Copper Sulfate

Livestock

Identification of Petitioned Substance

Chemical Names:

Copper sulfate

Other Names:

Copper (II) sulfate, cupric sulfate, copper sulfate pentahydrate also called bluestone, blue vitriol, Roman vitriol, and Salzburg vitriol

Trade Names:

Agritox, BSC Copper Fungicide, CP Basic Sulfate, TriBasic Copper Sulfate, Triangle Brand Copper Sulfate Crystal, Diamond Copper Sulphate (Bluestone).

CAS Numbers:

Refer to Table 1

Other Codes:

Refer to Table 1

Table 1 Chemical Abstract Service (CAS) registry numbers and U.S. EPA Pesticide Code[2]

Copper product	Formula	CAS Number	EPA PC Code	EPA Registered ?
Copper sulfate basic	$Cu(OH)_2 \cdot CuSO_4$	1344-73-6	008101	Yes
Copper sulfate pentahydrate	$CuSO_4 \cdot 5H_2O$	7758-99-8	024401	Yes
Copper sulfate (anhydrous)	$CuSO_4$	7758-98-7	024408	No
Copper sulfate (monohydrate)	$CuSO_4 \cdot H_2O$	1332-14-5	024402	No

[1]The International Union of Pure and Applied Chemistry (IUPAC) name for this active ingredient is copper (2^+) sulfate or copper (II) sulfate.
[2] Copper Compounds Listed in 40 CFR 180.1021

Summary of Petitioned Use

Currently, copper sulfate is listed on USDA National Organic Program's (NOP) National List of allowed synthetic substances for use in organic livestock production.

This falls under the following section:

§205.603 Synthetic substances allowed for use in organic livestock production

(b) As topical treatment, external parasiticide or local anesthetic as applicable.

Copper sulfate is scheduled to sunset on June 27, 2017. As required by the Organic Foods Production Act[1], the National Organic Standards Board requested a technical evaluation report of this substance under the sunset process.

[1] 7 USC Sec. 6517(d)

Characterization of Petitioned Substance

Composition of the Substance:

Copper sulfate is an inorganic compound that combines sulfur with copper. The salt exists as a series of compounds that differ in the degree of hydration. Copper sulfate, bluestone and blue vitriol are all common names for cupric sulfate pentahydrate, $CuSO_4{\cdot}5H_2O$, which is the best known and the most widely used of the copper salts (Merck Index, 1989, NPIC, 2012).

Sulfate (CAS no. 14808-79-8) is the salt of sulfuric acid and contains the anion SO_4^{2-} (molecular weight, 96.07 grams/mole equivalent). It is found widely in the environment both terrestrial and aquatic. Sulfate reducing bacteria use the reduction of sulfates coupled with the oxidation of organic compounds or hydrogen as an energy source for chemosynthesis (Merck Index, 1989).

Source or Origin of the Substance:

Copper sulfate is produced commercially by reacting various copper minerals and/or metal with sulfuric acid. In nature, the anhydrous form occurs as a rare mineral known as chalcocyanite. The hydrated copper sulfate occurs as chalcanthite (pentahydrate) mineral. The production of copper sulfate, using copper ore as the starting raw material, is rarely utilized. The bulk of production comes from nonferrous scrap. The scrap metal is refined and dissolved in dilute sulfuric acid. The saturated solution is allowed to cool and the copper sulfate crystals form.

Properties of the Substance:

The chemical properties for copper sulfate pentahydrate and copper sulfate are summarized Table 2 (Merck Index, 1989, NPIC, 2012).

Table 2 Chemical properties of Copper Sulfate

Active Ingredient	Formula	Form	Molecular weight (g/mol)	Density (g/cm^{3})	Solubility	Solubility (water)
Copper sulfate pentahydrate	$CuSO_4{\cdot}5H_2O$	Blue triclinic crystals, granules or powder	249.69	2.28	Soluble in methanol 10.4g/L (18°C) insoluble in ethanol	316 g/L (0 C) 2033 g/L (100 C)
Copper sulfate (anhydrous)	$CuSO_4$	Light gray/ blue green rhombic crystals or fine powder	159.61	3.60	Insoluble in ethanol	243 g/L (0 °C) 320 g/L (20 C) 618 g/L (60 C) 1140 g/L (100 C)

Commercially, copper sulfate contains 25 % metallic copper and is sold with a guaranteed minimum purity of 98 % copper sulfate. It is produced in a number of grades varying from large crystal lumps, of 25 mm or more in diameter from which it appropriately derives the name bluestone, to very fine powders of almost the fineness of talcum powder. The four commonest grades, based on crystal diameter sizes, are: large crystals (from 10 mm to 40 mm), small crystals (from 2 mm to 10 mm), granulated or snow crystals (less than 2 mm) and windswept powder (less than 0.15 mm) (Copper.org, 2015).

Specific Uses of the Substance:

Copper is ubiquitous in nature and a necessary nutritional element for both animals and plants. The daily recommended allowance of copper for human adult nutrition is 2 mg. Ground water used for drinking purposes contains copper ions. The actual amount varies from region to region. The Environmental Protection Agency (EPA) has set a maximum contaminant level for copper at 1.3 ppm. Copper sulfate also used in feed rations to treat copper deficiency in food producing animals (RED-Cu, 2009).

Copper sulfate is listed on NOP's National List of allowed synthetic substances for use in organic crop production. Copper sulfate in various forms is used as a fungicide and algicide. As a fungicide, a mix of copper sulfate pentahydrate and calcium hydroxide (Bordeaux mixture) can be effective against plant diseases caused by both fungi (such as powdery mildew, downy mildew) and by bacteria (such as bacterial leafspots and fireblight). Another application is a mixture of copper sulfate and ammonium carbonate that can be (cheshunt mix) used in conventional horticulture to prevent damping off in seedlings (RED-Cu, 2009, Beckerman, 2008).

