United States Department of Agriculture
Agricultural Marketing Service | National Organic Program
Document Cover Sheet
https://www.ams.usda.gov/rules-regulations/organic/national-list/petitioned

Document Type:

☐ **National List Petition or Petition Update**

A petition is a request to amend the USDA National Organic Program's National List of Allowed and Prohibited Substances (National List).

Any person may submit a petition to have a substance evaluated by the National Organic Standards Board (7 CFR 205.607(a)).

Guidelines for submitting a petition are available in the NOP Handbook as NOP 3011, National List Petition Guidelines.

Petitions are posted for the public on the NOP website for Petitioned Substances.

☒ **Technical Report**

A technical report is developed in response to a petition to amend the National List. Reports are also developed to assist in the review of substances that are already on the National List.

Technical reports are completed by third-party contractors and are available to the public on the NOP website for Petitioned Substances.

Contractor names and dates completed are available in the report.

Trace Minerals

Livestock

Identification of Petitioned Substance

“Trace minerals” is a term for multiple nutritional elements added to livestock, poultry, and companion animal diets in micro quantities only (i.e., measured in milligrams per pound or small units) (AAFCO 2019). While the Association of American Feed Control Officials (AAFCO) lists only cobalt, copper, iodine, iron, manganese, and zinc as trace minerals added to animal feeds (AAFCO 2019), this technical report also discusses chromium, molybdenum, and selenium, which are all commonly found in commercial trace mineral products on the market for inclusion in animal feeds. Because a technical evaluation was completed in 2013 for use of trace minerals in aquaculture (USDA 2013), the use of trace minerals in aquaculture will not be discussed in this review. Information on the trace minerals in this report can be found in Table 1 below. See *Appendix A* for the specific U.S. Food and Drug Administration (FDA) or AAFCO citations which are the regulatory basis for allowing the trace minerals identified below.

Table 1. Trace minerals used in livestock, poultry and companion animal feeds

Mineral	Compound	Other names	CAS number	EC number
Chromium	Chromium propionate	Propionic acid chromium (3+) salt, Chromium (III) propionate; Chromic propionate; KemTRACE chromium	85561-43-9	919-722-0
	Chromium picolinate	Chromium (III) picolinate; Chromium tripicolinate	14639-25-9	100-131-423
	Chromium-enriched yeast	Buffermin® Chromium Yeast; ChromoPrecise®	7440-47-3 (chromium) plus 8013-01-2 (yeast extract)	231-157-5 (chromium) plus 614-750-7 (yeast extract)
Cobalt	Cobalt acetate	Cobalt diacetate; Cobalt (II) acetate; Cobaltous diacetate	Anhydrous 71-48-7 Tetrahydrate 6147-53-1	Anhydrous 200-755-8 Tetrahydrate 612-153-6
	Cobalt carbonate	Cobalt (II) carbonate; Cobaltous carbonate; Cobalt (II) salt; Spherocobaltite	513-79-1	208-169-4
	Cobalt chloride	Cobalt (II) chloride; Cobalt muriate	Anhydrous: 7646-79-9 Hexahydrate: 7791-13-1	231-589-4
	Cobalt glucoheptonate	Copro®; Glucohetonic acid cobalt salt	Glucoheptonate 87-74-1	Glucoheptonate 201-769-7
	Cobalt gluconate	Gluconic acid, cobalt salt	71957-08-9	276-206-1
	Cobalt oxide	Cobalt (II) oxide; Cobalt monoxide; Cobalt black; Zaffre	1307-96-6	215-154-6
	Cobalt sulfate (British: sulphate)	Cobalt brown; Cobalt (II) sulfate; Cobaltous sulfate	10124-43-3	233-334-2
	Cobalt amino acid chelate			
	Cobalt amino acid complex			
	Cobalt choline citrate complex			
	Cobalt polysaccharide complex			
	Cobalt proteinate			
Copper	Copper acetate	Cupric acetate; Copper (II) acetate	Monohydrate 6046-93-1	205-553-3

Mineral	Compound	Other names	CAS number	EC number
	Copper carbonate	Copper (II) carbonate or Cupric carbonate	1184-64-1	214-671-4
	Copper chloride	Cupric chloride	7447-39-4	231-210-2
	Copper citrate	Cuprocitrol; Cupric citrate	10402-15-0	212-752-9
	Copper gluconate	Copper D-gluconate; Cupric gluconate	527-09-3	208-408-2
	Copper hydroxide	Cuprous hydroxide; Copper (I) hydroxide; Copper dihydroxide	1344-69-0	215-705-0
	Copper orthophosphate	Phosphoric acid, copper salt	10103-48-7	233-284-1
	Copper oxide	Copper (II) oxide or cupric oxide	1317-38-0	215-269-1
	Copper pyrophosphate	Dicopper pyrophosphate; Copper (II) pyrophosphate	10102-90-6	239-250-2
	Copper sulfate pentahydrate (British: sulphate)	Copper sulphate; Cupric sulfate; Blue vitriol; Bluestone; Chalcanthite	Anhydrous: 7758-98-7 Pentahydrate: 7758-99-8	231-847-6
	Cuprous iodide	Copper (I) iodide; Copper monoiodide; Iodocopper	7681-65-4	231-674-6
	Tribasic copper chloride	Dicopper chloride trihydroxide; Copper trihydroxyl chloride; Copper hydroxychloride; Copper chloride hydroxide	1332-65-6	215-572-9
	Copper amino acid chelate			
	Copper amino acid complex			
	Copper choline citrate complex			
	Copper lysine complex			
	Copper polysaccharide complex			
	Copper proteinate			
Iodine	Calcium iodate	Calcium diiodate	Anhydrous: 7789-80-2 Monohydrate: 10031-32-0	232-191-3
	Calcium iodobehenate	Iododocosanoic acid calcium salt; iodobehenate calcium; Calioben; Saiodin; Sajodin	1319-91-1	n/a
	Cuprous iodide	Copper (I) iodide; Copper monoiodide; Iodocopper	7681-65-4	231-674-6
	Diiodosalicylic acid	3,5-diiodosalicylic acid	133-91-5	205-124-0
	Ethylenediamine Dihydriodide	EDDI; Dihydroiodide ethanediamine; Hiamine; ethane-1,2-diamine, dihydroxide; Orgadine; Ethylenediammonium diodide	5700-49-2	227-186-8
	Potassium iodate	Iodic acid, Potassium salt	7758-05-6	231-831-9
	Potassium iodide	Iodic acid potassium salt; iOSAT; SSKI; ThyroSafe; ThyroShield	7681-11-0	231-659-4
	Sodium iodide	Ioduril; Sodium monoiodide; Soiodin; Anayjodin	7681-82-5	231-679-3

Mineral	Compound	Other names	CAS number	EC number
	Thymol iodide	Iodothymol; Iodistol; Iodohydromol; Annidol; Thymiode; Lothymol; Aristol	552-22-7	209-007-5
Iron	Ferric ammonium citrate	Iron ammonium citrate; Ammonium ferric citrate; Ferriseltz	1185-57-5	214-686-6
	Ferric chloride	Iron chloride; Iron trichloride; Molysite	7705-08-0	231-729-4
	Ferric formate	Iron triformate; Ferric triformate; Iron (III) formate	555-76-0	209-106-3
	Ferric phosphate	Iron (III) phosphate; Ferric orthophosphate; Iron phosphate	10045-86-0	233-149-7
	Ferric pyrophosphate	Iron (III) pyrophosphate; Tetrairon tris(pyrophosphate)	10058-44-3	233-190-0
	Ferric sodium pyrophosphate	Iron sodium pyrophosphate; Sodium ferric pyrophosphate	10045-87-1	233-150-2
	Ferric sulfate (British: Sulphate)	Iron (III) sulfate; Iron persulfate; Iron tersulfate	10028-22-5	233-072-9
	Ferrous carbonate	Iron (II) carbonate, Ferrous monocarbonate, Blaud's mass	563-71-3	209-259-6
	Ferrous chloride	Iron (II) chloride; Iron dichloride	Anhydrous: 7758-94-3 Dihydrate: 16399-77-2 Tetrahydrate: 13478-10-9	231-843-4
	Ferrous fumarate	Iron (II) fumarate; Fersamal; Feostat	141-01-5	205-447-7
	Ferrous gluconate	Iron gluconate	299-29-6	206-076-3
	Ferrous lactate	Iron (II) lactate; Iron dilactate; Ferrous 2-hydroxypropanoate	5905-52-2	227-608-0
	Ferrous phosphate	Triiron bis(orthophosphate)	14940-41-1	239-018-0
	Ferrous sulfate (British: sulphate)	Iron (II) sulfate, ferrosulfate, green vitriol, iron vitriol, copperas	Anhydrous: 7720-78-7 Monohydrate: 17375-41-6 Heptahydrate: 7782-63-0	231-753-5
	Ferrous oxide	Iron monoxide, Iron (II) oxide, Oxoiron	1345-25-1	215-721-8
	Ferric choline citrate			
	Ferric choline citrate complex			
	Ferric methionine complex			
	Ferrous glycine complex			
	Iron amino acid chelate			
	Iron amino acid complex			
	Iron polysaccharide complex			
	Iron proteinate			
	Iron yeast	Lyncide® Forte Fe^{+}	617-112-6 (iron) Plus 614-750-7 (yeast extract)	8053-60-9 (iron) plus

Mineral	Compound	Other names	CAS number	EC number
				614-750-7 (yeast extract)
Manganese	Manganese acetate	Manganese (II) acetate; Manganese diacetate; Manganous acetate; Diacetylmanganese	Anhydrous 638-38-0 Dihydrate 19513-05-4 Tetrahydrate 6156-78-1	211-334-3
	Manganese carbonate	Manganese (II) carbonate	598-62-9	209-942-9
	Manganese chloride	Manganese (II) chloride; Manganese dichloride; Hyperchloride of manganese	Anhydrous 7773-01-5 Dihydrate 38639-72-4 Tetrahydrate 13446-34-9	231-869-6
	Manganese citrate	Trimanganese dicitrate	10024-66-5	233-193-7
	Manganese gluconate	Manganese D-gluconate; Manganese (II) gluconate	6485-39-8	229-350-4
	Manganese glycerophosphate	Manganese glyceryl-1-phosphate; Manganese rac-glycerel-1-phosphate	1320-46-3	215-301-4
	Manganese hypophosphate	Manganese (II) hypophosphate; Manganous hypophosphate	7785-86-6	n/a
	Manganese orthophosphate	Manganese (III) orthophosphate	10124-54-6	233-341-0
	Manganese oxide	Manganese (II) oxide, Manganese monoxide; Hypomanganous oxide	1344-43-0	215-695-8
	Manganese phosphate	Manganese (II) phosphate; Manganese phosphate tribasic; Trimanganese bis(orthophosphate)	14154-09-7	237-997-9
	Manganese sulfate (British: sulphate)	Manganese (II) sulfate, Manganous sulfate	10034-96-5	232-089-9
	Manganese amino acid complex			
	Manganese amino acid complex			
	Manganese methionine complex			
	Manganese polysaccharide			
	Manganese proteinate			
Molybdenum	Sodium molybdate	Disodium molybdate	Anhydrous: 7631-95-0 Dihydrate: 10102-40-6	231-551-7
Selenium	Sodium selenate	N/A	10102-23-5	236-501-8
	Sodium selenite	N/A	Anhydrous: 10102-18-8 Hydrate: 26970-82-1	233-267-9
	Selenium yeast	Lynside® Forte Se$^+$; Vandex, eXselen	7782-49-2 (selenium) plus 8013-01-2 (yeast extract)	231-957-4 (selenium) plus 614-750-7 (yeast extract)

Mineral	Compound	Other names	CAS number	EC number
	Selenomethionine	2-Amino-4-(methlyselanyl)butanoic acid; MSE	1464-42-2 (D,L) 3211-76-5 (L)	100-014-525
Zinc	Zinc acetate	Acetic acid, zinc salt; zinc diacetate; zinc (II) acetate; Dicarbomethoxyzinc	557-34-6	209-170-2
	Zinc carbonate	Smithsonite; Zinc spar; Carbonic acid, zinc salt; Zinc monocarbonate	3486-35-9	222-477-6
	Zinc chloride	Zinc dichloride; Zinc (II) chloride; Zinc butter	7646-85-7	231-592-0
	Zinc chloride diammine complex	Metal ammine complexes are metal complexes containing at least one ammonia (NH3) ligand. Almost all metal ions bind ammonia as a ligand, but the most prevalent examples for ammine complexes are chromium, cobalt, nickel, and copper		
	Zinc gluconate	Gluconic acid zinc (II) salt; Gluconic acid zinc salt; Zinc (II) gluconate	4468-02-4	224-736-9
	Zinc oxide	Zinc white, Calamine, Philosopher's wool, Chinese white, Flowers of zinc	1314-13-2	215-222-5
	Zinc stearate	Zinc disterate	557-05-1	209-151-9
	Zinc sulfate (British: Sulphate)	White vitriol; Goslarite	Anhydrous: 7733-02-2 Monohydrate: 7446-19-7 Hexahydrate: 13986-24-8 Heptahydrate: 7446-20-0	231-793-3
	Zinc amino acid chelate			
	Zinc amino acid complex			
	Zinc lysine complex			
	Zinc methionine complex			
	Zinc polysaccharide complex			
	Zinc proteinate			

Macro-minerals of calcium, magnesium, phosphorus, potassium, and salt (sodium and chloride) are also added to animal feeds, although in greater amounts than milligrams per pound. As such, these minerals are not considered trace minerals and are beyond the scope of this technical report. The macro-minerals that are included in animal diets, however, are listed in this technical report (Table 2, below) since many macro-minerals are allowed under the same organic regulations as those that allow trace minerals. Because macro-minerals are beyond the purview of this technical report, they will not be discussed in detail.

