticides are used primarily as microbiocides on a variety of agricultural use sites, such as greenhouses, horticultural establishments and some orchards. Currently registered hydrogen peroxide products are labeled as algicides, antifoulants, bacteriocides/bacteriostats, disinfectants, fungicides/fungistats, nematicides, microbiocides/microbiostats, molluscicides, sporicides, sanitizers, sterilizers, tuberculocides and virucides. Most if not all of the fungicides containing hydrogen peroxides are also registered for antimicrobial use patterns (US EPA, 2009b). According to 40 CFR 180.1197, an exemption from the requirement of a tolerance has been established for residues of hydrogen peroxide in or on all food commodities at the rate of less than or equal to one percent ($\leq 1\%$) hydrogen peroxide per application on growing and postharvest crops.

In the United States, the Food and Drug Administration (FDA) has established legal uses of hydrogen peroxide in food, cosmetic and drug products. According to a recent Agency response, FDA believes that most peroxide-containing tooth whiteners would meet the definition of a cosmetic under the Food, Drug and Cosmetic (FD&C) Act, but acknowledged that some of these products may be regarded as drugs (FDA, 2014). FDA postponed a final decision on the status of peroxide-based tooth whitening products since "a better understanding of the mechanisms of action, conditions of use, safety, and formulation of specific peroxide-containing tooth whitener products is necessary to determine whether such products also meet the definition of drug under the FD&C Act" (FDA, 2014). For the time being, FDA will continue using a case-by-case regulatory approach based on the claims associated with individual whitening products

(Gaffney, 2014). Hydrogen peroxide is an FDA-approved indirect food additive allowed for use only as a component of adhesives (21 CFR 175.105). The substance is also Generally Recognized as Safe (GRAS) when used as a bleaching agent in animal drugs, feeds and related products in accordance with good manufacturing or feeding practice (21 CFR 582.1366). According to 21 CFR 184.1366, hydrogen peroxide is a direct food additive affirmed as GRAS when the ingredient is used to treat food only within the following limitations:

- **Milk** – For use during the cheesemaking process as permitted in the appropriate standards of identify for cheese and related cheese products at a maximum treatment level of 0.05%,
- **Whey** – For use during the preparation of modified whey by electrodialysis methods at a maximum treatment level of 0.04%,
- **Dried eggs, dried egg whites, and dried egg yolks** – Oxidizing and reducing agent in an amount sufficient for the purpose,
- **Tripe** – Bleaching agent,
- **Beef feet** – Bleaching agent,
- **Herring** – Bleaching agent,
- **Wine** – Oxidizing and reducing agent in an amount sufficient for the purpose,
- **Starch** – Antimicrobial agent at a maximum treatment level of 0.15%,
- **Instant tea** – Bleaching agent in an amount sufficient for the purpose,
- **Corn syrup** – Used to reduce sulfur dioxide levels in the finished corn syrup at a maximum treatment level of 0.15%,
- **Colored (annatto) cheese whey** – Bleaching agent at a maximum treatment level of 0.05%,
- **Wine vinegar** – Used to remove sulfur dioxide from wine prior to fermentation to produce vinegar at an amount sufficient for the purpose,
- **Emulsifiers containing fatty acid esters** – Bleaching agent at a maximum treatment level of 1.25%.

Action of the Substance:

As a pesticide class, fungicides kill by damaging cell membranes, inactivating critical enzymes or proteins, and/or interfering with key metabolic processes such as respiration. Specialized plant enzymes known as peroxidases produce hydrogen peroxide for disease control, and are associated with fungal cell wall degradation and plant defense signaling as part of the Salicylic Acid pathway (Matheron, 2001). In general, hydrogen peroxide works by producing destructive hydroxyl free radicals that can attack membrane lipids, DNA and other essential cell components (CDC, 2008). Catalase enzymes produced by aerobic organisms and facultative anaerobes that possess cytochrome systems can protect cells from metabolically produced hydrogen peroxide by degrading the substance to water and oxygen. This defense mechanism is overwhelmed by the concentration used for disinfection or, in the case of agriculture, fungicidal applications to crops and soils (CDC, 2008).

Combinations of the Substance:

Various active and inert ingredients may be added to commercially available fungicides and disinfectants containing hydrogen peroxide. Sixty-eight out of the 164 currently registered pesticide products containing hydrogen peroxide also contain peroxyacetic acid as an active ingredient at concentrations ranging from 0.08 to 15.2 percent (US EPA, 2014). According to USDA organic regulations, peroxyacetic acid is permitted in hydrogen peroxide formulations at a concentration of no more than 6% as indicated on the pesticide product label (7 CFR 205.601(a)(6) and (i)(8)). The active ingredients hydrogen peroxide, peroxyacetic acid and caprylic acid are co-formulated in a small number of commercial disinfectant products. Mono- and di-potassium salts of phosphorous acid are co-formulated with hydrogen peroxide as the active ingredients in one broad-spectrum fungicide product. Other active substances that are combined with hydrogen peroxide in registered disinfectants include quaternary ammonium compounds (e.g., alkyl dimethyl ethylbenzyl ammonium chloride), sodium nonanoyloxybenzene sulfonate, and metallic silver (US EPA, 2014).

The labels of most registered fungicides and disinfectants containing hydrogen peroxide list "other ingredients" for the inert portion of the formulation. Water is the primary inert ingredient in hydrogen peroxide pesticide products. In addition, a small number of product labels list salicylic acid and phosphoric acid (two products), benzyl alcohol (two products), acetic acid (one product), and citric acid and 1-(1-

butoxypropan-2-yloxy)propan-2-ol (one product) as formulated inert ingredients (US EPA, 2014). Product formulations are considered confidential business information, and companies may reformulate products following the registration process. As a result, it is not always possible to know the identity of adjuvants and other inert ingredients used in formulated products.

Status

Historic Use:

The US Environmental Protection Agency (US EPA) first registered pesticidal hydrogen peroxide products for use in the United States in 1977 (US EPA, 2009b). Since its registration, hydrogen peroxide has been formulated in an increasing number of pesticide products, with 164 hydrogen peroxide disinfectants and fungicides currently registered for use (US EPA, 2014). Historically, agricultural disinfectants containing hydrogen peroxide have been used for the disinfection of livestock housing surfaces and production equipment, production surfaces in greenhouses, crop production equipment, water storage tanks, irrigation lines and food contact surfaces in processing facilities. Hydrogen peroxide fungicide solutions have been used as foliar sprays, soil drenches and seed treatments for annual (e.g., cucurbits) and perennial (e.g., grapes, apples) crops in field and greenhouse settings (US EPA, 2014).

Organic Foods Production Act, USDA Final Rule:

USDA organic regulations currently allow the use of hydrogen peroxide in organic crop production under 7 CFR §205.601(a)(4) as an algicide, disinfectant and sanitizer, and under 7 CFR §205.601(i)(5) for plant disease control as a fungicide. Likewise, hydrogen peroxide is also permitted for use in organic livestock production as a disinfectant, sanitizer and medical treatment (7 CFR 205.603(a)(13)). Lastly, synthetic hydrogen peroxide may be used as an ingredient in or on processed products labeled as “organic” or “made with organic (specified ingredients or food group(s)).” (7 CFR 205.605(b)).

International

A subset of the international organizations surveyed have provided guidance on the application of hydrogen peroxide for disinfection and plant disease control in organic crop production. Among these are regulatory agencies (EU and Canada) and independent organic standards organizations (IFOAM and The Soil Association). International organic regulations and standards concerning hydrogen peroxide are described in the following sub-sections.

Canadian General Standards Board

The Canadian General Standards Board allows numerous uses of hydrogen peroxide in organic production. Under Section 4.3: “Crop production aids and materials,” hydrogen peroxide is not allowed in maple syrup production, but is allowed for use as a fungicide. Section 5.3: “Health care and production aids for livestock production” lists pharmaceutical grade hydrogen peroxide for external use as a disinfectant, and food-grade hydrogen peroxide for internal use (e.g., livestock drinking water). Hydrogen peroxide is also listed in Section 7.3: “Food-grade cleaners, disinfectants and sanitizers” that are allowed without mandatory removal of residues, and 7.4: “Cleaners, disinfectants and sanitizers allowed on food contact surfaces including equipment, provided that substances are removed from food contact surfaces prior to organic production” (CAN, 2011).