Copper pesticides in their various forms are EPA registered for use on numerous aquatic applications (EPA, 2008) .

- As an algicide, copper can control or eliminate algae and invasive aquatic weeds from aquaculture facilities, drainage systems ponds, crop and non-crop irrigation canals, and sewage lagoons and potable water lines.
- As a molluscicide, a dilute solution of copper sulfate can be used to remove snails from an aquarium, and control freshwater snails that may be a vector for harmful trematodes. Copper sulfate and has been used to control invertebrates, specifically tadpole shrimp (Godfrey and Espino, 1999), in rice production.
- An estimated 9-11 million pounds of elemental copper in the form of copper sulfate pentahydrate are applied each year solely for algae and weed control (RED-Cu, 2009).

In addition, Copper sulfate is listed on the National List of allowed synthetic substances for use in organic livestock production (§ 205.603) as a topical treatment, external parasiticide or local anesthetic. Copper ions have been reported to have antimicrobial activity against a wide range of aerobic and anaerobic bacteria and fungi. The exact mechanisms by which copper sulfate exerts its biocidal effect is a source of numerous ongoing investigations in the scientific literature.

Copper sulfate has been used as a footbath antiseptic to help control and prevent infectious hoof disease problems that affect the skin adjacent to the claw horn of dairy cattle and sheep i.e., digital dermatitis (DD) (hairy heel warts), foot rot lesions (interdigital area and invading the subcutaneous tissue), and heel erosions. Depending on the severity of the infection, the impact on managed cattle and or sheep ranges from minor discomfort to severe debilitating lameness, reproductive problems and in the dairy industry a reduction of milk production ranging from 20 to 50 percent (Brown, et al., 2000, Losinger, 2006).

The bacterial spirochetes, Treponema spp., are thought to be a major contributor to the cause and origin of DD. Other bacteria associated with causing the infectious hoof disease include Fusobacterium necrophorum, Staphylococcus aureus, Escherichia coli, and Actinomyces pyogenes (Hartshorn, et al., 2013, and Blezinger, 2004). Foot rot is caused by an interaction of two anaerobic, Gram negative bacteria, Bacteroides nodosus and Fusobacterium necrophorum. Fusobacterium necrophorum is a normal inhabitant of the ruminant digestive tract and in wet weather may interact with another bacterium, Corynebacterium pyogenes, to produce the infection (Tomlinson et al., 2014, Whittier et al., 2009).

Additional factors that contribute to the infection include poor animal hygiene, an injury to the skin of some type, continuous exposure to wet conditions, a housed free stall cubicle design and diagnosing and treating suspected lesions and infections. Copper sulfate solutions (5 to 10% w/v) are commonly used in footbaths. The higher the concentration of copper ions in the water solution, the higher the lethality rate for the targeted bacteria. It also is dependent on the frequency of changing solutions, footbath dimensions and location in the operation.

The bacteriostatic properties of copper sulfate are attributed to copper ions reacting with sulfhydryl-(SH) group of thiol-dependent enzymes, thus stopping the oxidizing process of the anaerobic bacteria

(Epperson et al., 2007). The popularity of copper sulfate footbaths can be attributed to both its relatively low cost per footbath and that it effectively controls the infectious lesions (Hoffman, 2012). Research has shown that using copper sulfate footbaths decreases both the incidence and severity of foot lesions over time. However, some data suggest that copper sulfate is rapidly neutralized by organic matter (Greenough et al., 1997) and is less effective as the infection becomes progressively worse.

Concerns with using copper sulfate include metal corrosion and disposal of the copper sulfate solution. On the farm, discarding the diluted copper sulfate solution with manure (and placed in wastewater lagoon) is a normal practice (Ippolito et al., 2013). For example, if a dairy operation is using a 50-gallon footbath containing a 5% w/v copper sulfate solution, twice a week, and changed the solution every 200 animal passes, 10.9 pounds of copper sulfate/animal per year will discarded. Although the copper solution is diluted when mixed with manure, there is a potential for copper levels to increase in the soil over time when the manure is added to agricultural land as a soil amendment or fertilizer. High copper levels in the soil impact crop yields due to phytotoxicity and could exceed EPA and state guidelines for copper loading of agricultural land (Ippolito et al., 2011 and 2013).

Some examples of copper sulfate non-agricultural uses include pyrotechnic compositions (firework displays), a mordant in textile dyeing, in preparation of azo dyes, in preserving hides and tanning leather, electroplating coatings, reagents in analytical chemistry, use as ingredient in human and veterinary medicine, and as a wood preservative

Approved Legal Uses of the Substance:

Environmental Protection Agency

40 CFR § 180.1021 Copper; exemption from the requirement of a tolerance.

(a) Copper is exempted from the requirement of a tolerance in cattle, meat; goat, meat; hog, meat; horse, meat; sheep, meat; milk, poultry, fat; poultry, meat; poultry, meat byproducts; egg, fish, shellfish, and irrigated crops when it results from the use of:

> **(1)** Copper sulfate as an algaecide or herbicide in irrigation conveyance systems and lakes, ponds, reservoirs, or bodies of water in which fish or shellfish are cultivated.