Table 2. Additional macro-minerals added to animal feeds

Mineral	Compound	Other names	CAS number	EC number
Calcium	Calcite	See calcium carbonate		
	Calcium Ascorbate	Calcium diascorbate; Calcium L-ascorbate; Hemicalcium ascorbatre	5743-27-1	611-529-7

Mineral	Compound	Other names	CAS number	EC number
	Calcium carbonate	Calcite; aragonite; chalk; lime; limestone; marble; oyster; pearl	471-34-1	207-439-9
	Calcium chloride	Calcium (II) chloride; Calcium dichloride	10043-52-4	233-140-8
	Calcium citrate	Tricalcium dicitrate	813-94-5	212-391-7
	Calcium gluconate	n/a	299-28-5	206-075-8
	Calcium glycerophosphate	Calcium glycerlphosphate; Calcium 1,3-hydroxypropyl phosphate	58409-70-4	261-240-1
	Calcium hydroxide	Slaked lime; Milk of lime; Calcium (II) hydroxide; Pickling lime; Hydrated lime; Calcium hydrate	1305-62-0	215-137-3
	Calcium lactate	Calcium salt pentahydrate; Calcium dilactate	814-80-2	212-406-7
	Calcium oxide	Quicklime; Calcium monoxide; Lime; Burnt lime	1305-78-8	215-138-9
	Calcium phosphate	Tricalcium phosphate tribasic; Tricalcium phosphate	10103-46-5	233-283-6
	Calcium pyrophosphate	Calcium diphosphate; Dicalcium phosphate	7790-76-3	232-221-5
	Calcium sulfate	Drierite; Karstenite; Sulfuric acid calcium salt	7778-18-9	231-900-3
	Chalk	See Calcium carbonate		
	Clam shells	See Calcium carbonate		
	Dicalcium phosphate	Calcium hydrogen phosphate dihydrate; Dibasic calcium phosphate; Calcium monohydrate phosphate	Anhydrous: 7757-93-9 Dihydrate: 7789-77-7	231-826-1
	Gypsiferous shale	See calcium sulfate dihydrate		
	Limestone	See calcium carbonate		
	Monocalcium phosphate	Calcium acid phosphate; Cabiophosphate; MCP; Calcium dihydrogen orthophosphate; Calcium hydrogen phosphate; Calcium superphosphate	7758-23-8	231-837-1
	Oyster shell	See calcium carbonate		
	Phosphate, defluorinated	Defluorinated phosphate	n/a	917-742-4
	Rock Phosphate	Denotes any rock with phosphate. Consists of calcium phosphate, mineral apatite together with quartz, calcite, dolomite, clay and iron oxide (MineralsEducationColation.org)		
	Tricalcium phosphate (TCP)	Tribasic calcium phosphate; Bone phosphate of lime (BPL)	7758-87-4	231-840-8
	Calcium amino acid chelate			
	Calcium amino acid complex			
	Calcium proteinate			
Magnesium	Limestone	See calcium carbonate		

Mineral	Compound	Other names	CAS number	EC number
	Magnesium carbonate	Carbonic magnesium; Magnesite	546-93-0	208-915-9
	Magnesium chloride	Magnesium dichloride	7786-30-3	232-094-6
	Magnesium gluconate	Magnesium digluconate	3632-91-5	222-848-2
	Magnesium hydroxide	Milk of magnesia	1309-42-8	215-170-3
	Magnesium mica	Phlogopite, vermiculite	n/a	n/a
	Magnesium oxide	Magnesia	1309-48-4	215-171-9
	Magnesium phosphate	Salts of magnesium and phosphate		
		Monomagnesium phosphate (Magnesium bis(dihydrogen orthophosphate)	13092-66-5	236-004-6
		Dimagnesium phosphate (Magnesium hydrogen orthophosphate)	7757-86-0	231-823-5
		Trimagnesium phosphate (Trimagnesium bis(orthophosphate)	10233-87-1	231-824-0
	Magnesium sulfate (British: sulphate)	Epsom salt	Anhydrous: 7487-88-9 Monohydrate: 14168-73-1 Tetrahydrate: 24378-31-2 Pentahydrate: 15553-21-6 Hexahydrate: 13778-97-7 Heptahydrate: 10034-99-8	231-298-2
	Magnesium amino acid chelate			
	Magnesium amino acid complex			
	Magnesium polysaccharide complex			
	Magnesium proteinate			
Phosphorus	Ammonium phosphate	Salt of ammonium phosphate; Triammonium phosphate	10361-65-6	269-789-9
	Ammonia polyphosphate solution	n/a	68333-79-9 + water	100-063-425 + water
	Calcium glycerophosphate	Glycerol hydrogen orthophosphate	27214-00-2	248-328-5
	Calcium phosphate	See calcium sources		
	Diammonium phosphate	Diammonium hydrogen orthophosphate	7783-28-0	231-987-8
	Dicalcium phosphate	Calcium hydrogen phosphate dihydrate; Dibasic calcium phosphate; Calcium monohydrate phosphate	Anhydrous: 7757-93-9 Dihydrate: 7789-77-7	231-826-1

Mineral	Compound	Other names	CAS number	EC number
	Disodium phosphate	Sodium hydrogen phosphate; Sodium phosphate dibasic	7558-79-4	231-448-7
	Manganese glycerophosphate	See Manganese sources		
	Manganese hypophosphate			
	Magnesium phosphate			
	Monoammonium phosphate	MAP; Ammonium dihydrogen phosphate	7722-76-1	231-764-5
	Monocalcium phosphate	See calcium sources		
	Monosodium phosphate	MSP; Monobasic sodium phosphate; Sodium biphosphate	7558-80-7	231-449-2
	Phosphate, defluorinated	See calcium sources		
	Phosphoric acid	Orthophosphoric acid	7664-38-2	231-633-2
	Rock phosphate	See calcium sources		
	Sodium phosphate	Generic for a several varieties of salts of sodium and phosphate – monophosphates, diphosphates and polyphosphates		
	Sodium tripolyphosphate			
	Tricalcium phosphate	Calcium phosphate tribasic	7758-87-4	231-840-8
	Trisodium phosphate	TSP; Sodium phosphate tribasic	7601-54-9	231-509-8
Potassium	Potassium bicarbonate	Potassium hydrogen carbonate; Potassium acid carbonate	298-14-6	206-059-0
	Potassium carbonate	Carbonate of potash	584-08-7	209-529-3
	Potassium chloride	Sylvite; Muriate of potash	7447-40-7	231-211-8
	Potassium citrate	Tripotassium citrate	866-84-2	212-755-5
	Potassium gluconate	n/a	299-27-4	206-074-2
	Potassium glycerophosphate	n/a	927-19-5	215-291-1
	Potassium hydroxide	Caustic potash; Lye; Potash lye; Potassium hydrate	1310-58-3	215-181-3
	Potassium iodate	See Iodide source		
	Potassium iodide			
	Potassium sulfate	British: Potassium sulphate	7778-80-5	231-915-5
	Potassium amino acid complex			
Sodium and chlorine	Sodium chloride	Halite, table salt	7647-14-5	231-598-3
Sodium	Disodium phosphate	See phosphorus sources		
	Monosodium phosphate	Sodium dihydrogen phosphate; Sodium biphosphate	7558-80-7	231-449-2
	Sodium acetate	Acetic acid sodium salt	179-09-3	204-823-8
	Sodium acid phyrophosphate	Disodium diphosphate; Disodium dihydrogen pyrophosphate	7758-16-9	231-835-0
	Sodium biocarbonate	Sodium hydrogen carbonate	144-55-8	205-633-8

Mineral	Compound	Other names	CAS number	EC number
	Sodium carbonate	Disodium carbonate; Soda ash; Carbonic acid disodium salt	487-19-8	207-838-8
	Sodium caseinate	Casein sodium salt; Nutrose; Casein sodium	9005-46-3	618-419-8
	Sodium citrate	One of three sodium salts of citric acid:		
		Monosodium citrate	18996-35-5	242-734-6
		Disodium citrate	144-33-2	205-623-3
		Trisodium citrate	68-04-2	200-675-3
	Sodium hexametaphosphate	SHMP; Calgon S; Glassy sodium; Graham's salt	10124-56-8	233-343-1
	Sodium hydroxide			
	Sodium iodide	See Iodide sources		
	Sodium pectinate	Pectin sodium salt	9005-59-8	
	Sodium phosphate	Generic for sodium plus phosphate		
	Sodium sesquicarbonate	Trisodium hydrogen dicarbonate	533-96-0	208-580-9
	Sodium sulfate (British: Sulphate)	Sulfate of soda	7757-82-6	231-820-9
	Sodium tripolyphosphate	STTP; Sodium triphosphate or STP; Tripolyphosphate, TPP	7758-29-4	231-838-7
	Trisodium phosphate	TSP; Sodium phosphate tribasic	7601-54-9	231-509-8
Sulfur	Ammonium sulfate (British: sulphate)	Diammonium sulfate; Sulfuric acid diammonium salt	7783-20-2	231-984-1
	Calcium sulfate	See calcium sources		
	Cobalt sulfate	See copper sources		
	Copper sulfate	See copper sources		
	Gypsiferrous shale	See calcium sulfate dihydrate in calcium sources		
	Manganese sulfate	See manganese sources		
	Potassium sulfate	See potassium sources		
	Sodium sulfate	See sodium sources		
	Sulfur (elemental)	British: Sulphate	7704-34-9	231-722-6

Summary of Petitioned Use

Trace minerals approved by the FDA for enrichment or fortification of animal feeds are currently listed at 7 CFR 205.603(d)(2) along with other synthetic feed additives (defined at 7 CFR 205.2 as "a substance added to feed in micro quantities to fulfill a nutritional need"). However, what constitute "trace minerals" is not indicated. For the essential elements of cobalt, copper, iron, iodine, manganese, selenium, and zinc, requirements are established for livestock species by several scientific bodies including, the U.S. National Research Council (NRC 2005).

FDA-approved trace minerals used for enrichment or fortification were included in the original National Organic Program (NOP) Standards (Federal Register 2000). Trace minerals underwent their first sunset review at the Fall 2005 meeting of the National Organic Standards Board (NOSB) and were re-listed. This set of substances underwent sunset reviews again in 2010 and 2015 and were recommended for relisting by NOSB in both years. Trace minerals are currently under review before their scheduled sunset date of September 2021.

Characterization of Petitioned Substance

Composition of the Substance:

Minerals are required in animal nutrition for their vital roles in various metabolic, enzymatic, and biochemical reactions in the animal body. Minerals are usually defined as macro- or micro-minerals; micro-minerals—as defined by AAFCO (2019)—are required in micro quantities measured in milligrams per pound or small units, whereas macro-minerals are required in larger quantities (Church and Pond 1988).

Minerals may be provided through the intake of plant matter feedstuffs or through synthetic supplements. Several factors directly or indirectly influence the levels of minerals in plants, including location, nature, and chemical composition of the soil; level of fertilization; and the presence of anti-nutritional factors that may reduce mineral bioavailability. As a result, the amounts of minerals for animals that depend on plants as feedstuffs will vary (Suttle 2010a; Soetan et al. 2010).

Bioavailability is defined as the total proportion of the nutrient in a feedstuff that is available for use in normal body functions. Examples of anti-nutritional factors that reduce mineral bioavailability include oxalic acid and phytic acid (Nadeem et al. 2010; Rackis 1974). The minerals present in plant feedstuffs, both macro- and micro-, are of low bioavailability, especially for non-ruminants. As a result, minerals are supplemented to animal diets. Micro-minerals are commonly supplemented in a trace mineral premix, while macro-minerals are usually added individually. The amount of supplementation will depend on the animal species, age, and level of production. The bioavailability of many trace minerals differs between ruminants and non-ruminants (Spears 2003). The microbial digestion in the rumen precedes "mammalian-like" digestion in the abomasum and small intestine. Diets for adult ruminants, especially those on pasture, are usually high in fiber, which may affect the bioavailability of trace minerals (Whitehead et al. 1985; Kabija and Smith 1988).