European Union

According to Annex VII of EU regulation 889/2008, hydrogen peroxide is allowed for cleaning and disinfection of buildings and installations for animal production. Specifically, hydrogen peroxide can be used to satisfy Article 23 (4), which states that “housing, pens, equipment and utensils shall be properly cleaned and disinfected to prevent cross-contamination and the buildup of disease carrying organisms.” Hydrogen peroxide is also permitted for use in the production of gelatin under Section B of Annex VIII: Products and substances for use in production of processed organic food (EC, 2008).

International Federation of Organic Agriculture Movements

Hydrogen peroxide is permitted under Appendix 4 – Table 2 of the IFOAM Norms as an equipment cleanser and disinfectants. In addition, Appendix 5 lists hydrogen peroxide as an approved substance for pest and disease control and disinfection in livestock housing and equipment (IFOAM, 2014). The Norms make not mention of hydrogen peroxide for plant disease control and prevention.

UK Soil Association

The Soil Association standards permit the use of hydrogen peroxide only as a cleaning product for livestock housing areas. No conditions are provided allowing the use of hydrogen peroxide for plant disease control and prevention (Soil Association, 2014).

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

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

(A) The primary use patterns reviewed in this report are the fungicidal applications of hydrogen peroxide. Hydrogen peroxide is also considered an equipment cleanser due to its permitted use as an algicide, disinfectant and sanitizer in organic crop (7 CFR 205.601(a)(4)) and livestock (7 CFR 205.603(a)(13)) production. In fact, OMRI has approved several "cleaning agents" and "equipment cleansers for farms" that contain hydrogen peroxide as the active ingredient.

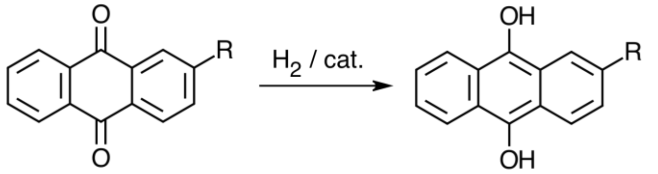
(B) Hydrogen peroxide is the active substance in several commercial disinfectant and fungicide products, and is therefore not considered an inert ingredient.

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

Virtually all modern production facilities manufacture commercial hydrogen peroxide solutions using large, strategically located anthraquinone autoxidation processes (Eul, 2001). Indeed, improved production methods and facilities based on the anthraquinone (AO) process have recently appeared in the commercial patent literature (Solvay, 2013).

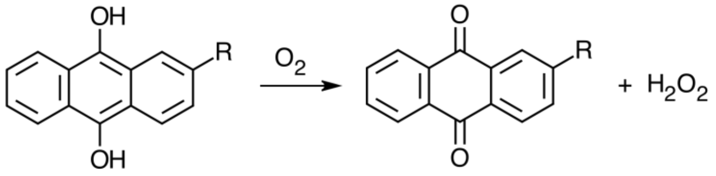
In the AO process, 2-alkyl-9,10-anthraquinones react with hydrogen (H_2) in the presence of a transition metal catalyst such as palladium or Raney nickel to form the corresponding hydroquinones (equation 2). Alkyl groups commonly employed in these anthraquinone systems include 2-ethyl, 2-isopropyl, 2-*sec* butyl, 2-*tert* butyl, 2-*sec* amyl, 1,3-dimethyl, 2,3-dimethyl, 1,4-dimethyl, and 2,7-dimethyl, among others (Porter, 1961). Following hydrogenation and removal of the metal catalyst, the hydroquinones are oxidized back to quinones with oxygen (usually air) with simultaneous quantitative formation of hydrogen peroxide (equation 3). Hydrogen peroxide is then extracted from the reaction mixture with water, and the quinones are returned to the hydrogenator to complete another round of the catalytic cycle (Goor, 2007). Therefore, AO processes lead to the net formation of hydrogen peroxide from gaseous hydrogen (H_2) and molecular oxygen (O_2).

Fixed bed catalyst systems have also been developed for the AO process. This enhancement involves incorporation of the transition metal catalyst into a fixed bed using a catalyst carrier/support (carbon, magnesium carbonate, silicon carbide, aluminum oxide, etc.) in contrast to other industrial processes using hydrogenation catalysts suspended within the reaction mixture. It generally involves a palladium catalyst and avoids the problem of filtration and recirculation of catalyst into the reaction between the hydrogenation and oxidation steps of the AO process. In addition, fixed catalysts reduce contact time between the reaction mixture and the hydrogenation catalyst, thereby minimizing undesired reduction reactions within the anthraquinone molecule (Porter, 1961).



(equation 2)

R = alkyl



(equation 3)

Solvent mixtures are almost always used to facilitate hydrogenation, oxidation and hydrogen peroxide extraction in the AO process because quinones and hydroquinones have different solubilities. Quinones dissolve readily in nonpolar, aromatic solvents (i.e., quinone solvents), while hydroquinones dissolve well in polar solvents, such as alcohols and esters (i.e., hydroquinone solvents). It is also important for the quinone and hydroquinone solvents to have low solubility in water and aqueous hydrogen peroxide solutions, as well as sufficiently lower density than water to encourage separation of the two phases during the extraction of hydrogen peroxide from the reaction mixture. Example quinone/hydroquinone solvent mixtures that have been utilized in the AO process include polyalkylated benzenes with alkyl phosphates, polyalkylated benzenes with tetraalkyl ureas, trimethylbenzenes with alkylcyclohexanol esters, and methylnaphthalene with nonyl alcohols (Goor, 2007).

The aqueous hydrogen peroxide produced following the extraction with water is impure. The crude product may be treated with polyethylene, activated carbon, ion exchangers or hydrocarbons to reduce the amount of dissolved organic compounds in hydrogen peroxide solutions. Water-soluble organic compounds are removed through oxidation (heating) followed by extraction with a suitable solvent (e.g., the quinone solvent). The purified crude hydrogen peroxide product is then fed to a distillation unit where it is purified further and concentrated to the usual commercial concentration of 50–70% by weight hydrogen peroxide. Reverse osmosis membranes can also be used to purify crude, distilled or concentrated (up to 70%) hydrogen peroxide (Goor, 2007).

Hydrogen peroxide can also be produced synthetically from compounds that contain the peroxy group; from water and oxygen by thermal, photochemical, or electrochemical processes; and by the uncatalyzed reaction of molecular oxygen with certain hydrogen-containing chemicals. Prior to industrialization of the AO process, hydrogen peroxide was commercially produced using the reaction of barium peroxide or sodium peroxide with an acid, the electrolysis of sulfuric acid and related compounds, and the autoxidation of isopropyl alcohol (Eul, 2001; Goor, 2007). In addition, systems for the direct synthesis of hydrogen peroxide from hydrogen (H_2) and oxygen (O_2) using finely dispersed catalysts have been developed, and companies continue to patent systems based on this methodology (Reuter, 2006). However, it is unlikely that any of these direct addition processes have achieved industrial-scale status (Goor, 2007).

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

According to USDA organic regulations, the NOP defines synthetic as "a substance that is formulated or manufactured by a chemical process or by a process that chemically changes a substance extracted from naturally occurring plant, animal, or mineral sources" (7 CFR 205.2). Hydrogen peroxide is a naturally occurring inorganic compound; however, the sources of hydrogen peroxide used in commercial fungicides, disinfectants and antiseptic products are produced through chemical synthesis. Indeed, industrial methods for the preparation of hydrogen peroxide are categorized as oxidation-reduction reactions. Modern commercial methods for hydrogen peroxide synthesis involve the transition-metal catalyzed chemical reduction of an alkyl anthraquinone with hydrogen (H_2) gas to the corresponding hydroquinone followed by regenerative oxidation of the latter species in air. We therefore conclude that hydrogen peroxide used for plant disease control is a synthetic substance based on NOP definition and the use of synthetic chemical reagents, catalysts and solvent in the production process. See the discussion in Evaluation Quesiton #2 for details regarding the anthraquinone autoxidation (AO) method.