(b) Copper compounds exempt from the requirement of a tolerance when applied (primarily) as a fungicide to growing crops using good agricultural practices are provided in Table 3:

Table 3 Exempt Copper Compounds

Copper compounds	CAS Reg. No.
Copper sulfate basic	1344-73-6
Copper sulfate pentahydrate	7758-99-8

(c) Copper sulfate pentahydrate (CAS Reg. No. 7758-99-8) is exempt from the requirement of a tolerance when applied as a fungicide to growing crops or to raw agricultural commodities after harvest, and as a bactericide/fungicide in or on meat, fat and meat by-products of cattle, sheep, hogs, goats, horses and poultry, milk and eggs when applied as a bactericide/fungicide to animal premises and bedding.

Food and Drug Administration

21 CFR § 184.1261 Copper sulfate. Direct Food Substances Affirmed as Generally Recognized as Safe

(a) Copper sulfate (cupric sulfate, CuSO4·5 H2O, CAS Reg. No. 7758–99–8) usually is used in the pentahydrate form. This form occurs as large, deep blue or ultramarine, triclinic crystals; as blue granules, or as a light blue powder. The ingredient is prepared by the reaction of sulfuric acid with cupric oxide or with copper metal.

(b) The ingredient must be of purity suitable for its intended use.

(c) In accordance with § 184.1(b) (1), the ingredient is used in food with no limitation other than current good manufacturing practice. The affirmation of this ingredient as generally recognized as safe (GRAS) as a direct human food ingredient is based upon the following current good manufacturing practice conditions of use:

> (1) The ingredient is used as a nutrient supplement as defined in § 170.3(o) (20) of this chapter and as a processing aid as defined in § 170.3(o) (24) of this chapter.
>
> (2) The ingredient is used in food at levels not to exceed current good manufacturing practice. Copper sulfate may be used in infant formula in accordance with section 412(g) of the Federal Food, Drug, and Cosmetic Act (the Act) or with regulations promulgated under section 412(a) (2) of the Act. (d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

Action of the Substance:

The copper ion is the component of copper sulfate with toxicological implications. Copper ions appear to bind to functional groups of protein molecules in bacteria, fungi and algae and cause protein denaturation, producing cell damage and leakage. Protein components that act as binding sites are sulfidal groups, phosphate (thiol), carboxyls, and imidazoles (Epperson et al., 2007, Gyawali et al., 2011)

Copper is highly toxic to most aquatic species (NPIC, 2012). The main cause of copper toxicity to fish and aquatic invertebrates is through rapid binding of copper ions to the gill membranes, which causes damage and interferes with osmoregulatory processes. The amount of cupric ion in the environment, and its toxicity to aquatic animals through gill damage, is dependent on a number of water quality parameters including pH, alkalinity, and dissolved organic carbon. In mollusks, copper sulfate disrupts surface epithelia function and peroxidase enzymes. Studies with sheep have shown high sensitivity to products containing copper sulfate, possibly due to inefficient copper excretion (NPIC, 2012).

Combinations of the Substance:

Copper sulfate is an inorganic compound that combines copper with sulfur. It is bought commercially as Copper sulfate pentahydrate.

Status

Historic Use:

Copper salts have been used widely used in domestic agriculture since late 18th century for its fungicidal and bactericidal properties (Van- Zwieten et al., 2004). Copper sulfate has been registered for use as a pesticide since 1956. The EPA completed the reregistration of copper sulfate in 2009. As a result, two pesticides, copper sulfate monohydrate and copper sulfate anhydrous, were cancelled. Products containing copper sulfate can be liquids, dust or crystals. The compound is listed on NOP's National List of allowed synthetic substances for use in organic production.

Organic Foods Production Act, USDA Final Rule:

7 CFR § 205.601 Synthetic substances allowed for use in organic crop production.

(a) As algaecide, disinfectants, and sanitizer, including irrigation system cleaning systems.

(3) Copper sulfate—for use as an algaecide in aquatic rice systems, is limited to one application per field during any 24-month period. Application rates are limited to those which do not increase baseline soil test values for copper over a timeframe agreed upon by the producer and accredited certifying agent.

(e) As insecticides (including acaricides or mite control).

(3) Copper sulfate—for use as tadpole shrimp control in aquatic rice production, is 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.

As plant disease control.

(1) Coppers, fixed—copper hydroxide, copper oxide, copper oxychloride, includes products exempted from EPA tolerance, Provided, That, copper-based materials must be used in a manner that minimizes accumulation in the soil and shall not be used as herbicides.

(2) Copper sulfate-Substance must be used in a manner that minimizes accumulation of copper in the soil.

As plant or soil amendments.

(6) Micronutrients-not to be used as a defoliant, herbicide, or desiccant. Those made from nitrates or chlorides not allowed. Soil deficiency must be documented by testing. Sulfates, carbonates, oxides or silicates of zinc, copper, iron, manganese, molybdenum, selenium, and cobalt.

7 CFR §205.603 Synthetic substances allowed for use in organic livestock production

(b) As topical treatment, external parasiticide or local anesthetic as applicable.

International

The allowed or prohibited use of Copper sulfate by other international organic standards organizations:

Canada - Canadian General Standards Board Permitted Substances List – CAN/CGSB-32.311-2006 Amended June 2011

Permitted Substances Lists for Crop Production:

1. Copper products --These products shall be used in a manner that prevents excessive copper accumulation in the soil. Buildup of copper in soil may prohibit future use. Use with caution. No visible residue shall be allowed on harvested crops. Basic copper sulphate, copper oxide, copper sulphate and copper oxysulphate may be used to correct documented copper deficiencies. Copper ammonia base, copper ammonium carbonate, copper nitrate and cuprous chloride are prohibited as sources of copper for plant nutrients.