Source or Origin of the Substance:

In most cases, biologically active forms of trace minerals cannot be obtained by mining, so many trace minerals used as feed additives are produced by chemical reactions resulting in inorganic forms of the mineral. Organic compounds are used for some of the trace minerals—the difference between organic and inorganic compounds is primarily the presence of the carbon atoms in the organic compounds. Organic compounds will contain at least one carbon atom (and usually a hydrogen atom as well, to form hydrocarbons) while almost all inorganic compounds do not contain carbon or hydrogen atoms (other than in the association with water—H_2O). Mineral products can also be sold as organically-bound compounds. For details regarding the production methods for the petitioned trace mineral compounds, refer to *Evaluation Question* #2. The Association of American Feed Control Officials (AAFCO 2019) definition of trace minerals includes metal proteinate (57.23), metal polysaccharide complex (57.29), metal amino acid chelates (57.142), metal amino acid complex (57.150), and metal (specific amino acid) complex (57.151). In organic systems, the use of synthetic amino acids is restricted. The use of synthetic D,L-methionine-hydroxy analog of calcium (CAS 922-50-9) is allowed at maximum levels set by the NOP. In addition, some mineral complexes allowed in organic production (e.g., manganese methionine complex) use synthetic methionine chelating agents in their production.

The term "complex" is used to describe the result of a metal ion reacting with a molecule or ion (ligand) that contains an atom which has a lone pair of electrons. The metal ions in a complex are bonded through donor atoms such as oxygen, nitrogen, or sulfur. When the ligands bond to a metal ion via two or more atoms, the complex formed contains one or more heterocyclic rings which contain the metal atom. Such complexes are referred to as "chelates." So, while all chelates are complexes, not all complexes are chelates. Chelates are prepared by reacting inorganic minerals with enzymatically prepared mixtures of amino acids and small peptides, under controlled conditions. Only the so-called transitional minerals, such as copper, iron, manganese, and zinc, have the necessary characteristics to allow them to form coordinate covalent bonds with amino acids and peptides resulting in biologically stable complexes (Murphy 2009).

Choline is included in some complexes such as cobalt choline citrate complex, copper choline citrate complex, and ferric choline citrate complex. Choline is a water-soluble, vitamin-like essential nutrient and has the CAS number 62-49-7 and ECHA number 200-655-4.

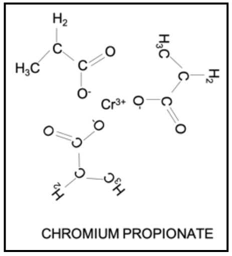
Properties of the Substance:

The different physical and chemical properties of the trace minerals from Table 1 are discussed below. The information was obtained, or confirmed, from several sources including PubChem, MSDS material provided by chemical providers, American Elements, ChemSpider, European Chemical Agency (ECHA), Common Chemistry, INCHEM (Chemical Safety Information from Intergovernmental Organizations), as well as websites for different chemical manufacturers.

Chromium

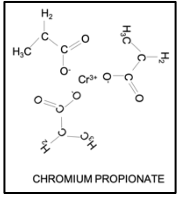
Chromium is a steely-gray, hard metal that occurs naturally in rocks, soil, and volcanic dust and gases (EPA 2016). Chromium can occur in several different oxidative states ranging from -2 to +6, but the biologically important forms are the trivalent and hexavalent (EPA 2016). Trivalent chromium is ubiquitous in nature, occurring in the air, water, soil, and biological materials. Hexavalent chromium is believed to be synthetic and does not occur naturally in the environment (NIEHS 2018).

Chromium propionate – $C_9H_{15}CrO_6$



Molar mass	Density	Melting point	Boiling point	Solubility
271.209 g/mol	n/a	n/a	n/a	n/a

Chromium picolinate – $Cr(C_6H_4NO_2)_3$



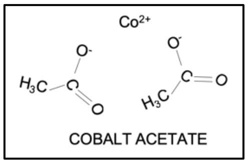
Molar mass	Density	Melting point	Boiling point	Solubility
418.33 g/mol	n/a	n/a	n/a	n/a

Chromium-enriched yeast is a product produced by the fermentation of *Saccharomyces cerevisiae* with the salts of chromium (EFSA 2009e). It has no CAS No. or molecular weight. It is a solid powder that is either off-white/gray or green. No information is available on the melting point or density. Yeast (CAS 84604-16-0; EC 283-294-5) is soluble in water (at least 200g of dry matter per kilogram of solution) and has a boiling point of 221°F/105°C (DSM 2012).

Cobalt

Cobalt is a hard ferromagnetic, silver-white, hard, lustrous, brittle element. Like iron, it can be magnetized (Lenntech 2019).

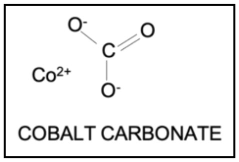
Cobalt acetate – $Co(CH_3CO_2)_2$



Cobalt (II) acetate is a cobalt salt of acetic acid and is usually found in the tetrahydrate form $(Co(CH_3CO_2)_2\bullet 4\ H_2O$. Cobalt acetate is a red-violet crystalline sold with a vinegar-like odor. The tetrahydrate form occurs as red crystals and decomposes on heating, producing irritating fumes.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	177.0 g/mol	1.70 g/cm³	140ºC (284ºF) decomposes	n/a	Soluble
Tetrahydrate	249.1 g/mol	1.70 g/cm³	140ºC (284ºF)	n/a	Soluble

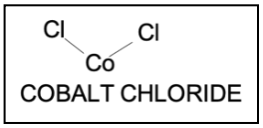
Cobalt carbonate – $CoCO_3$



Spherocobaltite is the natural form of cobalt carbonate. In its pure form (rare), spherocobaltite is a rose-red color, with impure forms varying from pink to pale brown in color. Anhydrous cobalt carbonate is red- or pink-colored crystals. The hexahydrate form is a pink, violet, or red crystalline powder.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	118.941 g/mol	4.13 g/cm³	427ºC (801ºF)	n/a	Insoluble
Hexahydrate	n/a	n/a	140ºC (284ºF)	n/a	Insoluble

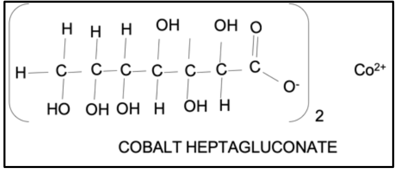
Cobalt chloride – $CoCl_2$



The anhydrous form of cobalt chloride is sky blue in color. The hexahydrate form is pink- or rose-red-colored crystals.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	129.839 g/mol	3.36 g/cm³	735ºC (1355ºF)	1049ºC (1920ºF)	0°C: 43.6 g/100ml 20°C: 52.9 g/100 ml
Hexahydrate	237.93 g/mol	1.92 g/cm³	86ºC (186.8ºF)	n/a	n/a

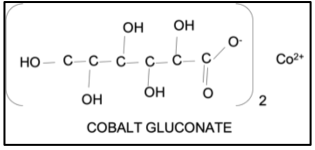
Cobalt glucoheptonate – a cobalt salt of glucoheptonic acid



Glucoheptonic acid is a carbohydrate acid that is heptonic acid with hydroxyl groups (OH) at six of the seven carbons (C)

Molar mass	Density	Melting point	Boiling point	Solubility
226.2 g/mol	n/a	145-148°C (293-298.4°F)	n/a	n/a

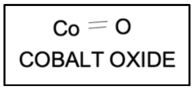
Cobalt gluconate – $C_{12}H_{22}CoO_{12}$



Cobalt gluconate is a rosy-pink or pinkish red crystalline or granular powder.

Molar mass	Density	Melting point	Boiling point	Solubility
449.2 g/mol	n/a	>300°C (>472°F)	n/a	Soluble

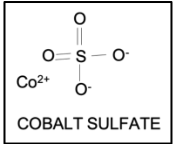
Cobalt oxide – CoO



Cobalt oxide can be in the form of a powder or cubic/hexagonal crystals. Colors vary from olive green to red depending on particle size. The commercial material is usually dark gray.

Molar mass	Density	Melting point	Boiling point	Solubility
74.94 g/mol	n/a	1935°C (3515°F)	n/a	4.88 mg/L (20°C) 3.27 mg/L (37°C)

Cobalt sulfate – $CoSO_4$



Cobalt sulfate is an odorless, rose-pink solid.

Molar mass	Density	Melting point	Boiling point	Solubility
155.0 g/mol	3.71 g/cm^3	735°C (1355°F)	n/a	330 mg/L (20°C)

Ruse et al. (2009) identified three cobalt (II) amino acid complexes: cobalt lysine complex, cobalt leucine complex, and cobalt methionine complex. They have melting points of 392°F (200°C), 365°F (185°C) and 356°F (180°C), respectively. They metal to ligand ratio is 1:2 in all cases. The amino acids were shown to act as bidentate ligands with coordination involving the carboxyl oxygen and the nitrogen atom of the amino group.

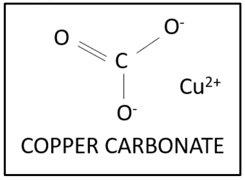
Copper

Copper is a soft, malleable, and ductile metal with a very high thermal and electrical conductivity.

Copper acetate – $Cu(CH_3COO)_2$

Molar mass	Density	Melting point	Boiling point	Solubility
199.65 g/mol	1.88 g/cm^3	n/a	240 ºC (464ºF)	7.2 g/100 ml (cold water) 20 g/100 ml (hot water)

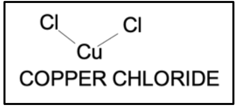
Copper carbonate – $CuCo_3$



Copper carbonate is a gray powder.

Molar mass	Density	Melting point	Boiling point	Solubility
123.5549 g/mol	n/a	n/a	200°C (392°F) decomposes	Reacts with water at normal conditions

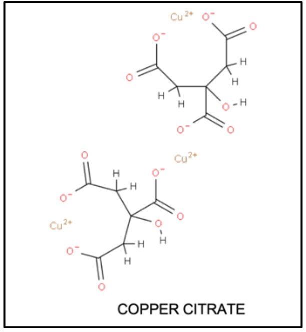
Copper chloride – $CuCl_2$



In the anhydrous form copper chloride is a yellowish-brown powder, while in the dihydrate form it is a green crystalline solid.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	134.45 g/mol	3.39 g/cm^3	498°C (928°F)	993°C (1819°F) decomposes	70.6 g/100 ml (0°C) 107.9 g/100 ml (100°C)
Dihydrate	170.48 g/mol	2.51 g/cm^3	100°C (dehydration of dihydrate)	n/a	n/a

Copper citrate – $Cu_3(C_8H_6O_7)_2$

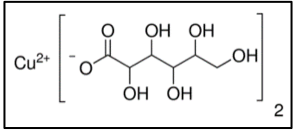


Copper citrate is a blue to green powder.

Molar mass	Density	Melting point	Boiling point	Solubility

568.84 g/mol	1.667 g/cm^3	350°C (662°F)	Decomposes	Slightly soluble

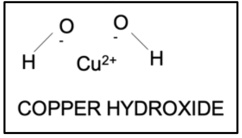
Copper gluconate – $Cu(C_6H_{11}O_7)_2$



Copper gluconate is the copper salt of D-gluconic acid. It is odorless and can be light blue or blue-green.

Molar mass	**Density**	**Melting point**	**Boiling point**	**Solubility**
453.84 g/mol	n/a	156°C (313°F)	n/a	30 mg/mL (20°C)

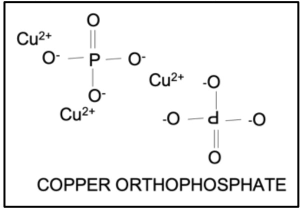
Copper hydroxide – $Cu(OH)_2$



Coper hydroxide is a pale, greenish blue, or bluish green solid.

Molar mass	**Density**	**Melting point**	**Boiling point**	**Solubility**
97.56 g/mol	n/a	n/a	80°C (176°F)	Insoluble in water

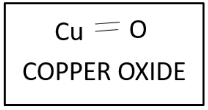
Copper orthophosphate – $Cu_3(PO_4)_2$



Copper orthophosphate is a light-blue powder.

Molar mass	**Density**	**Melting point**	**Boiling point**	**Solubility**
380.6 g/mol	6.315 g/cm^3	1326°C (2419°F)	158 °C (316.4 °F)	Insoluble in water

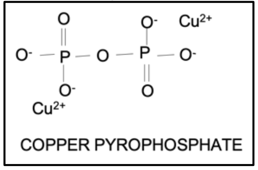
Copper oxide – CuO



Copper oxide is a black solid. As a mineral, it is known as tenorite.