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

Hydrogen peroxide is inherently unstable due to the weak peroxide (O–O) bond. At typical pesticide concentrations, hydrogen peroxide is expected to degrade rapidly to water and oxygen (US EPA, 2007). This section provides technical information on the fate, transport and persistence of hydrogen peroxide in the terrestrial, aquatic and atmospheric compartments of the environment.

When used as a fungicide, hydrogen peroxide is likely to contact soils under a variety of environmental conditions. Hydrogen peroxide degrades with an anaerobic (without oxygen) soil half-life of four hours in soils containing petroleum (US EPA, 2007). It was also found that soil texture, pH and temperature had little impact on the observed degradation rate. Under aerobic (with oxygen) soil conditions, dilute solutions of hydrogen peroxide degrade with a half-life of 1.4 hours. These results were extrapolated to an aerobic soil half-life of seven hours for concentrated solutions of hydrogen peroxide. Since the substance has physical properties very similar to those of water, hydrogen peroxide is unlikely to preferentially bind to soils when used in agricultural production (US EPA, 2007). Further, the calculated soil organic carbon-water partition coefficient (K_{oc}) of 0.2 suggests that hydrogen peroxide will be highly mobile in soils. The Henry's Law constant for hydrogen peroxide indicates that volatilization of the substance from moist soils and surface water is expected to be low (EC, 2003).

When released to water, hydrogen peroxide should be rapidly consumed through biodegradation and photolysis. The half-life of hydrogen peroxide metabolism in water generally decreases with increasing size of the microbial populations in the receiving water. Consequently, hydrogen peroxide degradation half-lives in natural waters range from a few hours to several days. Degradation in water is also catalyzed by transition metals, including iron, copper, manganese, and chromium (Goor, 2007). In one study, 20% of the applied hydrogen peroxide degraded (DT_{20}) within 25–35 minutes in seawater. Hydrogen peroxide degrades with a half-life of 1.1–5.3 hours under non-sterile aerobic aquatic conditions; however, the half-life increased to 80 hours under sterile aquatic conditions (US EPA, 2007). When microbial degradation is possible, direct photolysis is unlikely to be the primary mechanism for aquatic decomposition of hydrogen peroxide (Goor, 2007). Hydrogen peroxide is not expected to bioaccumulate in aquatic organisms due to its low octanol-water partition coefficient (K_{ow}) of 0.032 (US EPA, 2007).

Degradation of hydrogen peroxide released to the atmosphere is primarily a result of indirect photolysis reactions with smaller contributions from direct photolysis and chemical reaction with organic substances. Indirect photolysis is due to sensitization by secondary reactions with OH and O_2 radicals and organic substances. The most significant of these indirect degradation reactions is the reaction of hydrogen peroxide with the hydroxyl (OH) radical. Direct hydrogen peroxide photolysis is initiated at wavelengths of 280–380 nanometers (nm) with an estimated half-life of approximately two days. Light, oxygen, ozone, hydrocarbons and free radicals in the atmosphere mediate hydrogen peroxide formation and release to the atmosphere, likely at a significantly greater rate than the agricultural uses of the substance (Goor, 2007; Eul, 2001). Considering the various atmospheric degradation pathways, the overall tropospheric half-life of hydrogen peroxide is estimated to be 10–24 hours (Goor, 2007; EC, 2003).

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

Multiple EPA terrestrial effects characterizations have evaluated the toxicity of hydrogen peroxide and other "peroxy compounds" to mammals and birds. Studies submitted by the registrants indicate that hydrogen peroxide solutions used in pesticide products are corrosive to washed and unwashed eyes, as well as exposed skin (i.e., Toxicity Category I for eye and skin irritation). The acute systemic toxicity of hydrogen peroxide products depends upon the formulation; specifically, products formulated as mixtures of hydrogen peroxide and peroxyacetic acid are generally more toxic than those containing hydrogen peroxide alone. Results of the acute toxicity studies indicate that formulated hydrogen peroxide products are slightly to moderately toxic to rats (Toxicity Category II to III) via the oral, dermal and inhalation routes of exposure, with lower levels of toxicity observed for hydrogen peroxide alone. In addition, the results of a skin sensitization study suggest that hydrogen peroxide formulations are not likely to be a sensitizer in mammals (US EPA, 1993; US EPA, 2009c). The product label for OxiDate (27% hydrogen peroxide) carries a danger warning and the following precautionary statement (BioSafe, 2010):

> *Corrosive. Causes irreversible eye damage. May be fatal if swallowed or absorbed through the skin. Causes skin burns or temporary discoloration on exposed skin. Do not breathe vapor. Do not get in eyes, on skin or on clothing. Wear protective eyewear such as goggles or face shield. Wash thoroughly with soap and water after handling. Remove and washing contaminated clothing before reuse.*

Hydrogen peroxide is considered slightly toxic to practically non-toxic to birds on an acute oral basis. A study of mallard ducks force-fed hydrogen peroxide via gavage administration provided a dose lethal to 50% of experimental birds (LD_{50}) of 1,049 mg/kg, which indicates slight toxicity in birds. In addition, dietary exposure studies in which Bobwhite quail were administered hydrogen peroxide in feed did not result in significant mortality at any of the concentrations tested. No Observed Adverse Effect Concentrations (NOAEC) in food of 47 and 1,953 part per million (ppm) were determined based on unspecified adverse effects in the registrant submitted studies (US EPA, 2009c).

The substance has also been evaluated for systemic toxicity from chronic exposure, developmental and reproductive toxicity, and carcinogenicity. According to the Agency for Toxic Substances and Disease Registry (ATSDR), hydrogen peroxide is unlikely to cause chronic toxicity because hydrogen peroxide is rapidly decomposed in mammalian bodies. However, repeat exposure to vapors of hydrogen peroxide may cause chronic irritation of the respiratory tract and even partial or complete lung collapse (ATSDR, 2014). Laboratory exposure studies have not linked hydrogen peroxide exposure to adverse reproductive and developmental effects. Chronic exposure studies in which hamsters were administered hydrogen peroxide to their buccal cheek pouches (topical) five times per week for 20–24 weeks provided no evidence of carcinogenicity. Adenomas and carcinomas of the duodenum were reported following oral administration of hydrogen peroxide to mice in drinking water; however, the dermal exposure study in mice indicated that hydrogen peroxide has no cancer promoting activity (IARC, 1999).

The *in vitro* mutagenicity of hydrogen peroxide is well established in the scientific literature. For example, hydrogen peroxide induced DNA damage in several bacterial strains and mutation in *Salmonella typhimurium* (Ames test) and *Escherichia coli* in the absence of exogenous metabolic activation. However, the substance was not mutagenic in *S. typhimurium* in the presence of exogenous metabolic activation. Several studies demonstrated that hydrogen peroxide causes gene mutation, sister chromatid exchanges, chromosome aberrations and DNA single-strand breaks and fragmentations in mammalian cell lines, including Chinese hamster cell cultures and human lymphocytes. In addition, tumor development was observed in mice injected with mouse myeloid progenitor cells transformed through *in vitro* exposure to hydrogen peroxide (IARC, 1999). A more recent in vitro study demonstrated that high concentrations of hydrogen peroxide produced in the thyroid to oxidize iodide induces DNA double- and single-strand breaks in rat, pig and human thyroid cell lines (Driessens, 2009).

Aquatic studies indicate that hydrogen peroxide is slightly toxic to aquatic invertebrates and practically non-toxic to fish on an acute basis. Treatment of *Daphnia magna* (freshwater water flea) with 0.1, 1.0, 10 and 100 mg/L of a 35% hydrogen peroxide solution provided a 48-hour LC_{50} (concentration lethal to 50% of test water fleas) of 24 mg/L and a NOAEC of 10 mg/L. Likewise, Bluegill sunfish and rainbow trout were tolerant of hydrogen peroxide, with LC_{50} values and NOAECs ranging from 93–150 mg/L and 56–100 mg/L, respectively (US EPA, 2009c).