2. Includes copper hydroxide for use as a wood preservative or for disease control; copper sulphates for use as a fungicide; Bordeaux mix, copper oxychloride, copper oxide, fungicides or wood treatments, for fruits and vegetables. These products shall be used in a manner that prevents excessive copper accumulation in the soil. Buildup of copper in soil may prohibit future use. Use with caution. No visible residue shall be allowed on harvested crops. Basic copper sulphate, copper oxide, copper sulphate and copper oxysulphate may be used to correct documented copper deficiencies. Copper ammonia base, copper ammonium carbonate, copper nitrate and cuprous chloride are prohibited as sources of copper for plant nutrients.

Permitted Substances Lists for Livestock Production:

1. For use as an essential nutrient (source of copper and sulphur) and for topical use (footbaths). Sulphates produced using sulphuric acid are prohibited.

CODEX Alimentarius Commission, Guidelines for the Production, Processing, Labelling and Marketing of Organically Produced Foods (GL 32-1999) - –(CODEX-GL 32, 1999)[1] Amended by the 26th and 27th Sessions of the Codex Alimentarius Commission in 2003 and 2004 provides for use of copper sulfate for organic production (Table 4).

Table *4*: Codex Alimentarius Copper Use for Plant and Disease Control

Substance	**Description; compositional requirements; conditions of use**
Copper in the form of copper hydroxide, copper oxychloride, (tribasic) copper sulphate, cuprous oxide, Bordeaux mixture and Burgundy mixture	Need, prescription and application rates recognized by certification body or authority. As a fungicide on condition that the substance be used in such a way as to minimize copper accumulation in the soil.
The Codex has not established a MRL for copper sulfate pentahydrate (pesticide).	

European Economic Community (EEC) Council Regulation, EC No. 834/2007 and 889/2008

Please refer to Table 5.

Table 5. EEC: Copper use permitted in organic farming

Authorization	**Name**	**Description, compositional requirement, conditions for use**
Plant Protection Products referred to 6.5.1 Regulation (EC) No 834/2007	Copper compounds in the form of copper hydroxide, copper oxychloride, copper oxide, Bordeaux mixture, and tribasic copper sulphate	Only uses as bactericide and fungicide up to 6 kg copper per hectare per year. For perennial crops, CBs may, by derogation from the first paragraph, provide that the 6 kg copper limit can be exceeded in a given year provided that the average quantity actually used over a 5-year period consisting of that year and of the four preceding years does not exceed 6 kg. Risk mitigation measures shall be taken to protect water and non-target organisms such as buffer zones. Only products also specified in the Annex to implementing Regulation (EU) No 540/2011 (number 277).
Feed additives and certain substances used in animal nutrition referred to 6.7.20 Additives listed must have been approved under Regulation (EC) No 1831/2003 of the European Parliament and of the Council on additives for use in animal nutrition.	Cupric oxide, basic cupric carbonate, monohydrate, copper sulphate, pentahydrate;	
European Union's regulation on organic production and labeling of organic products was revised in September 2008 (EU-889/2008).		

Japan Agricultural Standard (JAS) for Organic Production-
http://www.ams.usda.gov/nop/NOP/TradeIssues/JAS.html

Standards and Individual Procedures for Judging Compliance of Substances Listed in Appendices 1 and 2 of Japanese Agricultural Standards for Organic Plants: Notice 1180, August 2009
3. Copper sulfate: Only for use in preparation of Bordeaux mixture.

Substances for Plant Pest and Disease Control (Table 2):

Copper wetable powder
Copper powdered agent

International Federation of Organic Agriculture Movements (IFOAM)-

Since 2002, the International Federation of Organic Agriculture Movements (IFOAM) has limited total copper input on organic farms to a maximum of 8 kg /ha/ year. These restrictions applied by the organic farming industry acknowledge the potential for copper levels in orchard top-soils to accumulate with repeated application.

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?

Copper sulfate pentahydrate is composed of copper (25.4%), oxygen and sulfur. The salt, in various hydrated states, can be used in crop (to control plant disease, invertebrate, and algae) and livestock production (as an antimicrobial agent). Depending on its final use, additional ingredients/elements could be added to the mixture, if bought commercially.

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)).

Copper sulfate is produced commercially by reacting various copper minerals and or metal with sulfuric acid (Copper Org, 2015).

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)).

The Copper Development Association, Inc. (Copper Org, 2015) reported that world-wide there were more than 100 producers, yielding 200,000 tons of the copper compounds annually. It is estimated that approximately three-quarters is used in agriculture, principally as a fungicide.

Copper Org, 2015 also reported that for the bulk of the production comes from nonferrous scrap and not copper ore. The scrap is dissolved in dilute sulfuric acid than allowed to cool slowly to form the traditional large crystals of copper sulfate. Other methods of producing the salt include:

- heating copper scrap with sulfur to produce copper sulfide and then oxidized to form copper sulfate,
- heating copper sulfide ores to produce copper oxide and then treat with sulfuric acid to form copper sulfate, and
- exposing low grade ore to the air and bacterial action.

Therefore, Copper sulfate is a synthetic compound produced by a chemical process.

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

Copper is an essential microelement to plant growth. Chlorophyll production, protein synthesis and respiration are important plant functions that need copper. About 70 percent of the copper in plants is found in the chlorophyll. Most crop tissues (leaves and stems) normally contain copper in the range of 5 - 30 ppm. The copper content of soils ranges from 2 to 100 ppm, with an average value of about 30 ppm. Most agricultural crops remove (i.e., alfalfa, corn and other small grains) remove less than 0.1 lb./acre of copper per year (Schulte et al.,1999; Stehouwer et al., 2004) The copper ion is held tightly by minerals and organic matter in the soil and most copper in the soil are unavailable to plants. Organic matter and soil pH are major factors influencing copper availability. Increasing the soil pH increases the ions bonding to organic matter. Although the soil rarely produces excessive amounts of copper on its own, copper toxicity can occur from over application of the micronutrient in agricultural production. For example, horticultural and viticultural operations with a long history of copper (Bordeaux mix) fungicide application have resulted in accumulations of copper in the soil (Gallagher et al., 2001 and Chaignon et al., 2003). The classic foliar symptom of copper toxicity is interveinal chlorosis (pale green yellow striping in leaves) and stunted growth due to root damage. Neutralizing copper soil toxicity is extremely difficult once the problem occurs. Copper has low solubility, which enables it to persist in the soil for years.