Molar mass	**Density**	**Melting point**	**Boiling point**	**Solubility**
79.545 g/mol	6.315 g/cm^3	1326°C (2419°F)	2000 °C (3630°F)	Insoluble in water

Copper pyrophosphate – $Cu_2P_2O_7 \bullet xH_2O$

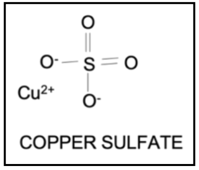


COPPER PYROPHOSPHATE

Copper pyrophosphate appears as light green powder. It is soluble in acid but not water.

Molar mass	Density	Melting point	Boiling point	Solubility
301.0 g/mol	n/a	1170ºC (2138ºF)	n/a	Insoluble in water

Copper sulfate – $CuSO_4(H_2O)_5$



COPPER SULFATE

Copper sulfate has the formula $CuSO_4(H_2O)_x$, where X can range from 0–5. The pentahydrate form (X=5) is the most common form, and the form used in animal feeds (Old Bridge Chemicals Inc.). It most often occurs as a salt and is bright blue in color. The anhydrous form is a white powder.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Pentahydrate	249.685 g/mol	2.286 g/cm³	Decomposes above 100°C	Decomposes above 150°C	≥ 31.6 g/100ml

Cuprous iodide – CuI

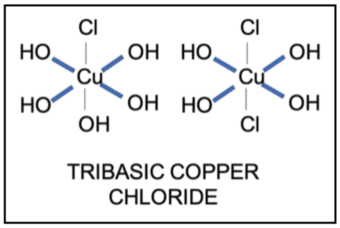
Cu^+ I^-

CUPROUS IODIDE

Pure cuprous iodide is white, but some products are often tan or reddish brown due to impurities. It is an odorless powder.

Molar mass	Density	Melting point	Boiling point	Solubility
190.45 g/mol	5.67 g/cm³	606ºC (1123ºF)	1290ºC (2350ºF) Decomposes	Low solubility

Tribasic copper chloride– $Cu_2(OH)_3Cl$



TRIBASIC COPPER CHLORIDE

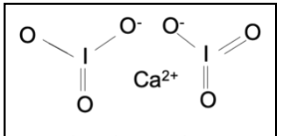
Tribasic copper chloride makes polymorphic crystals, the most common of which is atacamite. Atacamite is an orthorhombic (a crystal system or three-dimensional geometric arrangement having three unequal axes at right angles) with two crystallographically-independent copper atoms and hydroxyl groups in the asymmetric unit. Each copper is bonded to the four nearest hydroxyl groups. In addition, one of the copper atoms is bonded to two chlorine atoms to form a $[Cu(OH)_4Cl_2]$ octahedron, and the other copper atom is bonded to one chlorine atom and a distinct hydroxyl group to form a [$Cu(OH)_5Cl$] octahedron. The two different types of octahedrons are edge-linked to form a three dimensional framework with [$Cu(OH)_5Cl$] octahedron cross-linking the [$Cu(OH)_4Cl_2$] octahedron layers.

Molar mass	Density	Melting point	Boiling point	Solubility
213.56 g/mol	3.5 g/cm³	250ºC (482ºF)	Not applicable	Insoluble in water

Iodine

Iodine is a non-metallic, dark-gray/purple-black, lustrous, solid element, referred to as a halogen (reactive nonmetallic elements that form strongly acidic compounds with hydrogen, from which simple salts can be made). It is the most electropositive halogen and the least reactive of the halogens, though it can still form compounds with many elements. It has an acrid and stringent taste and smells somewhat like chlorine.

Calcium iodate – $Ca(IO_3)_2$

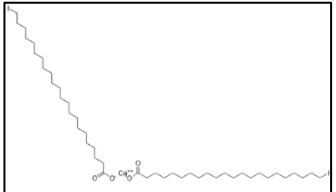


CALCIUM IODATE

There are two main forms of calcium iodate. The anhydrous form is $Ca(IO_3)_2$ and occurs naturally as lautarite. The monohydrate form is $Ca(IO_3)_2(H_2O)$ and occurs naturally as bruggenite. Lautarite is the most important non-synthetic source of iodine. Calcium iodate is a white to yellow crystalline powder with a slight acrid odor.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	389.88 g/mol	14.6 g/cm³	n/a	n/a	n/a
Monohydrate	407.90 g/mol	4.519 g/cm³	540ºC (1004ºF)	Decomposes	0°C: 0.09 g/100ml 20°C: 0.24 g/100 ml 90°C: 0.67 g/100 ml

Calcium iodobehenate – $Ca(C_{21}H_{42}ICO_2)_2$



CALCIUM IODOBEHENATE

Calcium iodobehenate is a white or yellowish powder. It is odorless or may have a slight fat-like odor.

Molar mass	Density	Melting point	Boiling point	Solubility
971.02 g/mol	n/a	n/a	n/a	n/a

Cuprous iodide – CuI

Cu^+ I^-

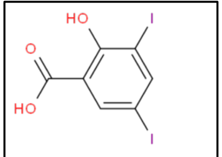
CUPROUS IODIDE

Pure cuprous iodide is white, but some products are often tan or reddish brown due to impurities. It is an odorless powder.

Molar mass	Density	Melting point	Boiling point	Solubility

190.45 g/mol	5.67 g/cm³	606°C (1123°F)	1290°C (2350°F) Decomposes	Low solubility

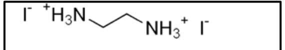
Diiodosalicylic acid – $C_7H_4I_2O_3$


3,5-DIIODOSALICYCLIC ACID

Diiodosalicyclic acid is on off-white to beige or grey powder that is light-sensitive.

Molar mass	Density	Melting point	Boiling point	Solubility
389.9 g/mol	2.43 g/cm³	235.5°C (455.9°F)	260°C (500°F) Decomposes	0.02 g/100 ml (25°C)

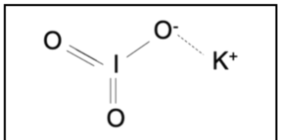
Ethylenediamine dihydroiodide – $NH_2CH_2CH_2NH_2 \bullet 2HI$


ETHYLENEDIAMINE DIHYDROIODIDE

EDDI is a white to off-white crystalline powder. It is a water-soluble salt derived from ethylenediamine and hydroiodic acid.

Molar mass	Density	Melting point	Boiling point	Solubility
315.93 g/mol	n/a	337°C(638.6°F)	n/a	Soluble

Potassium iodate– KIO_3


POTASSIUM IODATE

Potassium iodate is an odorless, white crystalline powder.

Molar mass	Density	Melting point	Boiling point	Solubility
214.001 g/mol	3.89 g/cm³	560°C (1040°F)	Decomposes	0°C: 4.74 g/100ml 25°C: 9.16 g/100 ml 100°C: 32.3 g/100 ml

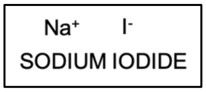
Potassium iodide – KI

K^+ I^-
POTASSIUM IODIDE

Potassium iodide is an odorless white solid.

Molar mass	Density	Melting point	Boiling point	Solubility
166.0 g/mol	3.13 g/cm³	681°C (1258°F)	1330°C (2430°F)	0°C: 1.28 g/100ml 20°C: 1.4 g/100 ml 100°C: 2.06 g/100 ml

Sodium iodide – NaI

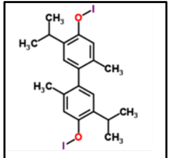


SODIUM IODIDE

Sodium iodide is an odorless, water-soluble, ionic compound with a crystal lattice.

Molar mass	Density	Melting point	Boiling point	Solubility
149.9 g/mol	3.67 g/cm³	660°C (1220°F)	1304°C (2739.2°F) Decomposes	25°C: 184 g/100ml 100°C: 302 g/100 ml

Thymol iodide – $C_{20}H_{24}I_2O_2$



THYMOL IODIDE

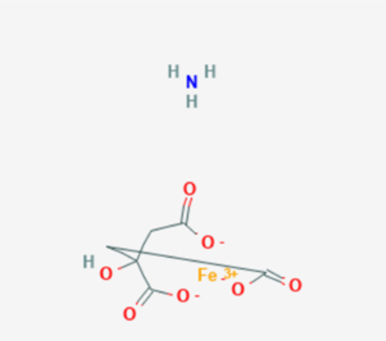
Thymol iodide is a reddish-brown or reddish-yellow bulky powder. It has a slight aromatic odor. It loses iodine on prolonged exposure to light.

Molar mass	Density	Melting point	Boiling point	Solubility
550.22 g/mol	n/a	n/a	n/a	Insoluble

Iron

Iron is a ductile, gray, and relatively soft metal which is a moderately good conductor of heat and electricity. It is attracted by magnets and can be easily magnetized.

Ferric ammonium citrate – C6H8FeNO7



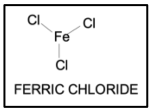
FERRIC AMMONIUM CITRATE

Ferric ammonium citrate is a yellowish brown to red solid with a faint odor of ammonia. When heated to decomposition it emits acrid smoke and irritating fumes.

Molar mass	Density	Melting point	Boiling point	Solubility

264.999 g/mol	1.8 g/cm³	n/a	n/a	Soluble

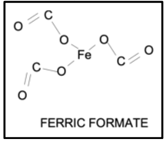
Ferric chloride – $FeCl_3$



Ferric chloride is an orange-brown liquid that has a faint hydrochloric acid odor.

Molar mass	**Density**	**Melting point**	**Boiling point**	**Solubility**
162.2 g/mol	2.9 g/cm³	304°C (579.2°F) Decomposes	315°C (599°F)	Cold water: 74.6 g/100 ml Hot water: 535.7g/100 ml

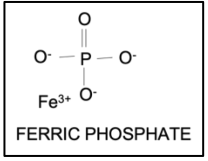
Ferric formate – $C_3H_3FeO_6$



Ferric formate is a red-yellow crystalline powder.

Molar mass	**Density**	**Melting point**	**Boiling point**	**Solubility**
190.9 g/mol	n/a	n/a	n/a	Soluble

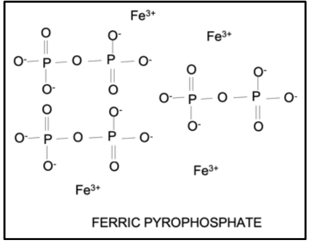
Ferric phosphate – $FePO_4$



Ferric phosphate is a white, grayish-white or light pink in color. It can be orthorhombic or monoclinic crystals or amorphous powder.

Molar mass	**Density**	**Melting point**	**Boiling point**	**Solubility**
150.8 g/mol	3.06 g/cm³	250ºC (482ºF)	n/a	Practically insoluble

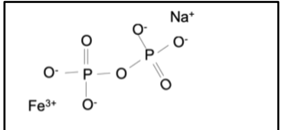
Ferric pyrophosphate – $Fe_4(P_2O_7)_3$



Ferric pyrophosphate is a yellowish-white powder.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	745.2 g/mol	n/a	Decomposes	n/a	Insoluble

Ferric sodium pyrophosphate – $FeNaO_7P_2$

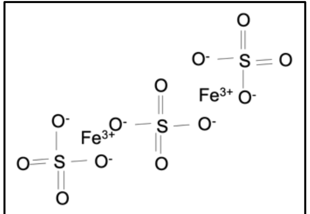


FERRIC SODIUM PYROPHOSPHATE

Ferric sodium pyrophosphate is a white powder.

Molar mass	Density	Melting point	Boiling point	Solubility
252.775 g/mol	1.5 g/cm^3	n/a	n/a	Insoluble

Ferric sulfate – $Fe_2(SO_4)_3$

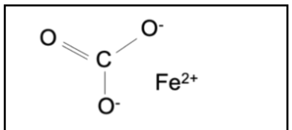


FERRIC SULFATE

Ferric sulfate is a yellow crystalline solid or grayish-white powder.

Molar mass	Density	Melting point	Boiling point	Solubility
399.86 g/mol	3.1 g/cm^3	480°C(896°F)	n/a	Slightly soluble

Ferrous carbonate – $FeCO_3$

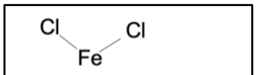


FERROUS CARBONATE

Ferrous carbonate is an iron salt of carbonic acid and occurs as white-colored powder or crystals.

Molar mass	Density	Melting point	Boiling point	Solubility
115.854 g/mol	3.9 g/cm^3	decomposes	n/a	0.0067 g/L

Ferrous chloride – $FeCl_2$



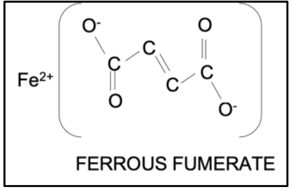
FERROUS CHLORIDE

Ferrous chloride is a greenish white crystalline solid.