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

Contamination is not expected when purified forms of hydrogen peroxide are released to the environment following normal use. At typical pesticide concentrations, hydrogen peroxide is expected to rapidly degrade to oxygen gas and water (US EPA, 2007). Large-volume spills and other releases of concentrated hydrogen peroxide could present a fire hazard since the substance readily decomposes to release oxygen gas. Pure hydrogen peroxide is not flammable and can be diluted with clean water to minimize the risk of fire (BioSafe, 2009). Although concentrated hydrogen peroxide is nonflammable, it is a powerful oxidizing agent that may spontaneously combust on contact with organic material and becomes explosive when heated (ATSDR, 2014; Eul, 2001). Combustion reactions and explosions resulting from accidental spills of concentrated hydrogen peroxide could therefore lead to environmental degradation.

Moderate spills of hydrogen peroxide to marine and estuarine environments are unlikely to adversely affect the receiving water bodies. On the contrary, a method describing the addition of hydrogen peroxide to natural waters as an oxidizing agent for oil spill remediation was recently published in the patent literature (Hoag, 2014). Likewise, hydrogen peroxide has been used to treat wastewater, and aids in the removal of soil contaminants, including creosote, polycyclic aromatic hydrocarbons (PAHs), and other inorganic and organic substances (Atagana, 2003; Conte, 2001; US EPA, 2007).

Toxic substances used in the manufacture of hydrogen peroxide, including alkyl anthraquinones, aromatic solvents and transition metal catalysts (e.g., Raney nickel and palladium), are generally removed from hydrogen peroxide prior to formulation of commercial pesticide products. Further, certain fractions of these reagents, catalysts and solvents are often returned to the reactors for use in subsequent synthetic reactions (Goor, 2007; Eul, 2001). Therefore, the chemicals used in the production of hydrogen peroxide should not be released to the environment when manufacturers adhere to standard operating procedures for safe handling and disposal of toxic substances.

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

Hydrogen peroxide reacts with oxidizable materials, including certain forms of the metals iron, copper, brass, bronze, chromium, zinc, lead, manganese and silver. Contact of pure hydrogen peroxide with organic materials may result in spontaneous combustion (ATSDR, 2014). Dilute hydrogen peroxide will oxidize dry or moist organic substances, but concentrated hydrogen peroxide will react violently with dried organic materials such as dehydrated compost or soil. Dilute and concentrated hydrogen peroxide will oxidatively damage or destroy soil microorganisms (see Evaluation Question #8). In the well-known Fenton reaction, iron cycles between the +2 and +3 oxidation states leading to the conversion of hydrogen peroxide to reactive oxygen species, including the hydroxyl radical (US EPA, 2007). Because of their highly reactive nature, these transient radical species are rapidly consumed through oxidative reactions with organic materials or other processes that form water and oxygen gas as the byproducts. Further, hydrogen peroxide does not deplete iron as part of the Fenton reaction and therefore should not adversely affect the availability of this trace mineral in soils. Similar activation reactions are facilitated when hydrogen peroxide is subjected to other naturally occurring transition metals (e.g, copper and chromium), as well as iron-containing enzymes, such as catalase (US EPA, 2007).

Evaluation Question #8: Describe any effects of the petitioned substance on biological or chemical interactions in the agro-ecosystem, including physiological effects on soil organisms (including the salt index and solubility of the soil), crops, and livestock (7 U.S.C. § 6518 (m) (5)).

Non-target soil organisms may be damaged or destroyed following application of hydrogen peroxide fungicides to plants and soils. Currently registered hydrogen peroxide products are labeled as algicides, antifoulants, bacteriocides/bacteriostats, disinfectants, fungicides/fungistats, nematicides, microbiocides/microbiostats, molluscicides, sporicides, sanitizers, sterilizers, tuberculocides and virucides (BioSafe, 2010). For example, the downy mildew fungal organisms *Pseudoperonospora cubensis* and the pink rot of potato fungus *Phytophthora erythroseptica* are susceptible to the oxidizing effects of hydrogen peroxide (Kuepper, 2003; Al-Mughrabi, 2006). It therefore follows that populations of beneficial soil fungi, such as *Mycorrhizal* fungi, and nitrogen-fixing bacteria may be negatively impacted by large-scale soil treatments of fungicides containing hydrogen peroxide. Other soil organisms, including nematodes, earthworms, snails and grubs are also at risk depending on the concentration and volume of hydrogen peroxide applied to soil. Indeed, recent studies demonstrated that soil drenches of dilute hydrogen peroxide adversely impact reproduction in the root-knot nematode *Meloidogyne javanica* (Karajeh, 2008), suggesting that similar treatments may impact populations of beneficial soil nematode species. The effects of hydrogen peroxide fungicides on beneficial soil organisms should be manageable at the population level since the substance degrades rapidly to water and oxygen in the environment and provides no residual activity.

Direct application or drift of concentrated hydrogen peroxide foliar sprays to treatment and non-target plants may result in phytotoxicity. The OxiDate product label states that use of solutions more concentrated than prescribed may result in leaf necrosis (cell death) in some plants. Applicators are advised to use 1:100 dilutions of the Oxidate product; since the concentrate is 27% hydrogen peroxide, this dilution ratio provides a working spray solution consisting of approximately 0.3% hydrogen peroxide (BioSafe, 2010). While plant damage is not expect at label application rates, plant sensitivity to hydrogen peroxide solutions should be assessed before applying the substance to a large area.

Overall, the available information suggests that large volumes of concentrated hydrogen peroxide solutions will adversely affect the viability and reproduction of non-target microorganisms, including beneficial soil fungi and nematodes. Information was not identified on the potential or actual impacts of hydrogen peroxide upon endangered species, populations, viability or reproduction and the potential for measurable reductions in genetic, species or eco-system biodiversity.

<u>Evaluation Question #9:</u> Discuss and summarize findings on whether the use of the petitioned substance may be harmful to the environment (7 U.S.C. § 6517 (c) (1) (A) (i) and 7 U.S.C. § 6517 (c) (2) (A) (i)).

Hydrogen peroxide is an unstable inorganic compound and is expected to degrade rapidly to water and oxygen in the environment. The half-lives for aerobic and anaerobic degradation of hydrogen peroxide in various soils are between one and seven hours. Hydrogen peroxide is mobile in soils, but does not readily volatilize from moist soils and surface waters (EC, 2003; US EPA, 2007). When released to water, hydrogen peroxide is rapidly consumed through biodegradation and photolysis. The half-life for biodegradation of hydrogen peroxide in water generally ranges from minutes to several hours (Goor, 2007; US EPA, 2007). Light, oxygen, ozone, hydrocarbons and free radicals contribute to hydrogen peroxide formation in the atmosphere, likely at significantly greater rates than the agricultural uses of the substance. The overall tropospheric half-life of hydrogen peroxide is estimated to be 10–24 hours (EC, 2003; Eul, 2001; Goor, 2007). Under typical use conditions, diluted and pure forms of hydrogen peroxide are reactive with transition metals (e.g., iron, copper, chromium) and organic materials (US EPA, 2007; ATSDR, 2014).

Ecological receptors are insensitive to moderately sensitive to hydrogen peroxide solutions. Hydrogen peroxide is considered slightly toxic to practically non-toxic to birds on an acute oral basis. Likewise, aquatic toxicity studies indicate that hydrogen peroxide is slightly toxic to aquatic invertebrates and practically non-toxic to fish on an acute exposure basis. In contrast to birds and aquatic animals, microorganisms are particularly sensitive to various concentrations of hydrogen peroxide. The scientific literature and agricultural experience have demonstrated that hydrogen peroxide is toxic to pathogen soil organisms, such as the downy mildew fungus *Pseudoperonospora cubensis* and pink rot of potato fungus *Phytophthora erythroseptica* (Kuepper, 2003; Al-Mughrabi, 2006). Considering the oxidizing mode of action for hydrogen peroxide, it is likely that the substance is also toxic to beneficial soil organisms, including *Mycorrhizal* fungi and nitrogen-fixing bacteria. This non-target effect is most relevant for spray drift and soil drench scenarios, and should not present a population-level concern for controlled hydrogen peroxide applications.