<u>Evaluation Question #5:</u> 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)).

Copper sulfate footbath has been used as management strategy to treat hoof related diseases in dairy cattle and sheep. However, several papers in the scientific literature and state agricultural extension service bulletins raise the concerns about disposing used copper sulfate solution into the manure pit or wastewater lagoons (Epperson et al 2007, Ippolito et al., 2011, Moore, 2009, Stehouwer et al., 2004). The additional copper ions can increase the overall concentration significantly in manure slurry, from approximately 5.0 grams per 1,000 liters to 90.0 grams per 1,000 liters. This enriched dairy waste is then applied to agricultural land, thus raising concerns about how soils and plants are impacted by the increase in the copper load (Ippolito et al. 2013).

Copper is bound, or adsorbed, to organic materials, and to clay and mineral surfaces. The degree of copper adsorption to soils depends on the level of acidity or alkalinity of the soil. Dairy manure is rich in organic matter and will naturally have greater Cu adsorption than dairy lagoon water which is low in organic matter. In soils with pH values greater than 7.0, soluble Cu^{+2} will react with water to form either copper hydrate or associations with Fe-oxides (Ippolito et al., 2013). Thus, almost all Cu added to soil will remain in the soil and accumulate in the upper soil layers (Stehouwer et al., 2004). The potential for groundwater contamination increases in sandy, acidic soils or under irrigated conditions. However, most studies suggest that soluble Cu transported through soils does not exceed the national drinking water standard of 1.3 mg/L.

Ippolito et al., 2013 noted that the potential for Cu toxicities in plants is relatively small given the amount of Cu that is added through dairy-waste application. With the strong binding of soluble Cu to soils, very little of the applied Cu is plant-available. Preliminary results from the USDA–ARS in Kimberly, Idaho, showed that extractable soil Cu concentrations ranging from 1 to 154 parts per million (ppm) in a calcareous soil had no effect on alfalfa or corn silage biomass yields, while plant survival was drastically impeded at concentrations greater than 323 ppm. Copper application rates used in this study to achieve reductions in yields and plant survival greatly exceeded rates typically seen for dairy manure applications. In a similar study conducted in New York, $CuSO_4$ was applied at 0, 6.3 and 12.6 pounds Cu per acre to corn silage, orchard grass, and timothy grass using Cu rates equivalent to those typical to dairy waste applications. Similar soil Cu concentrations were 11, 13 and 18 ppm, respectively. The varying Cu application rates had no effect on grass or corn silage yields, although plant shoot growth rates were significantly reduced for the grasses (Moore, 2009).

Although these studies were short in duration, repeated applications of dairy manures could potentially raise Cu concentrations to levels toxic to plants, with very limited possibilities for remediation (Ippolito et al., 2013).

<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)).

Walk-through footbaths are used to help control and prevent hoof relate diseases in dairy cattle and sheep. A five to ten percent copper sulfate solution is commonly used as the antimicrobial agent in the footbath and is considered effective for 150 to 300 animal passes. Spent solution is mixed with manure waste and ultimately disposed by land application. Regulators in several states (Ippolito et al., 2013, Rankin, 2012) have expressed concern that soil copper could be increased to an unhealthy level by this practice and have established maximum (lifetime) loading rates of copper. An 8 ft. x 2.5 ft. x 5 inch foot footbath will contain approximately 62 gallons of water and 26 pounds of copper sulfate (charged at the 5% concentration). Since copper sulfate is 25% copper, each time the footbath is dumped, 6.5 pounds of copper is added to the disposal burden. The environmental effect of this copper depends on the volume of footbath solution disposed (a function of the number of animals and intensity of footbath use), concentration of copper sulfate, and the land area of application. Without careful attention, maximum soil copper loading rates may be exceeded in relatively short times (5 to 30 years) (Epperson et al., 2007). Depending on the agricultural crop, the annual removal rate for copper is less than 0.5 pound/acre per year.

Federal, state and local levels environmental regulations require the development of manure management plans to protect water resources and soil quality. The EPA has specific guidelines for copper loading to agricultural land when sewage sludge or biosolids are applied. The EPA §503.13 standard limits annual loading of copper from biosolids to 66 pounds copper per acre and limits lifetime loading to 1,339 pounds copper per acre (limits are based on biosolids land application) (EPA, 2014). Reaching these limits is almost impossible with dairy waste applications, and would devastate most agricultural crops long before the lifetime loading limits were met.

Some states have lower limits for copper application. New York and Illinois have set lower lifetime loading limits for Copper at 75 and 250 pounds per acre, respectively, in order to avoid the potential of irreversible toxic accumulations of Cu in the soil (Socha et al., 2007, Ippolito et al., 2013, Rankin, 2012). While more studies are needed, Ippolito et al. 2013 recommended that alkaline soils with greater than 50 ppm extractable copper should not have additional copper load added to soil. This value is advisable for producers raising alfalfa for dairy cow consumption in order to avoid copper accumulation above the NRC 2005 recommendations for the maximum tolerable Cu level for cattle and sheep. Ippolito et al., 2013 suggested that soil samples be tested for extractable copper every two to three years from an accredited soil testing laboratory to determine if a copper accumulation problem exists.