Molar mass	Density	Melting point	Boiling point	Solubility
126.75 g/mol	3.16 g/cm^3	674°C(1245.2°F)	1023°C(1873.4°F)	0°C: 64.4 g/100 ml

				20ºC 68.5 g/100 ml 100ºC 105.7 g/100 ml

Ferrous fumarate – $C_4H_2FeO_4$

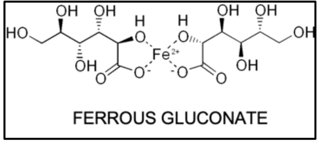


FERROUS FUMERATE

Ferrous fumarate is an iron (II) salt of fumaric acid and occurs as a reddish-orange powder. It does not have an odor.

Molar mass	Density	Melting point	Boiling point	Solubility
169.9 g/mol	2.435 g/cm^3	280ºC (536ºF)	n/a	Slightly soluble

Ferrous gluconate – $C_{12}H_{22}FeO_{14}$

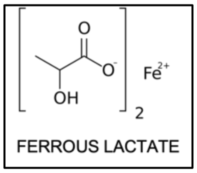


FERROUS GLUCONATE

Ferrous gluconate is a light yellow to brown powder depending on the pH. It is the iron (II) salt of gluconic acid. It has a slight caramel odor.

Molar mass	Density	Melting point	Boiling point	Solubility
446.14 g/mol	n/a	188ºC (370ºF)	n/a	Soluble

Ferrous lactate – $Fe(C3H_5O_3)_2$

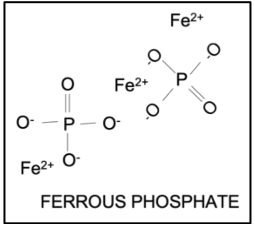


FERROUS LACTATE

Ferrous lactate is a greenish-white or light green powder with a characteristic smell.

Molar mass	Density	Melting point	Boiling point	Solubility
233.99 g/mol	n/a	500ºC (932ºF)	n/a	Soluble

Ferrous phosphate – $Fe_3(PO_4)_2$

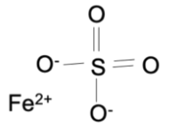


FERROUS PHOSPHATE

Ferrous phosphate is an iron salt of phosphoric acid. It is a brown powder.

Molar mass	Density	Melting point	Boiling point	Solubility
357.475 g/mol	2.61 g/cm^3	180ºC (356ºF) Decomposes	n/a	Insoluble

Ferrous sulfate – $FeSO_4$

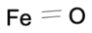


FERROUS SULFATE

Ferrous sulfate is the sulfate salt of iron (II) ion. Ferrous sulfate has the formula $FeSO_4(H_2O)_x$, where X can be 0–7. Ferrous sulfate most commonly exists as heptahydrate (X=7). The crystals of the anhydrous form are brownish-white. The monohydrate crystals are whitish-yellow, and the heptahydrate is bluish-green. Ferrous sulfate heptahydrate occurs as pale, bluish-green crystals or granules. When heated, it produces ferrous sulfate monohydrate with varying amounts of ferrous sulfate tetrahydrate. Dried ferrous sulfate occurs as a grayish-white to buff-colored powder.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	151.91 g/mol	3.65 g/cm^3	680ºC (1256ºF)	n/a	n/a
Monohydrate	169.93 g/mol	3 g/cm^3	300ºC (572ºF)	n/a	77°C: 44.69 g/100 ml 90.1°C: 35.97 g/100 ml
Heptahydrate	278.02 g/mol	1.895g/cm^3	60-64ºC 140-147ºF)	n/a	0°C: 15.65 g/100ml 20°C: 29.51 g/100 ml 90°C: 51.35g/100 ml

Ferrous oxide – FeO



FERROUS OXIDE

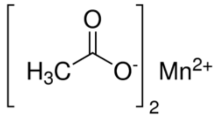
Iron (II) oxide is referred to as ferrous oxide—"ferrous" refers to the iron atom losing only two electrons (FeO). Iron (III) oxide is referred to as ferric oxide, or rust—"ferric" refers to the iron atom losing three electrons (Fe_2O_3). The mineral form of ferrous oxide is known as wurtzite, a black-colored powder often confused for ferric oxide.

Molar mass	Density	Melting point	Boiling point	Solubility
71.844 g/mol	5.745 g/cm^3	1377ºC (2511ºF)	3414ºC (6177ºF)	Highly insoluble

Manganese

Manganese is a gray-white material that resembles iron but is harder and very brittle.

Manganese acetate – $Mn(CH_3CO_2)_2$

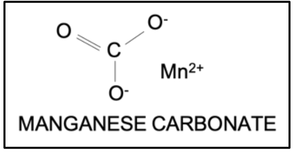


MANGANESE ACETATE

Manganese acetate is a white to pinkish red crystals or crystalline powder.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	173.027 g/mol	1.74 g/cm^3	210°C (410°F)	n/a	Soluble
Tetrahydrate	245.087 g/mol	1.59 g/cm^3	80°C (176°F)	n/a	Soluble

Manganese carbonate – $MnCO_3$

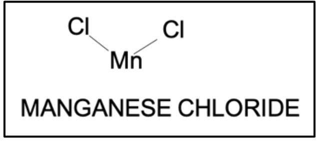


MANGANESE CARBONATE

Manganese carbonate occurs naturally as the mineral rhodochrosite but is typically produced industrially. It is a pale pink, water-soluble solid. It gradually becomes light brown in air.

Molar mass	Density	Melting point	Boiling point	Solubility
114.9 g/mol	3.7 g/cm^3	>200°C (>392°F) Decomposes	n/a	Negligible

Manganese chloride – $MnCl_2 \bullet H_2O$

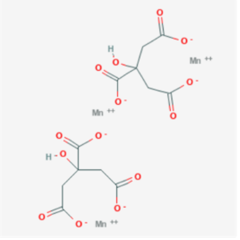


MANGANESE CHLORIDE

Manganese chloride exists as $MnCl_2 \bullet xH_2O$ where x can be 0, 2 or 4. The tetrahydrate is the most common form. The salts are pink. Anhydrous manganese chloride serves as the starting point for the synthesis of a variety of different manganese compounds.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	125.8 g/mol	2.98 g/cm^3	654°C (1209°F)	1225°C (2237°F)	0°C: 63.4 g/100ml 20°C: 73.9 g/100 ml 100°C: 123.8 g/100 ml
Dihydrate	161.9 g/mol	2.27 g/cm^3	Dehydrates at 135°C (275°)	n/a	n/a
Tetrahydrate	197.9 g/mol	2.01 g/cm^3	Dehydrates at 58°C (136.4°F)	n/a	n/a

Manganese citrate – $Mn_3(C_6H_5O_7)_2$

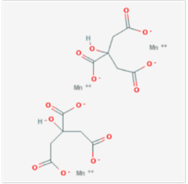


MANGANESE CITRATE

Manganese is a white powder.

Molar mass	Density	Melting point	Boiling point	Solubility
543.01 g/mol	3.7 g/cm³	>300ºC (>572ºF)	n/a	Soluble in water in the presence of sodium citrate

Manganese gluconate – $C_{12}H22Mn_2O_{14}$

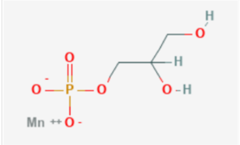


MANGANESE GLUCONATE

Manganese gluconate is a pink powder.

Molar mass	Density	Melting point	Boiling point	Solubility
445.24 g/mol	n/a	n/a	n/a	Very soluble in cold water

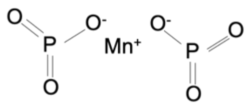
Manganese glycerophosphate – $C_3H_3MnO_7P$



MANGANESE GLYCEROPHOSPHATE

Molar mass	Density	Melting point	Boiling point	Solubility
243.01 g/mol	n/a	n/a	n/a	Very soluble in cold water

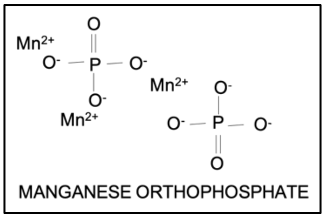
Manganese hypophosphate – $Mn(PO_3)_2$



MANGANESE HYPOPHOSPHATE

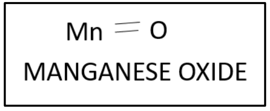
Molar mass	Density	Melting point	Boiling point	Solubility
212.88 g/mol	n/a	n/a	n/a	n/a

Manganese orthophosphate – $Mn_3(PO_4)_2$


MANGANESE ORTHOPHOSPHATE

Molar mass	Density	Melting point	Boiling point	Solubility
354.8 g/mol	n/a	n/a	n/a	n/a

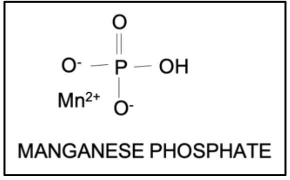
Manganese oxide – MnO


MANGANESE OXIDE

Manganese oxide is made up of green crystals or powder.

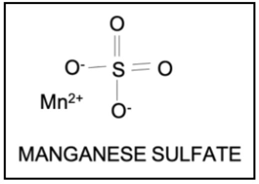
Molar mass	Density	Melting point	Boiling point	Solubility
70.9374 g/mol	5.43 g/cm^3	1945ºC (3533ºF)	n/a	Insoluble in water

Manganese (II) phosphate – $MnPO_4H$


MANGANESE PHOSPHATE

Molar mass	Density	Melting point	Boiling point	Solubility
150.9 g/mol	n/a	n/a	n/a	n/a

Manganese sulfate – $MnSO_4$


MANGANESE SULFATE

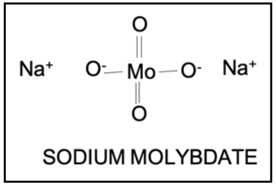
Typically, manganese ores are purified by their conversion to manganese (II) sulfate, a pale pink, granular, odorless product. Manganese sulfate minerals are very rare in nature and occur as hydrates. The monohydrate form of the mineral is known as szmikite, while the tetrahydrate form is called ilesite.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	151.001 g/mol	3.25 g/cm^3	710ºC (1310ºF)	850ºC (1310ºF)	0°C: 52 g/100ml 70°C: 70 g/100 ml
Monohydrate	169.02 g/mol	2.95 g/cm^3	n/a	n/a	n/a
Tetrahydrate	223.07 g/mol	2.107 g/cm^3	27ºC (80.6ºF)	n/a	n/a

Molybdenum

Molybdenum is a silvery-grey metal.

Sodium molybdate – Na_2MoO_4



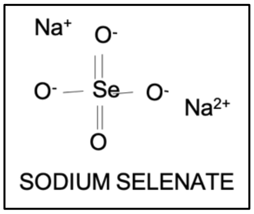
Sodium molybdate is often found as the dihydrate $Na_2MoO_4(H_2O)_2$.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	205.92 g/mol	3.78 g/cm^3	687ºC (1269ºF)	n/a	100°C: 8 g/100ml
Dihydrate	241.95 g/mol	n/a	n/a	n/a	n/a

Selenium

Selenium is a non-metal and occurs in several allotropic forms. The most stable form—crystalline hexagonal selenium—is metallic gray. Crystalline monoclinic selenium is a deep red in color.

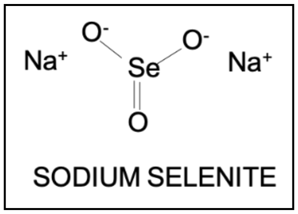
Sodium selenate – Na_2SeO_4



Sodium selenate should not be confused with sodium selenite. It exists in the anhydrous, heptahydrate and decahydrate forms. They are white solids.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	143.0 g/mol	3.1 g/cm^3	Decomposes	Decomposes	Soluble

Sodium selenite – Na_2SeO_3



Sodium selenite is a colorless solid. The pentahydrate form $Na_2SeO_3(H_2O)_5$ is the most common form and is water soluble.

Molar mass	Density	Melting point	Boiling point	Solubility
172.95 g/mol	3.1 g/cm^3	Decomposes at 710ºC (1310ºF)	n/a	20°C: 85 g/100ml

Selenomethionine - $(CH_3Se(CH_2)_2CH(NH_4)COOH)$

Selenomethionine can be made with D,L-methionine or L-methionine (Schrauzer 2000). L-selenomethionine is a white to off-white powder. D,L-selenomethionine is a colorless, glistening powder.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
L-form[1]	n/a	n/a	267-269ºC (512.6 – 516.2ºF) decomposes	n/a	5 g/100ml
D,L-form[2]	n/a	n/a	265ºC (509ºF) decomposes	n/a	n/a

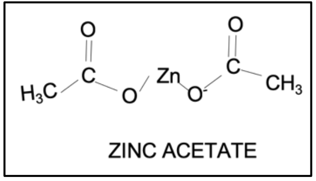
Selenium yeast

As with chromium yeast, selenium yeast is produced by fermenting *Saccharomyces cerevisiae* in a selenium-rich media. The predominant form of the selenium is selenomethionine, which accounts for about 60–85 percent of all selenium species (EFSA 2008). It has no CAS No. or molecular weight. No information is available on the melting point or density. Yeast (CAS 84604-16-0; EC 283-294-5) is soluble in water (at least 200g of dry matter per kilogram of solution) and has a boiling point of 221°F/105°C (DSM 2012).