Environmental contamination is not expected when purified forms of hydrogen peroxide are released to the environment. At typical pesticide concentrations, hydrogen peroxide is expected to rapidly degrade to oxygen gas and water (US EPA, 2007). The toxic solvents and reagents used in the manufacture of hydrogen peroxide are removed prior to product formulation and, in many cases, are reused in subsequent synthetic reactions (Eul, 2001; Goor, 2007). As such, it is unlikely that these chemicals are readily introduced into the environment as a result of hydrogen peroxide production.

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

Hydrogen peroxide is generally considered safe for human exposure at low doses. Indeed, the US Food and Drug Administration (FDA) affirmed hydrogen peroxide as Generally Recognized as Safe (GRAS) when used as a direct food additive with certain limitations (see "Approved Legal Uses of the Substance" for details). Acute irritation and systemic toxicity is possible in humans exposed to moderate to high doses of hydrogen peroxide. Systemic effects of the substance generally result from the release of oxygen gas and water as the enzyme catalase decomposes available hydrogen peroxide. Specifically, venous embolism (gas bubble in bloodstream) may occur when the amount of oxygen gas produced exceeds its blood solubility (ATSDR, 2014).

Ingestion of household solutions (3%) typically causes mild gastrointestinal irritation and vomiting. Gastric distension (bloating of the stomach) may occur due to liberation of oxygen, but hollow-organ (e.g., stomach) rupture is unlikely when dilute solutions are ingested. In contrast, the ingestion of concentrated solutions (≥ 10%) can cause extreme irritation, inflammation, burns of the alimentary tract, and hollow-organ distension and rupture. Vapors, mists or aerosols of hydrogen peroxide can cause upper airway irritation, inflammation of the nose, hoarseness, shortness of breath, and tightness or a burning sensation in the chest. Inhalation or ingestion of hydrogen peroxide at high concentrations may lead to seizures, cerebral embolism or even tissue death (infarction). Dermal exposure to dilute hydrogen peroxide solutions can irritation and temporary bleaching of the skin, whereas concentrated solutions can cause severe skin burns with blistering. In addition, contact of dilute hydrogen peroxide solutions with the eyes can cause stinging pain and tearing, while solutions that are 5% or greater can cause injury to the eye surface (ATSDR, 2014).

The most recent US EPA Human Health Scoping Document for peroxy compounds provides a summary of incidents and associated symptoms associated with hydrogen peroxide exposure. As of the 2009 review, a total of 98 individual human incidents were submitted to the Agency, which summarized the symptoms observed in those cases as follows (US EPA, 2009d):

> *The most common symptoms reported were acute symptoms based on acute corrosion and irritation effects. The symptoms include eye irritation, skin burns, esophageal burns, nausea, dizziness, rash, and headaches. Inhalation effects include chest congestion, respiratory irritation, coughing of blood, tightness of chest and shortness of breath. Dermal effects include edema, erythema, skin burns, blistering, and swelling. These cases led to hospitalization in some cases.*

Hydrogen peroxide is unlikely to cause chronic toxicity in humans because it is rapidly decomposed in the body. The available toxicity and epidemiology studies provide no evidence of reproductive or developmental toxicity in experimental animals and humans (ATSDR, 2014). Although oral administration of hydrogen peroxide resulted in the formation of adenomas and carcinomas in mice, carcinogenic effects were not observed in topical application studies using mice and hamsters. Further, a 1991 case-control study found no association between hydrogen peroxide exposure in hairdressers, textile bleachers and furriers and the occurrence of several types of cancer, including esophageal, stomach, colon, rectum, pancreatic, lung, prostate, bladder, and kidney cancer, as well as skin melanoma and lymphoma (IARC, 1999). On the other hand, hydrogen peroxide is a known mutagen and is associated with genotoxicity in mammalian and human cell lines (IARC, 1999; Driessens, 2009). IARC determined that there is *inadequate evidence* in humans and *limited evidence* in experimental animals for the carcinogenicity of hydrogen peroxide, classifying the substance as *Group 3 – Not classifiable as to its carcinogenicity to humans* (IARC, 2014).

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

Numerous alternatives exist for hydrogen peroxide solutions used as disinfectants, sanitizers and algicides on crop production tools and equipment, as well as plant disease control agents (fungicides) in the organic production of crop commodities. This section provides a summary of available naturally occurring and synthetically produced substances that may serve as alternatives for hydrogen peroxide according to the use patterns under sunset review with the National Organic Standards Board.

Alternative Algicides, Disinfectants and Sanitizers

Technical information regarding the efficacy of natural, nonsynthetic agricultural commodities or products that could substitute for hydrogen peroxide as a sanitizer in organic crop production is limited. Nonsynthetic (natural) sources of ethanol may substitute for hydrogen peroxide disinfectants. Certain essential oils exhibit antiviral and antibacterial properties, and are commonly used in homemade hand sanitizers. Examples of the strongest and most commonly used antiseptic essential oils include clove oil, melaleuca oil, and oregano oil. In addition, pine oil, basil oil, cinnamon oil, eucalyptus oil, helichrysum oil, lemon and lime oils, peppermint oil, tea tree oil, and thyme oil are also used as antiseptic substances. Aloe vera contains six antispectic agents (lupeol, salicylic acid, urea nitrogen cinnamonic acid, phenols and sulfur) with inhibitory action on fungi, bacteria and viruses (Surjushe, 2008). Depending on the required potency and intended application, essential oils may be used in pure form or as a mixture in carrier, such as water. University agricultural extension literature databases contained no articles related to the practice of using essential oils as disinfectants or any performance data for these oils relative to hydrogen peroxide. It is therefore uncertain whether essential oil mixtures could serve as viable, naturally derived alternatives to hydrogen peroxide for the disinfection of tools and equipment used in organic crop production.

A wide variety of synthetic substances are available for sanitizing and disinfecting the surfaces of cutting tools and other implements in crop production. Laboratory experiments have evaluated the efficacy of Clorox (sodium hypochlorite ($NaClO$; 7 CFR 205.601(a)(2)(iii)), Lysol (soap, *o*-phenylphenol, *o*-benzyl-*p*-chlorophenol, ethanol, xylenols, isopropanol, tetrasodium ethylenediamine tetraacetate), Pine-Sol (pine oil), rubbing alcohol (isopropanol), Lysterine (thymol, eucalytol, methyl salicylate, menthol, ethanol, benzoic acid, poloxamer 407), hydrogen peroxide (H_2O_2; 7 CFR 205.601(a)(4)), Agrimycin 17 (streptomycin sulfate), and Kocide 101 (cupric hydroxide and metallic copper) for preventing the transmission of fire blight bacteria in 'Granny Smith' apple and 'Shinseiki' Asian pear fruit (Teviotdale, 1991). The combined results indicate that spray and 3–5 minute soaking treatments of Clorox, Lysol, and Pine-Sol were superior to corresponding treatments of the other products as well as dip treatments of all commercial disinfectants. In addition, quaternary ammonium chloride salts, chlorine dioxide (ClO_2; 7 CFR 205.601(a)(2)(ii)) and sodium carbonate peroxyhydrate (7 CFR 205.601(a)(8)—which produces hydrogen peroxide (H_2O_2) and sodium carbonate (Na_2CO_3) when dissolved in water—have been used as effective algicides, bactericides, virucides, and fungicides for greenhouse surface disinfection (Benner, 2012).