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)).

Copper sulfate has been used as a footbath antiseptic to help control and prevent infectious hoof disease problems. The hoof bath solutions usually contain one or a mixture of synthetic substances compounds with known antimicrobial properties. There is a lack of well documented and reported trials under farm conditions that show the effect of foot bathing when accompanied by proper hoof trimming. Additionally, the available trial data does not always address the full range of foot diseases. A number of researchers have expressed concern about the procedures employed, the selection of commercially available products, footbath dimensions, placement and animal hygiene and number of cow passes before cleaning and refilling (Hoffman 2012, Durkin et al. 2004)

Tomlinson et al. (2014) reported that the effectiveness of a footbath solution is dependent upon the antimicrobial activity of the solution and the impact of soil load (organic matter). For example, sodium hypochlorite (chlorine) has a broad range of activity against pathogenic bacteria; however, it has limited utility in footbath solutions where organic material such as manure reacts with the chlorine, resulting in loss of antimicrobial activity.

Schultz et al. (2013) undertook a study to evaluate the efficacy of salicylic acid (SA) applied topical (within a bandage) to treat dairy cows with digital dermatitis (DD) lesions. The findings suggested that topical treatment with SA proved to be 1.75 fold better than an antibiotic in terms of clinical improvement in heeling the DD lesions. The topical application of SA should be considered as a useful alternative to antibiotics in the treatment of DD in cattle as it appears to be more effective and has a reduced environmental impact. Aspirin (i.e., salicylic acid) is a listed substance in §205.603 allowed for use in organic livestock production; however, it is currently only approved for health care use to reduce inflammation.

Hoffman (2012) reported that Speijers et al. (2010) compared 5% copper sulfate used twice daily for two days every week to an untreated control group and found that more treated cows had no DD or healing DD lesions compared to the control group. Almost 60% of the herd was affected by DD at the start of their study. In a second experiment, Speijers compared the efficacy of 2 and 5 percent copper sulfate solutions. They found that the proportion of cows with no DD lesion at the beginning of the study that remained free of DD lesions was the same for these two concentrations, but a greater proportion of cows in the 5% copper sulfate group had no DD lesions by the end of the study. These authors also compared using 5% copper sulfate twice daily for two days in a row every two weeks to tap water or saltwater (10% sodium chloride) in alternating weeks with the same copper sulfate treatment. They concluded that there appears to be no advantage to using tap water or saltwater versus no treatment in alternating weeks.

Recently, zinc sulfate has been petitioned to be added to USDA's National Organic Program's (NOP) National List of allowed synthetic substances for use in organic livestock production for use in foot baths.

Several papers in the scientific literature and state agricultural extension service bulletins suggests some success in controlling DD with the use of footbaths containing 5 to 20% (w/v) zinc sulfate solutions (Tomlinson et al., 2014, Hoffman 2012). Zinc sulfate solutions have antibacterial properties and are relatively inexpensive to use in footbaths. It has not been widely accepted because of difficulty in dissolving most sources of zinc sulfate in water. One advantage of using zinc sulfate is the zinc ion is a microelement needed in corn fertilization programs. However, like copper sulfate, used zinc sulfate footbath solutions will be mixed with manure waste and ultimately disposed by land application. According to EPA Standard 503, the cumulative loading limit for zinc is 2499 lbs/acre at an annual application limit of 125 lbs/acre (EPA, 2014). Potential concerns with this level of zinc disposal include exceeding EPA and state guidelines for zinc loading of agricultural land.

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)).

Copper is an essential element and required by all organisms. However, elevated concentrations of copper in soils are toxic and may result in a range of effects including reduced biological activity and subsequent loss of fertility (Ma, Wei-chun 1988).

Walk-through footbaths are used to help control and prevent hoof related diseases in dairy cattle and sheep. Five to 10 percent copper sulfate solutions are commonly used as the antimicrobial agent in the footbath and are considered effective for 150 to 300 animal passes. Spent solution is mixed with manure waste and ultimately disposed by land application.

Copper is bound, or adsorbed, to organic materials, and to clay and mineral surfaces. The degree of copper adsorption to soils depends on the level of acidity or alkalinity of the soil. Dairy manure is rich in organic matter and will naturally have greater Cu adsorption than dairy lagoon water which is low in organic matter. In soils with pH values greater than 7.0, soluble Cu^{+2} will react with water to form either copper hydrate or associations with Fe-oxides (Ippolito et al., 2013). Thus, almost all Cu added to soil will remain in the soil and accumulate in the upper soil layers (Stehouwer et al. 2004). The potential for groundwater contamination increases in sandy, acidic soils or under irrigated conditions. However, most studies suggest that soluble Cu transported through soils does not exceed the national drinking water standard of 1.3 mg/L (NPIC, 2012 , RED-Cu, 2009).

Earthworms are an important soil invertebrate in promoting soil fertility (Duiker et al., Valenzuela, 2010). Their feeding and burrowing activities break down organic matter and release nutrients and improve aeration, drainage, and aggregation of soil. Feeding and burrowing habits of earthworms determine their exposure to chemicals in soil and litter. In a review of copper sulfate literature, Paoletti(1999) stated at the laboratory level, tests specifically developed for lumbricid species (living only in manure) suggest copper sulfate is lethal only when applied at high doses over 1000 ppm and the toxicity would decrease as the quantity of organic matter increases in the soil. Treatment of orchards and vineyards with copper sulfate fungicides strongly affects soil invertebrates, especially earthworms in terms of both biomass and species population response (Paoletti et al., 1988).