Zinc

Zinc is a bluish-white, moderately hard metal.

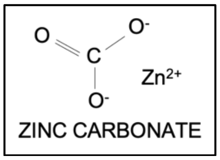
Zinc acetate – $Zn(CH_3COO)_2$



Both the anhydrous and dihydrate forms of zinc acetate are white crystalline solids.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	183.5 g/mol	n/a	Decomposes at 237°C (459°F)	Decomposes	n/a
Dihydrate	219.5 g/mol	1.735 g/cm^3	Dehydrates at 100°C (212°F)	Decomposes	20°C: 53g/100 ml

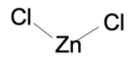
Zinc carbonate – $ZnCO_3$



Zinc carbonate is a mineral ore of zinc. It is an odorless, white crystalline solid or powder that is insoluble in water.

Molar mass	Density	Melting point	Boiling point	Solubility
125.4 g/mol	4.398 g/cm^3	Loses CO_2 at 300ºC (572ºF)	n/a	15°C: 0.001 g/100g

Zinc chloride – $ZnCl_2$



ZINC CHLORIDE

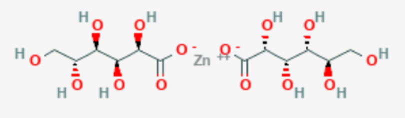
Zinc chloride is an odorless, colorless liquid.

Molar mass	Density	Melting point	Boiling point	Solubility
136.3 g/mol	2.91 g/cm^3	293°C (559.4°F)	732°C (1350°F)	25°C: 432g/100g

Zinc chloride diamine complex – $[Zn(NH_3)_4]^{2+}$

Metal ammine complexes are metal complexes that contain at least one ammonia (NH_3) ligand. Zinc (II) forms a colorless tetraamine and has a tetrahedral structure.

Zinc gluconate - $Zn(C_6H_{11}O_7)_2$

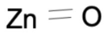


ZINC GLUCONATE

Zinc gluconate is a zinc salt of gluconic acid.

Molar mass	Density	Melting point	Boiling point	Solubility
454.03 g/mol	2.91 g/cm^3	172-175°C (342-347)	n/a	Moderately soluble

Zinc oxide - ZnO



ZINC OXIDE

Zinc oxide is a white powder that is insoluble in water.

Molar mass	Density	Melting point	Boiling point	Solubility
81.38 g/mol	5.606 g/cm^3	Decomposes at 1975°C (3587°F)	Decomposes at 1975°C (3587°F)	17.8°C: 0.0004%

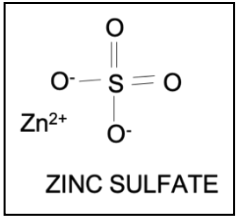
Zinc stearate – $ZnC_{36}H_{70}O_4$

ZINC STEARATE

Zinc stearate is a soft white powder with a slight, characteristic odor.

Molar mass	Density	Melting point	Boiling point	Solubility
632.33 g/mol	1.095 g/cm^3	120-130°C (248-265°F)	Decomposes	Insoluble

Zinc sulfate – $ZnSO_4$



Commercially, the hydrate of zinc sulfate is the most common form ($ZnSO_4(H_2O)_7$). It is a white, odorless powder.

Form	Molar mass	Density	Melting point	Boiling point	Solubility
Anhydrous	161.47 g/mol	3.54 g/cm³	680ºC (1256ºF) decomposes	740ºC (1360ºF)	20°C: 57.7 g/100ml
Monohydrate	179.47 g/mol	3.31 g/cm³	At 280°C decomposes to zinc oxide and sulfur trioxide	n/a	n/a
Heptahydrate	287.53 g/mol	2.072 g/cm³	100ºC	280ºC (536ºF) decomposes	n/a

Specific Uses of the Substance:

Minerals are added to animal feeds in order to meet the nutritional requirements for each of the micro- and macro-minerals. The dietary importance of each micro-mineral will depend on the animal species in question.. A discussion of the specific uses of each of the minerals in Table 1 follows.

Chromium

Based on a review of trace mineral products advertised online, chromium supplements are normally only given to swine and rabbits. Some studies, however, have shown that chromium supplementation can improve immune status of weaned pigs (Lien et al. 2005), broiler chickens (Rao et al. 2012), and calves (Uyanik et al. 2008). Chromium supplementation of broiler chickens was also reported to increase carcass weight while decreasing the amount of abdominal fat (Hossain et al. 1998). On the other hand, Lambertini et al. (2014) reported no effect of chromium supplementation on growth performance and meat quality in rabbits. Chromium supplementation to lactating dairy cows under heat stress has been shown to improve milk yield and feed intake without affecting milk components (Al-Saiady et al. 2004). Chang et al. (1992) reported that continuous supplementation of chromium to unstressed growing-finishing steers had no effect on growth rate or carcass composition.

Rat and human absorbability (i.e., the ability to be absorbed into the body) for several chromium compounds as reported by the European Food Safety Authority (2009a) are below.

Species	Chromium compound	Absorbability (%)
Rats	Chromium chloride	0.9
	Chromium nicotinate	1.3
	Chromium picolinate	1.1
	Chromium dinicotinic acid-diglycine-cysteine-glutamic acid	0.6
Humans	Chromium chloride	0.1–0.4
	Chromium picolinate	2.8
	Chromium-enhanced yeast	5-10

Cobalt

Cobalt is primarily a trace mineral supplement of ruminants, horses, and rabbits, which have large populations of microflora that can use the cobalt to synthesize vitamin B12 (EFSA 2009b). Coprophagous animals, rabbits, and horses receive some supplies of vitamin B12 from microbial fermentation in the hindgut (Van Paemel et al. 2010). The production of vitamin B12 would occur too far down the digestive tract to allow for substantial absorption by young ruminants, poultry, and swine. As a result, vitamin B12 supplement is added to these diets rather than cobalt (EFSA 2009b). There is no evidence that cobalt is needed for monogastrics when dietary vitamin B12 levels are adequate.

Under grazing conditions, lambs are the most sensitive to cobalt deficiency, followed by mature sheep, calves, and mature cattle (McDowell 2003). Cobalt toxicosis in animals is very rare because the concentrations of cobalt included in animal diets are much lower than those needed to cause toxicosis (Van Paemel et al. 2010). Characteristic signs of chronic cobalt toxicity for most animal species include reduced feed intake and body weight, anemia, hyperchromemia, debility, increased liver cobalt concentrations, and increased disease susceptibility (McDowell 2003).

Absorbability of various cobalt compounds in humans and animals (Van Paemel et al. 2010) based on different reference sources are included below.

Species	**Cobalt source**	**Dose**	**Absorbability (%)**
Hamster	Cobalt oxide	-	< 0.5
Rats	Cobalt chloride	-	30
	Cobalt chloride	0.01μg/rat	11
	Cobalt chloride	1000μg/rat	34
	Cobalt oxide	-	1–3
	Cobalt chloride	-	13–34
Humans	Cobalt chloride	-	5–44
	Cobalt chloride	-	18–97

Different factors that may affect absorption and solubility of the cobalt compound include the presence of amino acids and sulfhydryl groups in the diet as well as the iron status of the animal.

Copper

Copper deficiencies can occur in plants grown in coarse-textured and calcareous soils, which are typically low in copper. Copper deficiencies can also occur in soils high in organic matter where copper is readily chelated. As a result, copper deficiencies in cattle occur in many parts of the world (Underwood and Suttle 1999). However, for cattle raised under confined rearing conditions, routine supplementing with copper is not justified to maintain adequate copper levels in the animal or to improve productive parameters (García-Vaquero et al. 2011). Copper availability for cereals in concentrated feeds is more available than from forage.

An excess of molybdenum in the diet can lead to copper deficiencies in ruminants (Miltmore et al. 1970). High molybdenum levels found in some hays in British Columbia, Canada could cause copper deficiencies; lower copper concentrations in the hay could also result in copper deficiencies even without high molybdenum levels.

Copper fed at high levels is only known to have a practical growth promoting effect in pigs (Cromwell et al. 1998), broilers (Smith 1969; Jegede et al. 2011), and potentially laying hens (Lim and Paik 2006; Van Paemel et al. 2010). Lim and Paik (2006) also reported that copper supplementation of laying hen diets increased egg weight and reduced the production of soft-shelled eggs. However, Chowdhury et al. (2004) reported that copper supplementation of broiler chickens had no significant effect on growth rate, but negatively affected feed efficiency. Similarly, Chiou et al. (1999) reported that copper supplementation of broilers had no beneficial effect on growth performance but resulted in severe damaged to the morphology of the digestive tract at high levels (500 mg/kg). In addition, basal concentrations of copper in laying hen diets were enough to maintain egg production and shell quality—no supplementation was found to be needed (Shřivan et al. 2006).

With both copper sulfate and copper tribasic chloride available, the choice for dietary copper source is one of preference. The bioavailability of copper between these two sources is similar for poultry (Miles et al. 1998), swine (Cromwell et al. 1998), and cows (Spears et al. 2004). The absorption of copper from the diet is much lower in ruminants than in non-ruminants due to complex interactions that occur in the rumen (Spears 2003). The sulfur and molybdenum interact in the rumen and form insoluble complexes with copper, making it unavailable for ruminants (Suttle 1991). When given a choice, pigs have been shown to prefer tribasic copper chloride (Cable et al. 2013). As with most minerals, young animals absorb copper more efficiently than older animals, but have a higher requirement (Borah and Sarmah 2013).

Copper sulfate supplementation has also been shown to reduce gram negative bacteria in the gut, such as streptococci (Van Paemel et al. 2010; Jensen 2016). The Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) evaluated the use of copper in animal nutrition on the development of antibiotic resistance in gut and soil bacteria (EFSA 2015). They concluded that the high copper concentrations in the microbial environment increases the number of copper-resistant bacteria. In addition, copper resistance is correlated with more frequent resistance to several antibiotics in certain bacterial species. They were not able to quantify the extent to which copper-resistant bacteria contribute to overall antibiotic resistance.

Below are the relative bioavailability assessments (%)[1] of copper compounds compared to copper sulfate in livestock (Jongbloed et al. 2002):

Copper compound	**Pigs**	**Broilers**	**Ruminants**
Copper sulfate	100	100	100
Copper carbonate	100	64	93
Copper oxide	74	24	76
Copper methionine	100	91	-
Copper lysine	94	100	104

[1]Criterion: liver copper concentration

Iodine

Iodine deficiency reduces the production of thyroid hormones and results in a slowing down of many metabolic processes. Iodine deficiency reduces reproductive capacity as well as the growth and development of the progeny (Van Paemel et al. 2010). Symptoms of iodine deficiencies include sluggishness, decreased feed intake, decreased body weight gain in young animals, reduced production or performance, dry hair or wool, puffy appearance, decreased resistance to cold, decreased resistance to infection, stunted growth, and dwarfism (EFSA 2005).

Toxic levels of iodine are more common than deficits, and more likely to be fatal in extreme cases (Hallas-Kilcoyne 2013). High dietary iodine levels result in hypothyroidism because of feedback inhibition of T3 synthesis (Van Paemel et al. 2010). In cattle, clinical signs include excessive nasal and ocular discharge, coughing, nervousness, tachycardia, decreased appetite, dermatitis, alopecia (the partial or complete absence of hair from areas of the body where it normally grows), exophthalmos (abnormal protrusion of the eyeball or eyeballs), weight loss, decreased milk production, susceptibility to infectious and respiratory diseases, reduced milk production in dairy cattle, and increased mortality of dams (Van Paemel et al. 2010; Paulíková et al. 2002). For pigs, iodine toxicosis reduces growth rate, feed intake, and hemoglobin levels. In sheep, toxic levels of iodine may result in depression, anorexia, hyperthermia, cough, changes in the respiratory system, and sometimes death (Paulíková et al. 2002). In sheep, a copper deficiency also results in “swayback” problems (EFSA 2005). Iodine toxicity in poultry results in depressed growth and neurological signs. Additionally, laying hens and breed hens (chickens and turkeys) have decreased egg production, egg size, and hatchability. Toxic iodine levels also result in low fertility and enlarged thyroids in hatching chicks (Van Paemel et al. 2010; Christensen and Ort 1991; Lewis 2004).