In addition to hydrogen peroxide (7 CFR 205.601(a)(4)), the National List of Allowed and Prohibited Substances permits the use of the following synthetic materials as algicides, disinfectants, and sanitizers, including irrigation system cleaning, in organic crop production:

- **Ethanol.** Molecular formula of CH_3CH_2OH; allowed according to the listing for alcohols (7 CFR 205.601(a)(1)(i)).
- **Isopropanol.** Molecular formula of $(CH_3)_2CHOH$; allowed according to the listing for alcohols (7 CFR 205.601(a)(1)(ii)).
- **Calcium hypochlorite.** Molecular formula of $Ca(ClO)_2$; allowed according to the listing for chlorine-based materials (7 CFR 205.601(a)(2)(i)).
- **Chlorine dioxide.** Molecular formula of ClO_2; allowed according to the listing for chlorine-based materials (7 CFR 205.601(a)(2)(ii)).
- **Sodium hypochlorite.** Molecular formula of $NaClO$; allowed according to the listing for chlorine-based materials (7 CFR 205.601(a)(2)(iii)).
- **Copper sulfate.** Molecular formula of $CuSO_4$. Allowed for use as an algicide in aquatic rice systems; limited to one application per field during any 24-month period (7 CFR 205.601(a)(3)).
- **Ozone gas.** Molecular formula of O_3. Allowed for use only as an irrigation system cleaner (7 CFR 205.601(a)(5)).
- **Peracetic acid.** Molecular formula of CH_3CO_3H. Allowed for use in disinfecting equipment, seed, and asexually propagated plant material. Also permitted in hydrogen peroxide formulations as allowed in §205.601(a) at concentration of no more than 6% as indicated on the pesticide product label (7 CFR 205.601(a)(6)).
- **Soap-based algicide/demossers.** Consist of mixtures of ammonium or potassium salts of fatty acids with varying molecular weight components; allowed according to 7 CFR 205.601(a)(7).

- **Sodium carbonate peroxyhydrate.** Molecular formula of 2 $Na_2CO_3 \bullet 3 H_2O_2$. Allowed for use according to 7 CFR 205.601(a)(8); federal law restricts the use of this substance in food crop production to approved food uses identified on the product label.

Alternative Plant Disease Control Agents

A number of naturally occurring, non-synthetic substances exist for the control and prevention of pathogenic microorganisms that cause plant diseases. Natural sources of elemental sulfur have been used to manage grapevine powdery mildew for almost 200 years (Vasquez, 2009); however, the sulfur used in modern formulated products is likely produced synthetically from fossil fuels (Nehb & Vydra, 2006). Sulfur operates through a multi-site mode of action involving inhibition of fungal spore germination and production of toxic vapors that impair cellular respiration in target organisms (Vasquez, 2009). Other natural active ingredients used to manage plant diseases in organically grown crops include botanical oils, plant extracts and microorganisms.

Natural products and horticultural oils derived from plant sources are commonly used to combat and prevent the development of plant pathogens. Neem oil containing the active ingredients azadirachtin and salannin is a botanical fungicide, insecticide and miticide derived from the neem tree (Pottorff, 2010). Commercially available neem oil products, such as the OMRI-listed product Neem Oil 70% manufactured by Certis USA, are used to control anthracnose, scab and leaf blight, as well as aphids, psyllids, mealybugs, leafhoppers and scale insects on a variety of crops and ornamentals (Certis USA, 2014). Natural plant oils, including oil of thyme, sesame, clove and rosemary, and extract of *Reynoutria sachalinensis* (Giant Knotweed) have also been used as active ingredients in OMRI-approved fungicides, insecticides and miticides (McGrath, 2010). Lastly, it has been noted that foliar sprays of compost tea are successful in managing a number of plant diseases (Kuepper, 2003). Horticultural oils produced synthetically are included on the National List for organic crop production (see list below).

Certain bacterial and fungal strains are used as active ingredients in commercially available fungicide products. Beneficial microorganisms provide control of plant diseases through various modes of action: (1) outcompeting the pathogen for nutrients and space, (2) producing a chemical compound that acts against the pathogen, (3) directly attacking the pathogen, and/or (4) triggering a defensive response in the host plant that limits the invading ability of the pathogen (Swain, 2014). For example, the gram-positive bacterium *Bacillus subtilis* is used as the active ingredient in several biological fungicides, including the Serenade® products manufactured by Bayer CropScience, by producing proteins that inhibit spore germination in fungi that cause powdery mildew and other plant diseases (Vasquez, 2009). Likewise, the gram-negative bacterium *Pseudomonas fluorescens* (Frostban™ by Nufarm Americas, Inc) is used as a foliar spray to compete with fire blight bacterium for nutrients in apple and pear tree blossoms. Biofungicides work best when applied preventatively (Swain, 2014).

In addition to naturally occurring materials, several synthetic substances are also permitted for use as plant disease control agent in organic crop production:

- **Elemental sulfur.** In addition to natural sources, synthetic elemental sulfur (i.e., derived from petroleum materials) is approved for use in organic crop production as an insecticide (7 CFR 205.601(e)(5)) and for plant disease control (7 CFR 205.601(i)(10) without restrictions.
- **Horticultural oils.** Narrow range oils, such as dormant, suffocating and summer oils may be used for plant disease control in organic crop production (7 CFR 205.601(i)(7)). In addition, synthetic oils are allowed for use as insecticides (7 CFR 205.601(e)(8)).
- **Aqueous potassium silicate (CAS # 1312-76-1).** According to the final rule, the silica used in the manufacture of potassium silicate must be sourced from naturally occurring sand when used in organic crop production for plant disease control (7 CFR 205.601(i)(1)) and for insecticidal and miticidal purposes (7 CFR 205.601(e)(2)).
- **Copper sulfate.** The synthetic substance may be used for plant disease control in a manner that minimizes accumulation of copper in soil (7 CFR 205.601(i)(3)). As an insecticide, only allowed for use as tadpole shrimp control in aquatic rice production. Treatments are limited to one application per field during any 24-month period. Application rates are limited to levels which do not increase

baseline soil test values for copper over a timeframe agreed upon by the producer and accredited certifying agent (7 CFR 205.601(e)(4)).

- **Coppers, fixed.** Copper hydroxide, copper oxide, copper oxychloride (includes products exempted from EPA tolerance) may be used for plant disease control provided that copper-based materials are used in a manner that minimizes accumulation in the soil and shall not be used as herbicides (7 CFR 205.601(i)(2)).
- **Hydrated Lime.** The reaction of lime with water produces synthetic hydrated or "slaked" lime (calcium hydroxide). Hydrated lime is allowed for use as a plant disease control agent in organic crop production (7 CFR 205.601(i)(5)).
- **Lime Sulfur.** Consists of a mixture of elemental sulfur and hydrated lime (calcium hydroxide). The synthetic substance is permitted for use as a plant disease control agent in organic crop production (7 CFR 205.601(i)(6)). In particular, lime sulfur is commonly used to control pathogenic organisms in organic apple and grape production.
- **Peracetic acid.** Used to control fire blight bacteria. Also permitted in hydrogen peroxide formulations as allowed in §205.601(i) at a concentration of no more than 6% as indicated on the pesticide product label (7 CFR 205.601(i)(8)).
- **Potassium bicarbonate.** The synthetic substance is allowed for use as a plant disease control agent in organic crop production (7 CFR 205.601(i)(9)).

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

Proper implementation of crop rotation and incorporation of cover crops can effectively minimize the occurrence of plant diseases and corresponding applications of chemical fungicides. Crop rotations are critical for reducing the adverse impacts plant pathogens, pest insects and weeds on various crop varieties. By changing environmental conditions in the field and removing food sources to prevent pest buildup, crop rotations have enabled organic and conventional farmers to reduce pest populations (McGuire, 2003). Crops of the same family should not follow one another in the field, and should typically be separated by at least two years and as much as five years to minimize the occurrence of pests and pathogens in the soil (Baldwin, 2006). A rotation of crop families might include *Brassicaceae* (cole crops), followed by *Asteraceae* (lettuce, cut flowers), followed by *Solanaceae* (tomatoes, potatoes, peppers, eggplants), followed by *Curbitaceae* (squashes, cucumbers and melons). Specific plant diseases will require tailored crop rotations; for example, detection of *Sclerotium rolfsii* (southern blight) in vegetable crops may require a rotation of corn, grass, hay or pasture crop for two or three years (Baldwin, 2006).