Soil microorganisms play a critical role in nutrient cycling. As primary consumers of soil organic matter, soil microbes convert nutrients to plant-available forms and serve as a food source for higher trophic levels. The soil microbiota is a heterogeneous collection of highly adaptable organisms exploiting the many micro-niches in the soil.

Ippolito et al. 2011 investigated the effect of copper applications on alfalfa growth and copper concentration and the soil bacterial load. Copper application up to 250 mg/kg did not affect alfalfa growth nor impacted the bacterial diversity of the soil. The higher concentrations did impact both the plant and bacterial load of the soil. Ippolito et al. 2011 suggested available soil copper not exceed 63 mg/kg in agroecosystems associated with these soils in order to prevent excessive alfalfa copper accumulation and negative impacts on the soil bacterial community.

Lejon et al. 2008 also investigated the copper load impact in vineyard soil amended with varying types of organic matter on soil microcosms. The results showed that copper distribution, speciation, and bioavailability are different between organically amended and unamended soils. It also showed that organic matter controlled copper toxicity and the level of microorganisms in the soil.

Van Zwieten et al., 2004 reviewed the copper impacts on soil biota. Significant impacts were observed when copper concentrations were greater the 150mg/kg. The study observed few earthworms and reduced surface activity with fewer castings visible at the soil surface. The evidence reviewed in this paper demonstrates that copper residues originating from fungicide application reduce soil microbial biomass, while stressing the microorganisms that are present. In addition, copper- has resulted in an elimination of earthworms in the orchard where residues averaged between 180-338 mg/kg. This has influenced soil processes by reducing bioturbation and chemical processes.

Evaluation Question #9: 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)).

Copper sulfate is listed on the National List of allowed synthetic substances for use in organic livestock production (§ 205.603) as a topical treatment, external parasiticide or local anesthetic. Copper ions have been reported to have antimicrobial activity against a wide range of aerobic and anaerobic bacteria and fungi. The exact mechanisms by which copper sulfate exerts its biocidal effect is a source of numerous ongoing investigations in the scientific literature (Hoffman, 2012).

Copper sulfate has been used as a footbath antiseptic to help control and prevent infectious hoof disease problems that affect the skin adjacent to the claw horn of dairy cattle and sheep i.e., digital dermatitis (DD) (hairy heel warts), foot rot lesions (interdigital area and invading the subcutaneous tissue), and heel erosions. Depending on the severity of the infection, the impact on managed cattle and/or sheep ranges from minor discomfort to severe debilitating lameness, reproductive problems and in the dairy industry a reduction of milk production ranging from 20 to 50 percent (Brown, et al., 2000). The bacterial spirochetes, Treponema spp., are thought to be a major contributor to the cause and origin of DD. Other bacteria associated with causing the infectious hoof disease include Dichelobacter nodosus, Fusobacterium necrophorum, Staphylococcus aureus, Escherichia coli, and Actinomyces pyogenes.

Additional factors that contribute to the infection include poor animal hygiene, an injury to the skin of some type, continuous exposure to wet conditions, a housed cubicle design and diagnosing and treating suspected lesions and infections. Copper sulfate solutions (5 to 10% w/v) are commonly used in footbaths. The higher the concentration of copper ions in the water solution, the higher the lethality rate for the targeted bacteria. It also is dependent on the frequency of changing solutions, footbath dimensions and location in the operation.

The bacteriostatic properties of copper sulfate are attributed to copper ions reacting with sulfhydryl-(SH) group of thiol dependent enzymes, thus stopping the oxidizing process of the bacteria (Epperson et al., 2007). The popularity of copper sulfate footbaths can be attributed to both its relatively low cost per footbath and that it effectively controls the infectious lesions. Research has shown that using copper sulfate footbaths decrease both the incidence and severity of foot lesions over time. However, some data suggest that copper sulfate is rapidly neutralized by organic matter (Greenough, 1997) and is less effective as the infection becomes progressively worse.

Concerns with using copper sulfate include metal corrosion and disposal of the copper sulfate solution. On the farm, discarding the diluted copper sulfate solution with manure (and placed in wastewater lagoon) is a normal practice (Ippolito et al., 2011). For example, if a dairy operation is using a 50-gallon footbath containing a 5% w/v copper sulfate solution, twice a week, and changed the solution every 200 animal passes, 10.9 pounds of copper sulfate/animal per year will discarded. Although the copper solution is diluted when mixed with manure, there is a potential for copper levels to increase in the soil over time when the manure is added to agricultural land as a soil amendment or fertilizer. High copper levels in the soil impact crop yields due to phytotoxity and could exceed EPA and state guide lines for copper loading of agricultural land (Rankin, 2012, Ippolito et al., 2008).

In high concentrations, copper damages the plant's root system. In some locations, (Downing et al., 2010, Ippolito et al., 2010 and 2013, Rankin, 2012, Rehm et al., 2009) crop yields have been greatly reduced as a result of copper toxicity. At current rates of application many dairy operations will achieve the lifetime accumulative load within a period of 10-15 years. All farm operations that use copper sulfate should calculate the load that will be applied per acre in order to determine if the soil is reaching EPA or state lifetime accumulative loads. This assessment may be made by multiplying the pounds of copper sulfate purchased annually by 0.25 to determine the actual amount of copper; then divide this amount by the number of acres that are receiving manure applications (Shearer, 2006).