Horses are more sensitive to excess iodine than other farm animals (EFSA 2005). The symptoms of iodine deficiency and toxicosis are the same, complicating a diagnosis. The symptoms include hypothyroidism, goiter, or hypertrophy of the thyroid gland; a dry, dull hair coat; hair loss; flaky skin; thickened skin of the lower legs; birth of hairless foals; lethargy, dullness and timid behavior; and cold intolerance and low body temperature (EFSA 2015). In horses, iodine deficiencies symptoms may result in goiter (enlarged thyroid gland) on the underside of the throat along the jaw, poor coat and hair loss, low body temperature, and increased susceptibility to infectious diseases (Hallas-Kilcoyne 2013). Iodine deficiency in mares also tends to result in stillborn or weak foals.

Excess iodine intake also results in increased iodine excretion via milk and eggs (EFSA 2005). However, all available data on iodine content of foods of animal origin, as well as estimates of dietary intake in Europe, do not indicate a risk of excessive iodine intake in humans when iodine is included in animal feeds at the current recommended levels (EFSA 2005). They also reported that feed manufacturing practices in the European Union (EU) do not make full use of the maximum levels approved.

Below are relative bioavailability assessments (%) of iodine compounds compared to potassium iodide in livestock (Jongbloed et al. 2002):

Compound	Pigs	Poultry	Ruminants
Potassium iodide	100	100	100
Calcium iodate	-	95	106
Calcium iodide	-	-	110
Ethylenediamine dihydroiodide	99	-	111
Iodine humate	71	-	-
Diiodosalicylic acid	-	-	36
Pentacalcium orthoperiodate	-	-	111

Iron

Iron deficiency can occur worldwide in several crops (Zuo and Zhang 2011), often in calcareous soils because of their high pH and low iron content. Plant species that are typically low in available iron are soybeans and sorghum.

Iron deficiency is of limited practical significance in most livestock species, and may occur in newborn pigs, calves raised for veal, copper-supplemented pigs, and animals with parasitic infections (Soetan et al. 2010). There is a high tolerance for dietary iron in all animal species (Van Paemel et al. 2010) and limited intestinal absorption when iron intakes are high. The powerful mucosal block to iron absorption affords protection against toxicity (Van Paemel et al. 2010; EFSA 2014a). Characteristic signs of chronic iron toxicity include reduced feed intake, growth rate, and feed efficiency (Van Paemel et al. 2010).

Below are relative bioavailability assessments (%) of iron compounds compared to ferrous sulfate in livestock (Jongbloed et al. 2002):

Iron compound	Pigs	Meat chickens (broilers)
Ferrous sulfate•7 H_2O	100	100
Ferrous sulfate•H_2O	100	100
Ferrous carbonate	82	27
Ferric oxide	-	52
Ferric choline citrate	118	-
Ferric citrate	114	-
Ferric ammonium citrate	-	115

EFSA (2016a) reported that ferrous carbonate has the potential to be efficacious in adult animals only.

Manganese

Manganese deficiency as a practical problem is primarily confined to avian species (McDowell 2003; Underwood and Suttle 1999). The most commonly observed manganese deficiency disorder in poultry is perosis or slipped tendon. The disease results from malformation of bones characterized by enlarged and malformed tibio-metatarsal joints, twisting and bending of the tibia and the tarso metatarsus, thickening and shortening of the long bones, and slippage of the Achilles tendon from the condyles. Manganese deficiency in breeding hens results in chondrodystrophy in embryonic chicks. Manganese deficiency in laying hens and breeding hens reduces egg production and hatchability and increases the incidence of thin-shelled and shell-less eggs.

While supplementing laying hen diets with manganese had no significant effect on egg production, egg weight, feed intake, or feed efficiency, it was shown to have positive effects on eggshell quality, with reduced percentages of cracked eggs (Venglovská et al. 2014). Thickness, weight, proportion, and index of eggshells were significantly higher in all manganese-supplemented groups. Manganese supplementation from organic sources was also more effective in preventing yolk lipid oxidation during cold storage of eggs than supplementation with manganese sulfate, thus improving shelf-life of the eggs.

The main indications of a manganese deficiency in livestock include impaired growth, skeletal abnormalities, depressed reproductive function, ataxia of the newborn, and defects in lipid and carbohydrate metabolism (Van Paemel et al. 2010).

In pigs, manganese deficiency causes decreased growth and feed efficiency and impaired reproduction. In ruminants, a manganese deficiency may cause suboptimal soft tissue and skeletal growth, decreased breaking strength of bones, abnormal bone shape, ataxia, muscular weakness, excess accumulation of body fat, reduced milk production, delayed or absent estrus, resorption of fetus, fetal deformities, and small birth weights (McDowell 2003; Underwood and Suttle 1999).

Manganese is one of the least toxic of the essential trace elements (Van Paemel et al. 2010). Manganese toxicosis symptoms include depressed iron status and hematological changes, even when animals receive a diet typically adequate in iron. Pigs are more sensitive to manganese toxicity than other livestock. Some of the differences in sensitivities are related to the dietary iron levels as well as zinc and copper levels.

Below are relative bioavailability assessments (%) of manganese compounds compared to manganese sulfate monohydrate in livestock (Jongbloed et al. 2002):

Form	**Pigs**[1]	**Poultry**[2]	**Ruminants**[3]
Manganese sulfate monohydrate	100	100	100
Manganese carbonate	95	66	69
Manganese oxide	96	85	91-80
Manganese methionine	-	101	113

[1]Criterion: absorption of manganese (Mn); [2]Criterion: tibia ash Mn concentration; [3]Criterion: liver, kidney and bone Mn concentration

Molybdenum

Molybdenum requirements for livestock are low and typically met by feeding practical diets (Van Paemel et al. 2010). Pigs are the most tolerant to excess molybdenum. Ruminants are less tolerant of excess molybdenum than non-ruminants (Van Paemel et al. 2010); the higher susceptibility is due to the formation of thiomolybdates in the rumen. Cattle are the most sensitive, followed by sheep. The clinical signs of molybdenum excess are similar to secondary copper deficiency and include diarrhea, anorexia, depigmentation of hair or wool, anemia, neurological disturbances, impaired reproduction, and premature death (Van Paemel et al. 2010). An excess of molybdenum in the diet can lead to copper deficiencies in ruminants (Miltmore et al. 1970). High molybdenum levels were found in some hays in British Columbia, Canada, which could cause copper deficiencies.

Regarding relative bioavailability of dietary molybdenum sources, Jongbloed et al. (2002) concluded that there were no studies available in pigs and poultry. For ruminants, the relative bioavailability of molybdenum compounds compared to sodium molybdate were 114 percent for ammonium molybdate, 121 percent for molybdenum trioxide, and 60 percent for molybdenum metal.

Selenium

Most grains and forages are produced in areas of the United States that are either deficient or marginally deficient in selenium, making selenium supplementation necessary (Saha et al. 2016). Selenium-deficient soils have been reported in New England, New York, New Jersey, Delaware, Pennsylvania, Maryland, West Virginia, Florida, Ohio, Indiana, Illinois, Michigan, Wisconsin, Washington, Oregon, Arizona, and the coastal regions of Virginia, the Carolinas, and Georgia.

Selenium deficiencies in calves and lambs result in myodystrophy (white muscle disease), exudative diathesis (vascular disorders causing capillary leakage), impaired functions of the liver and pancreas, and a reduction in performance and reproductive ability (EFSA 2006). White muscle disease involves degeneration and necrosis of both the skeletal and cardiac muscles. In addition, subclinical selenium deficiencies may cause delayed development of immunocompetence and raise susceptibility to infectious disease (EFSA 2006). In older ruminants, selenium deficiencies result in unthriftiness and poor reproductive performance, including early embryonic death, impaired immunity, and placenta retention. In horses and foals, deficiencies result in white muscle disease. In swine, a deficiency results in hepatosis dietetica (damage to vital organs like the liver, kidney, or pancreas), white muscle disease, and mulberry heart disease. In poultry, a deficiency results in exudative diathesis and exocrine pancreatic atrophy (Saha et al. 2016). Sheep are more susceptible to selenium deficiency than cattle, and goats are more susceptible than lambs and calves.

Acute selenium toxicity is characterized by abnormal posture, unsteady walk, diarrhea, abdominal pain, increased pulse and respiratory rates, hypotension due to vasodilation, foamy nasal discharge, prostration, and a typical garlic smell on the breath because of the presence of volatile dimethyl selenide in the air (EFSA 2006). Selenium toxicity in cattle may result in deformities, cracking and loosing of hooves, lameness, stiffness of joints, dullness, lack of vitality, emaciation, and loss of hair (EFSA 2006). High selenium soils have been reported in South Dakota, Montana, Wyoming, Nebraska, Colorado, and New Mexico, though the level of available selenium in these areas will depend on soil conditions (Saha et al. 2016). There are reported cases of selenium toxicity in grazing animals due to consumption of selenium-accumulating plants (e.g., species of *Astragalus* and *Stanleya*) when they are grown in soils high in selenium. Most of these plants, however, have an unpleasant garlic-sulfur odor that makes them unpalatable to livestock. Typically, livestock will only consume these plants if the pastures are overgrazed or if other forages are not available. Lethal doses of selenium can occur if there is an error in weighing the selenium for premixes, or if there is a mis-formulation of supplement products.

Selenium toxicity in poultry has been reported to reduce hatching rates due to deformities of the embryos (Van Paemel et al. 2010). When selenium toxicity was experimentally induced in growing chickens, it resulted in severe diarrhea, dyspnea (difficult or labored breathing), and somnolence (a strong desire for sleep) in the chickens (EFSA 2006).

Below are relative bioavailability assessments (%) of selenium compounds compared to sodium selenite in livestock (Jongbloed et al. 2002):

Selenium compound	Pigs	Meat chickens (broilers)	Ruminants
Sodium selenite	100	100	100
Sodium selenate	-	-	107
Selenomethionine	102	78	124
Yeast selenium	108	-	109

Zinc

In livestock, zinc deficiencies typically result in reduced feed intake and growth retardation or cessation. Zinc deficiencies are also characterized by skin lesions, and skin outgrowths of hair, wool, and feathers. Impaired immunity often occurs as well (Van Paemel et al. 2010).

Livestock exhibit a considerable tolerance to high zinc intakes (Van Paemel et al. 2010); typical signs of zinc toxicity include reduced feed intake and growth rate, as well as well as signs typical of secondary deficiencies of other minerals such as copper. High zinc levels in weaned piglets have been shown to increase growth production and have a preventive effect on diarrhea of the piglets (SCAN 2003b), and zinc supports a large diversity of coliforms in weaned piglets that reduces susceptibility to *E. coli* infections. However, the effect of zinc on growth remains questionable (Pouslon and Carlson 2008).

Below are relative bioavailability assessments of zinc compounds compared to zinc sulfate (Jongbloed et al. 2002):

Zinc compound	Pigs	Ruminants	Poultry
Zinc sulfate	100	100	100

Zinc carbonate	98	58	93
Zinc chloride	-	42	107
Zinc oxide	92	95	67
Zinc amino acid chelate	102	102	131

Calcium

The requirements and metabolism of calcium and phosphorus are closely related (Cheeke 2005). Calcium and phosphorus deficiency symptoms reflect their metabolic functions as well as vitamin D status. Vitamin D functions in calcium and phosphorus absorption and in bone mineralization. In growing animals, the first signs of a calcium, phosphorus, and/or vitamin D deficiency is rickets, which causes spongy, poorly mineralized bones and typically results in lameness, broken bones, and death. This is also referred to as osteomalacia. In older animals, including humans, osteoporosis can result in decreased bone mass even with normal mineral composition (Cheeke 2005).

The use of calcium and phosphorus is influenced by the relative dietary amounts of each (Cheeke 2005). High calcium-to-phosphorus ratios are more common in laying hens and lactating animals. For most other animals, the optimal calcium-to-phosphorus ratio is in the range of 2:1 to 1:2 depending on the species as well as the stage of production.

The most common sources of calcium in animal diets include ground limestone (calcium carbonate), calcium sulfate (gypsum), bone meal, and crushed oyster shells (Cheeke 2005). Dietary ingredients containing both calcium and phosphorus include dicalcium phosphate and tricalcium phosphate.

Magnesium

Plant forage and animal feeds are often deficient in the levels of magnesium needed for healthy animal nutrition. Magnesium deficiencies result in symptoms of hyper-irritability, convulsions, muscle twitching, and death, a condition called grass tetany in cattle and sheep (Cheeke 2005).

Sources of magnesium for dietary supplementation include magnesium oxide and magnesium sulfate, both of which have high bioavailability (Cheeke 2005).