Planting cover crops for biological fumigation has the potential to curtail the use of chemical fungicides during the growing season by reducing the populations of soil borne pathogens prior to planting. Certain varieties of mustard cover crops (e.g., Ida Gold, Mighty Mustard and Pacific Gold) planted in a resting field are grown for a certain period of time and then plowed under before reaching full maturity in order to maximize the concentration of nutrients and allelochemicals available from the mustard crop (Johnson, 2009). Specifically, damaged plant tissues of mustard plants naturally release the biofumigant allyl isothiocyanate. Green manures from various cover crops may also serve as energy sources for beneficial microorganisms that out-compete plant pathogens and potentially confer disease resistance to crops (McGuire, 2003).

Crop rotation and the incorporation of cover crops are commonly employed methods of controlling soil-borne pests and pathogens in annual cropping systems. However, these methods are incompatible with the growing requirements of perennial fruit trees, grape vines and bushes (e.g., raspberries and blackberries) typically treated with hydrogen peroxide to prevent and control diseases caused by various plant pathogens. Despite these limitations, several alternative strategies have been developed to minimize the use of chemical fungicides on perennial crops.

Providing effective control of plant diseases on tree crops and ornamentals requires an integrated approach. Starting with certified and disease-free plant material will allow for faster growth and heightened resistance to environmental stressors and less susceptibility to fungal pathogens (Holb, 2009). Using apple scab control as an example, sanitation practices such as picking up and disposing of fallen leaves in the fall can be effective for smaller operations but is not always practical for large orchards. In conventional production, urea can be applied to apple trees just before leaves drop or directly to leaves on the ground followed by tilling the fallen leaves into the soil or chopping them into small pieces to accelerate leaf decomposition. This practice significantly decreases the amount of apple scab pathogen available the next growing season (Vaillancourt, 2005). Although similar mechanical strategies can be employed in organic orchards, urea—a synthetic nitrogen fertilizer—is not approved for use in organic crop production. Flaming using a torch-directed flame sears the leaf litter on the orchard floor and ruptures fungal cells on the affected leaves (Holb, 2009). Regular pruning of apple trees enables direct management of several fungal diseases through removal of diseased shoots, fruit, stems or dead wood that can harbor pathogens (Holb, 2009). Pruning also enhances air movement and the penetration of sunlight within the canopy, thus hastening the drying process for leaves and fruit. Likewise, it is generally recommended that growers avoid overhead irrigation, especially when weather conditions are favorable for apple scab development. Both of the latter two strategies minimize the occurrence of moist conditions that support fungal infections (Vaillancourt, 2005; Holb, 2009).

Physical methods are also available for postharvest control of pathogens on raw agricultural commodities. Using table grapes as an example, ultraviolet light at wavelengths between 200–280 nanometers (UV-C) as well as temperature and pressure changes are viable options for controlling various mold species. For example, UV-C treatment at 254 nm effectively controlled gray mold, which was reduced from 22 and 52% in control to 14 and 38% in grapes. Laboratory scale applications of hyperbaric pressures such as 1140 mmHg (1.5 atm) successfully decreased the percentage of infected berries and lesion diameter of gray mold on artificially inoculated berries. The authors note that antimicrobial treatments involving pressures higher than atmospheric require additional study in large-scale tests before the widespread deployment of this method in agricultural production (Romanazzi, 2012). Postharvest heat treatments such as hot water treatment, short hot water rinsing and brushing, and hot air treatment may reduce rot development and enhance fruit resistance to chilling injury in cold-sensitive cultivars. However, it is noted that complete control of decay is rarely achieved using heat therapy alone (Schirra, 2011).

The cultural practices summarized above may minimize but are unlikely to eliminate the need for natural or synthetic pesticides during periods of intense disease pressure. Alternatives substances to hydrogen peroxide for plant disease control are summarized in Evaluation Question #11.

References

ATSDR. 2014. Medical Management Guidelines for Hydrogen Peroxide. Agency for Toxic Substances & Disease Registry. Retrieved November 13, 2014 from http://www.atsdr.cdc.gov/MMG/MMG.asp?id=304&tid=55.

Al-Mughrabi KI. 2006. Sensitivity to Hydrogen Peroxide in vitro of North American Isolates of Phytophthora erythroseptica, the Cause of Pink Rot of Potatoes. Plant Physiology Journal 5: 7–10.

Atagana HI. 2003. Bioremediation of creosote-contaminated soil: a pilot-scale landfarming evaluation. World Journal of Microbiology and Biotechnology 19: 571–581.

Baldwin KR. 2006. Crop Rotations on Organic Farms. Center for Environmental Farming Systems. North Carolina State University. Retrieved September 10, 2014 from http://www.cefs.ncsu.edu/resources/organicproductionguide/croprotationsfinaljan09.pdf.

Benner R. 2012. Spotlight: Starting the Season Clean. Penn State Extension. College of Agricultural Sciences. The Pennsylvania State University. Retrieved January 12, 2015 from http://extension.psu.edu/plants/green-industry/news/2012/starting-the-season-clean.

BioSafe. 2010. Label: OxiDate® Broad Spectrum Bactericide/Fungicide. Retrieved November 5, 2014 from http://iaspub.epa.gov/apex/pesticides/f?p=PPLS:102:::NO::P102_REG_NUM:70299-2.

BioSafe. 2009. MSDS: OxiDate® Broad Spectrum Bactericide/Fungicide. Material Safety Data Sheet. Retrieved November 5, 2014 from http://www.cdms.net/LabelsMsds/LMDefault.aspx?manuf=262.

CAN. 2011. Organic Production Systems Permitted Substances Lists: CAN/CGSB-32.311-2006. Canadian General Standards Board. Retrieved November 11, 2014 from http://www.tpsgc-pwgsc.gc.ca/ongc-cgsb/programme-program/normes-standards/internet/bio-org/documents/032-0311-2008-eng.pdf.

CDC. 2008. Guideline for Disinfection and Sterilization in Healthcare Facilities, 2008. Centers for Disease Control and Prevention. Retrieved November 5, 2014 from http://www.cdc.gov/hicpac/disinfection_sterilization/7_0formaldehyde.html.

Certis USA. 2014. Master Label/Sublabel A – Neem Oil 70%. Retrieved October 27, 2014 from http://iaspub.epa.gov/apex/pesticides/f?p=PPLS:102:::NO::P102_REG_NUM:70051-2.

Conte P, Zena A, Pilidis G, Piccolo A. 2001. Increased retention of polycyclic aromatic hydrocarbons in soils induced by soil treatment with humic substances. Environmental pollution 112: 27–31.

Driessens N, Versteyhe S, Ghaddhab C, Burniat A, De Deken X, Van Sande J, et al. 2009. Hydrogen peroxide induces DNA single- and double-strand breaks in thyroid cells and is therefore a potential mutagen for this organ. Endocrine Related Cancer 16: 845–856; doi:10.1677/ERC-09-0020.

EC. 2008. Commission Regulation (EC) No. 889/2008. European Commission. Retrieved November 11, 2014 from http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:250:0001:0084:EN:PDF.

EC. 2003. Hydrogen Peroxide: Summary Risk Assessment Report. European Commission. Retrieved November 12, 2014 from http://echa.europa.eu/documents/10162/590965ca-33e7-43a0-a109-3a9148870d07.

El-Mougy N, El-Gamal N, Abdalla M. 2008. The Use of Fungicide Alternatives for Controlling Postharvest Decay of Strawberry and Orange Fruits. Journal of Plant Protection Research 48: 385–396.

Eul W, Moeller A, Steiner N. 2001. Hydrogen peroxide. In *Kirk-Othmer Encyclopedia of Chemical Technology*. John Wiley & Sons, Inc.

FDA. 2014. Citizen Denial Response from FDA CDER to American Dental Association. US Food and Drug Administration. Retrieved January 12, 2015 from http://www.regulations.gov/#!documentDetail;D=FDA-2009-P-0566-0005.

Gaffney A. 2014. Are Products Used to Whiten Your Teeth Drugs or Cosmetics? FDA Weighs in. Regulatory Affairs Professionals Society (RAPS). Retrieved January 12, 2015 from http://www.raps.org/regulatoryDetail.aspx?id=18525.

Goor G, Glenneberg J, Jacobi S. 2007. Hydrogen Peroxide. In *Ullmann's Encyclopedia of Industrial Chemistry*. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany.