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

Copper sulfate is an inorganic salt that is highly soluble in water. The disassociated copper ions bind to organic matter. Human exposure to copper is primarily from food (organ meats, seafood, beans, nuts, and whole grains) and drinking water sources (RED-Cu, 2009). The estimated total daily oral intake of copper is between 1 and 2 mg day. These values are higher than the recommended dietary allowance (RDA) of copper, as established by the National Academy of Science, ranging from 0.34 mg/day in young children to 1.3 mg/day for pregnant and lactating females.

RED-Cu, 2009 stated that the mechanisms for regulating total copper in the body appear to be efficient in maintaining a generally consistent level of copper needed for homeostasis. The efficiency of copper absorption varies greatly, depending on dietary intake. When dietary copper is high and more copper is absorbed, mainly through the gastrointestinal tract, excretion of copper from the body increases, protecting against excess accumulation of copper in the body. Depending on the copper status in the body at the time, approximately 20 to 60% of dietary copper may be absorbed. Copper absorption is also affected by other factors such as species, age, chemical form, and pregnancy. When copper intake is low, little copper is excreted from the body, protecting against copper depletion.

The usual routes by which humans can receive toxic exposure to the copper sulfate are through eye or skin contact as well as by inhaling powders and dusts (MSDS-Copper 1 and 2).

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)).**

There are no natural (non-synthetic) products available that can be used as a management strategy to treat hoof relate diseases and lameness in dairy cattle and sheep operations. However, there are various management tools available that could help reduce the cost of treatment and prevent hoof related diseases. These include the use additional dietary supplements (i.e., feeding of iodine, feeding of zinc methionine) , free stall (cubicle) design, limit contact with gravel or rocky surfaces, and hoof trimming practices (Maas 2009).

Copper sulfate has been used as a footbath antiseptic to help control and prevent infectious hoof disease problems. The hoof bath solutions usually contain one or a mixture of synthetic substances compounds with known antimicrobial properties. There is a lack of well documented and reported trials under farm conditions that show the effect of foot bathing when accompanied by proper hoof trimming. Additionally, the available trial data does not always address the full range of foot diseases. A number of researchers have expressed concern about the procedures employed, the selection of commercially available products, footbath dimensions, placement and animal hygiene and number of cow passes before cleaning and refilling (Hoffman, 2012, Durkin et al., 2004).

Tominson et al., (2014) reported that the effectiveness of a footbath solution is dependent upon the antimicrobial activity of the solution and the impact of soil load (organic matter). For example, when used properly, sodium hypochlorite (chlorine) can an effective method to eliminating pathogenic bacteria and viruses from work surfaces and water (McGlynn, 2004). Its use would be limited in footbath solutions where organic material such as manure reacts with the chlorine, resulting in a loss of antimicrobial activity (McGlynn, 2004, Tomlinson et al., 2014).

Schultz et al. 2013 under took a study to evaluate the efficacy of salicylic acid (SA) applied topical (within a bandage) to treat dairy cows with DD lesions. The findings suggested that topical treatment with SA proved to be 1.75 fold better than an antibiotic in terms of clinical improvement in heeling the DD lesions. The topical application of SA should be considered as a useful alternative to antibiotics in the treatment of DD in cattle as it appears to be more effective and has a reduced environmental impact. Aspirin (i.e., salicylic acid) is a listed substance in §205.603 allowed for use in organic livestock production; however, it is currently only approved for health care use to reduce inflammation.

Hoffman (2012) reported that Speijers et al. (2010) compared 5% copper sulfate used twice daily for two days every week to an untreated control group and found that more treated cows had no DD or healing DD lesions compared to the control group. Almost 60% of the herd was affected by DD at the start of their study. In a second experiment, Speijers compared the efficacy of 2 and 5 percent copper sulfate solutions. They found that the proportion of cows with no DD lesion at the beginning of the study that remained free of DD lesions was the same for these two concentrations, but a greater proportion of cows in the 5% copper sulfate group had no DD lesions by the end of the study. These authors also compared using 5% copper sulfate twice daily for two days in a row every two weeks to tap water or saltwater (10% sodium chloride) in alternating weeks with the same copper sulfate treatment. They concluded that there appears to be no advantage to using tap water or saltwater versus no treatment in alternating weeks.

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

Below are several alternative management practices that could employed to help control and prevent infectious hoof disease problems. They are:

1. Foot trimming**:** This reduces the number of cracks and crevices where bacteria can hide, removes infected hoof, and exposes the wound to air. Foot trimming should be done at least one to two times per year as a part of normal management practices. When trimming feet, it is important to disinfect the trimming instruments (foot shear, hoof parer, or knife) between animals to prevent spreading of the infection. Prevent mechanical injury damage to cattle and sheep feet as caused by frozen or dried mud and minimizing the time cattle must spend standing in wet areas.
2. Recently, zinc sulfate has been petitioned to be added to USDA's National Organic Program's (NOP) National List of allowed synthetic substances for use in organic livestock production for use in foot baths. According to Tomlison et al., 2014, zinc sulfate (5 to 20%) solutions have antibacterial properties and may also act as a hardening agent in controlling infectious claw lesions. The zinc sulfate can be added to the copper sulfate solution or can be as a standalone solution.
3. Tomlinson et al., 2014 suggested that proper use and management of walk-through footbaths can reduce the frequency of changing the solutions. For example, footbaths should be located in frequently traveled areas such as the return alley from the milking parlor. A prebath using water or salt solution to remove manure buildup on feet of the cattle should be used prior to the treatment footbath (Cook, 2007 and Cook et al., 2012).
4. Tomlinson et al., 2014 recommended footbath solutions be changed every 150 to 200 animals to maximize effectiveness of the treatment solutions. The optimal interval for changing footbath solutions depends on cleanliness of animals, footbath size and the concentration of the treatment solution.

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