HSDB. 2005. National Library of Medicine, TOXNET. *Hydrogen Peroxide*. Hazardous Substances Data Bank. Retrieved November 5, 2014 from http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

Hoag GE, Collins JB, Ayers JT. 2014. Compositions and methods for oil spill remediation. Patent # US20140110344 A1. Retrieved November 13, 2014 from http://www.google.com/patents/US20140110344.

Holb IJ. 2009. Fungal Disease Management in Environmentally Friendly Apple Production – A Review. In *Climate Change, Intercropping, Pest Control and Beneficial Microorganisms* (E. Lichtfouseed.), pp. 219–292, Springer Netherlands, Dordrecht.

IARC. 2014. Agents Classified by the *IARC Monographs*, Volumes 1–111. International Agency for Research on Cancer. Retrieved November 13, 2014 from http://monographs.iarc.fr/ENG/Classification/.

IARC. 1999. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Hydrogen Peroxide. International Agency for Research on Cancer. Retrieved November 5, 2014 from http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-29.pdf.

IFOAM. 2014. The IFOAM Norms for Organic Production and Processing. International Federation of Organic Agriculture Movements. Retrieved November 11, 2014 from http://www.ifoam.org/en/ifoam-norms.

Johnson G. 2009. Fumigation Alternatives – Biofumigants. University of Delaware. Retrieved September 8, 2014 from http://agdev.anr.udel.edu/weeklycropupdate/?p=837.

Karajeh MR. 2008. Interaction of root-knot nematode (*Meloidogyne javanica*) and tomato as affected by hydrogen peroxide. Journal of Plant Protection Research 48(2): 181–187.

Kuepper G. 2003. Down Mildew Control in Cucurbits. ATTRA (National Sustainable Agriculture Information Service). Retrieved November 5, 2014 from http://www.carolinafarmstewards.org/wp-content/uploads/2012/12/4-ATTRA-Downy-Mildew-Control-in-Cucurbits.pdf.

Matheron M. 2001. Modes of Action for Plant Disease Management Chemistries. University of Arizona Cooperative Extension. Retrieved November 5, 2014 from http://cals.arizona.edu/crop/diseases/papers/dischemistry.html.

McGrath MT. 2010. Efficacy of Various Biological and Microbial Fungicides – Does That Really Work? Cornell University. Retrieved November 7, 2014 from nofavt.org/sites/default/files/biologicals.pdf

McGuire A. 2003. Using Green Manures in Potato Cropping Systems. Center for Sustaining Agriculture and Natural Resources. Washington State University. Retrieved September 10, 2014 from http://cru.cahe.wsu.edu/CEPublications/eb1951e/EB1951E.pdf.

Newman SE. 2004. Disinfecting Irrigation Water for Disease Management. 20th Annual Conference on Pest Management on Ornamentals, Society of American Florists. Colorado State University – Greenhouse Extension. Retrieved November 5, 2014 from http://ghex.colostate.edu/pdf_files/DisinfectingWater.pdf.

Nehb W, Vydra K. 2006. Sulfur. In *Ullmann's Encyclopedia of Industrial Chemistry*. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany.

Phillips M. 2005. *The Apple Grower: Guide for the Organic Orchardist, 2nd Edition*. White River Junction, VT, Chelsea Green Publishing.

Porter DH. 1961. Production of hydrogen peroxide by anthraquinone process in the presence of a fixed bed catalyst. Patent # US3009782 A. Retrieved November 7, 2014 from http://www.google.com/patents/US3009782.

Pottorff LP. 2010. Some Pesticides Permitted in Organic Gardening. Colorado State University Cooperative Extension. Retrieved October 27, 2014 from http://www.colostate.edu/Depts/CoopExt/4DMG/VegFruit/organic.htm.

Romanazzi G, Lichter A, Gabler FM, Smilanick JL. 2012. Recent advances on the use of natural and safe alternatives to conventional methods to control postharvest gray mold of table grapes. Postharvest Biology and Technology 63: 141–147; doi:10.1016/j.postharvbio.2011.06.013.

Rueter M. 2006. Direct hydrogen peroxide production using staged hydrogen addition. Patent # US7067103 B2. Retrieved November 7, 2014 from http://www.google.com/patents/US7067103.

Schilder A. 2011. Late-season fungicide sprays in grapes and potential effects on fermentation. Michigan State University Extension. Retrieved November 7, 2014 from http://msue.anr.msu.edu/news/late_season_fungicide_sprays_in_grapes_and_potential_effects_on_fermentatio.

Schirra M, D'Aquino S, Cabras P, Angioni A. 2011. Control of Postharvest Diseases of Fruit by Heat and Fungicides: Efficacy, Residue Levels, and Residue Persistence. A Review. Journal of Agricultural and Food Chemistry 59: 8531–8542; doi:10.1021/jf201899t.

Soil Association. 2014. Soil Association organic standards, farming and growing. Revision 17.2. United Kingdom Soil Association. Retrieved November 11, 2014 from http://www.soilassociation.org/LinkClick.aspx?fileticket=1-LqUg6illo%3d&tabid=353.

Solvay. 2013. Plant for hydrogen peroxide production and a process using it. Patent # EP2639200 A1. Retrieved November 7, 2014 from http://www.google.com/patents/EP2639200A1.

Surjushe A, Vasani R, Saple DG. 2008. Aloe Vera: A Short Review. Indian J Dermatol 53: 163–166; doi:10.4103/0019-5154.44785.

Swain S. 2014. Biological Fungicides: Do They Work and Are They Safe? University of California Cooperative Extension | Agricultural Experiment Station. Retrieved October 27, 2014 from http://ucanr.edu/blogs/blogcore/postdetail.cfm?postnum=13543.

Teviotdale BL, Wiley MF, Harper DH. 1991. How disinfectants caompare in preventing transmission of fire blight. California Agriculture 45: 21–23.

US EPA. 2014. Pesticide Product Information Systems (PPIS). US Environmental Protection Agency. Retrieved November 10, 2014 from http://www.epa.gov/opp00001/PPISdata/.

US EPA. 2009a. Summary of Product Chemistry, Environmental Fate, and Ecotoxicity Data for Hydrogen Peroxide, Peroxyacetic acid, and Potassium Peroxymonosulfate for Registration Review. US Environmental Protection Agency. Retrieved November 5, 2014 from http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0546-0002.

US EPA. 2009b. Peroxy Compounds Summary Document: Registration Review. US Environmental Protection Agency. Retrieved November 5, 2014 from http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0546-0005.

US EPA. 2009c. Summary of Ecotoxicity Data for Peroxy Compounds, hydrogen peroxide and peroxyacetic acid for the Registration Review Decision Document. US Environmental Protection Agency. Retrieved November 5, 2014 from http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0546-0004.

US EPA. 2009d. Summary of Human Health Effects Data for the Peroxy Compounds Registration Review Decision Document. US Environmental Protection Agency. Retrieved November 5, 2014 from http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0546-0003.

US EPA. 2007. Peroxy Compounds: Hydrogen Peroxide and Peroxyacetic Acid Environmental Fate Science Chapter. US Environmental Protection Agency. Retrieved November 12, 2014 from http://www.epa.gov/pesticides/chem_search/cleared_reviews/csr_PC-000595_12-Jul-07_a.pdf.

US EPA. 1993. Reregistration Eligibility Decision: Peroxy Compounds. US Environmental Protection Agency. Retrieved November 12, 2014 from http://www.epa.gov/opp00001/chem_search/reg_actions/reregistration/red_G-67_1-Dec-93.pdf.

Vaillancourt LJ, Hartman JR. 2005. Apple Scab. American Phytopathological Society; doi: 10.1094/PHI-I-2000-1005-01. Retrieved October 27, 2014 from http://www.apsnet.org/edcenter/intropp/lessons/fungi/ascomycetes/Pages/AppleScab.aspx.

Vasquez SJ. 2009. Minimizing fungicide resistance. University of California Cooperative Extension | Agricultural Experiment Station. Retrieved October 27, 2014 from http://ucanr.edu/blogs/blogcore/postdetail.cfm?postnum=1185.