Phosphorus

The availability of phosphorus in plant materials is usually low because of the presence of phytate, which binds the phosphorus present. The most common sources of phosphorus for animal diets include rock phosphate (defluorinated), phosphoric acid, diammonium phosphate, sodium phosphate (monobasic), and sodium tripolyphosphate (Cheeke 2005). Dietary ingredients containing both calcium and phosphorus include dicalcium phosphate and tricalcium phosphate. The excretion of phosphorus by swine and poultry can be minimized by adding phytase in the animals' diet to reduce the need for supplemental phosphorus (Cheeke 2005).

Sources of phosphorus tend to be expensive, so accurate information on diets is important to prevent using excess amounts and increasing costs (Cheeke 2005). In addition, phosphorus, along with nitrogen, is a major water pollutant. As result, there are legal limits on the number of livestock animals that can be raised in some European countries, such as the Netherlands. The amount of animal manure that can be applied to land in the United States is regulated based on phosphorus content.

See the *Calcium* section above for information on calcium/phosphorus requirements.

Potassium

Potassium deficiency is not commonly found in livestock production but can occur under certain circumstances (Cheeke 2005). Most feed ingredients contain sufficient potassium, although the levels in grains tend to be lower than in good-quality roughages; mature, weathered, poor-quality roughages may also be deficient in potassium. Feedlot cattle on high-concentrate diets sometimes respond to dietary potassium supplementation. Stressful conditions, such as transporting and marketing, may increase potassium excretion in feeder cattle and pigs. Any dehydration or diarrhea will also increase the loss of potassium (Cheeke 2005). Potassium requirements rise during thermal stress of monogastric animals, during milk production, and in tail biting situations in pig production. Ruminants have a higher potassium requirement than nonruminants since potassium is essential for rumen microorganisms (Armstrong 1998).

Alfalfa and grains have fairly high potassium content, so forage crops grown in association with dairy farms may have a high potassium content (Cheeke 2005). Feeding these high-potassium forages to dairy cattle causes an increase in water consumption and urine volume. High potassium intakes also interfere with magnesium and calcium absorption and can result in hypo-magnesemia and milk fever (Cheeke 2005).

Sodium and chlorine

Sodium, potassium, and chlorine are typically considered together in animal feed as they are closely related in their metabolism (Cheeke 2005). Common salt (NaCl) is routinely added to animal feeds and often provided free-choice to grazing animals. In North America and Europe, the addition of salt to livestock is almost universal (Cheeke 2005). This is mainly because animals—ruminants in particular—have an innate desire to consume salt, often interpreted as a physiological and nutritional need. It should be noted that animals, especially herbivores, have a salt appetite and can consume much more salt than required for optimal health. If water availability is limited, salt toxicity can occur. Herbivore diets tend to be high in potassium, and the ratio of sodium to potassium may be a contributing factor in an appetite for salt (Cheeke 2005).

Most plants do not provide sufficient sodium for animal feeding and may lack chloride content (Salt Institute, "Salt and trace minerals"). Even if the sodium requirement is met, the chloride requirement may not be met. Studies have shown a close correlation between potassium and chloride in the urine of cows. It was hypothesized that the necessity for ruminants to eliminate high amounts of dietary potassium as potassium chloride could dramatically increase their chloride requirements. Since many ruminant feedstuffs are high in potassium, the potassium to chloride ratio in the diet is important (Salt Institute, "Salt and trace minerals").

Ruminants have an ability to conserve sodium (Cheeke 2005) since the rumen acts as a sodium storehouse. When sodium-deficient diets are consumed, rumen sodium is used to counteract blood sodium depletion. In addition, potassium, which is abundant in grass, replaces sodium in saliva. These mechanisms allow ruminants to adapt to sodium-deficient areas of the world (Cheeke 2005), including most noncoastal land areas. Northern ruminants, like moose, eat large amounts of sodium-containing aquatic plants during a three-month season and draw on the rumen sodium pool during the rest of the year (Cheeke 2005).

Salt is often a carrier for trace minerals since all farm animals have an appetite for salt (Salt Institute, "Agricultural salt"). This is particularly true for animals on ranges where little or no levels of concentrate feed are produced. Producers supply trace-mineralized salt free-choice in the form of a mineral block or as a loose trace mineral salt in a box. Different levels of various minerals are added to salt for specific and different situations (Salt Institute, "Agricultural salt").

Sulfur

Sulfur is a mineral found in the amino acids methionine, cysteine, cystine, homocysteine and taurine (Goodrich and Garrett 1986). Other sulfur containing amino acids can be produced metabolically from methionine, but methionine is not produced by non-ruminants from other sulfur containing amino acids. As a result, methionine is the essential amino acid for non-ruminants, although half the methionine requirement can be met by cysteine.

In addition to being a key ingredient in the formation of these amino acids, sulfur is also important for the formation of collagen, hormones, vitamins biotin and thiamin and oxygen carriers (Goodrich and Garrett 1986).

Approved Legal Uses of the Substance:

21 CFR Part 573 addresses food additives permitted in the feed and drinking water of animals.

- 21 CFR §573.304 specifically addresses chromium propionate, which can be used with a restriction of 0.2 ppm in complete feed.
- 21 CFR §573.580 specifically addresses iron-choline citrate complex, which can be used as an iron source in animal feeds.
- 21 CFR §573.920 specifically addresses selenium. It states that selenium may be added, at specific levels, as sodium selenite, sodium selenate, or selenium yeast. There are specific regulations with regards to levels in complete feed, feed supplements, and salt-mineral premixes.

21 CFR §582.80 addresses the trace minerals that can be added to animal feeds. The following list of substances are Generally Recognized as Safe (GRAS) "when added at levels consistent with good feed practice." The substances listed may be in anhydrous or hydrated forms. Chromium and selenium are not listed in this section but are addressed above. Molybdenum is also not mentioned. It should be noted that all the compounds listed in Table 1 are considered GRAS and safe for use in animal feeds.

Cobalt:
- Cobalt acetate, cobalt carbonate, cobalt chloride, cobalt oxide, cobalt sulfate
  Note: While cobalt chloride can be supplemented to animal feeds, the direct use of cobalt chloride in human food is prohibited in the United States (21 CFR §189.120)

Copper:
- Copper carbonate, copper chloride, copper gluconate, copper hydroxide, copper orthophosphate, copper oxide, copper pyrophosphate, copper sulfate

Iodine
- Calcium iodate, calcium idobehenate, cuprous iodide, 3,5-Diiodosalicylic acid, Ethylenediamine dihydroiodide, potassium iodate, potassium iodide, sodium iodate, sodium iodide, thymol iodide

Iron:
- Iron ammonium citrate (note: 21 CFR §573.560 states that this is to be used as an anti-caking agent in salt), iron carbonate, iron chloride, iron gluconate, iron oxide, iron phosphate, iron pyrophosphate, iron sulfate, reduced iron

Manganese
- Manganese acetate, manganese carbonate, manganese citrate (soluble), manganese chloride, manganese gluconate, manganese orthophosphate, manganese phosphate (dibasic), manganese sulfate, manganous oxide

Zinc:
- Zinc acetate, zinc carbonate, zinc chloride, zinc oxide, zinc sulfate

The Association of American Feed Control Officials (AAFCO) allows for the use of metal amino acid complexes (57.150), metal (specific amino acid) complexes (571.151), metal amino acid chelate (57.142), metal proteinate (57.23), metal methionine hydroxy analogue chelate (57.28), and metal polysaccharide complex (57.29) in animal feeds. Note that 7 CFR §205.237 prohibits the feeding of mammalian or poultry slaughter byproducts to mammals and poultry. For organic production of the metal amino acid complexes, metal amino acid chelates, metal proteinates, and metal polysaccharide complexes, the protein used cannot come from slaughter-derived byproducts.

In 2007, the FDA's Center for Veterinary Medicine (CVM) signed a Memorandum of Understanding (MoU) with the AAFCO that allows FDA to formally recognize the AAFCO's list of feed ingredients and defines the role FDA can play in deciding on the suitability of feed ingredients offered for addition to the list. Under the memorandum, CVM assigns scientists to work with AAFCO in reviewing petitions for new feed ingredients or for modifications to existing ingredient definitions.

A discussion of the approved legal uses for each of the minerals in Table 1 follows.

Chromium

While the U.S. NRC considers chromium to be an essential trace mineral, it was unable to give specific recommendation levels for cattle, poultry, and swine (NRC 2005). The European Food Safety Authority (EFSA) does not consider chromium to be an essential trace mineral (EFSA 2009a; EFSA 2014c). The EFSA does not feel that deficiency symptoms have been recognized in field conditions but does consider chromium to be of nutritional or beneficial effect for human supplements. The Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) also concluded that there is no evidence of essentiality for chromium (III) as a trace element in animal nutrition (EFSA 2014c). Therefore, while the EU does not authorize the use of chromium supplements in food animals, it does authorize chromium supplements for humans (EFSA 2009a). A 2017 publication discussed new evidence that concludes that chromium is not an essential trace mineral, especially in humans (Vincent 2017). The author defined an essential nutrient as having a defined biochemical function, where its absence results in death or failure to reproduce, and its addition to the diet can prevent these effects. They also found no evidence of chromium deficiencies in the general population.

Chromium is usually added to animal feeds as chromium propionate, chromium picolinate, or chromium yeast. Chromium propionate can be added to broiler and swine feeds at a level not to exceed 0.2 mg per kilogram of feed (AAFCO 2019; 21 CFR §573.304). In cattle diets, chromium can be added at a level not to exceed 0.5 mg per kilogram of feed. Chromium propionate must be premixed with dry ingredients before adding to high moisture ingredients or forages (AAFCO 2019). Chromium picolinate can be used as a source of supplemental chromium in swine diets, not to exceed more than 200 ppb. Chromium from all sources of supplemental chromium cannot exceed this limit (AAFCO 2019).

Cobalt

Although cobalt carbonate, cobalt oxide, and cobalt sulfate are the main inorganic sources of cobalt typically added to livestock and poultry diets, 21 CFR §582.80 and AAFCO (2019) identify other approved cobalt compounds including cobalt acetate, cobalt chloride, cobalt gluconate, cobalt amino acid complex, cobalt proteinate, and cobalt choline complex.

Cobalt compounds are approved for inclusion in animal feeds in Europe under EC 1334/2003 and include cobaltous acetate tetrahydrate, basic cobaltous carbonate monohydrate, cobaltous chloride hexahydrate, cobaltous sulfate heptahydrate, cobaltous sulfate monohydrate, and cobaltous nitrate hexahydrate. The maximum allowed content of cobalt in animal feeds is a total of 2 mg/kg (Van Paemel et al. 2010). The EFSA, however, concluded that the toxicological and carcinogenic aspects of cobaltous chloride hexahydrate pose a safety concern for its use as a food supplement for humans as a source of cobalt (2009a).

Copper

Copper sulfate is used as a mineral supplement in animal feeds and is approved as GRAS per 21 CFR §184.1261. In accordance with 21 CFR §184.1(b)(1), copper sulfate can be used with no limitation other than current good manufacturing practices (GMPs). Other copper sources approved as GRAS for inclusion in animal feeds as nutritional dietary supplements according to good feeding practices include copper acetate, copper carbonate, and cobalt oxide (AAFCO 2019) as well as copper gluconate (21 CFR §582.5260), copper carbonate, copper chloride, copper gluconate, copper hydroxide, copper orthophosphate, copper oxide, and copper pyrophosphate (21 CFR §582.80).

In Europe, copper compounds are authorized for inclusion in animal feeds under EC 1334/2003, EC 479/2006, and EC 1253/2008 (Van Paemel et al. 2010). Approved compounds include cupric acetate monohydrate, basic cupric carbonate monohydrate, cupric chloride dihydrate, cupric methionine, cupric oxide, cupric sulfate pentahydrate, cupric chelate of amino acids hydrate, copper lysine sulfate, cupric chelate of glycine hydrate, and copper chelate of hydroxyl analogue of methionine. For the copper chelate of hydroxyl analogue of methionine, the maximum allowed total copper content for fattening meat chickens is 25 mg/kg. For the other compounds, the maximum total copper content for piglets up to 12 weeks old is 170 mg/kg; for pigs over 12 weeks, the maximum is 25 mg/kg; for bovines before the start of rumination, the maximum in milk replacers as well other complete feedstuffs is 15 mg/kg; for other bovines, the maximum is 35 mg/kg; for ovines, the maximum is 15 mg/kg; and for all other species, the maximum is 25 mg/kg (Van Paemel et al. 2010).

Iodine

Calcium iodate is considered GRAS and used as a dough stabilizer in the production of bread (21 CFR §184.1206). As with calcium iodate, potassium iodate is considered GRAS and approved for use as a dough strengthener in the production of bread (21 CFR §184.1635).

Calcium iodate and potassium iodate are both considered GRAS for use in animal dietary supplements when added at levels consistent with good feeding practices (21 CFR §582.80). Other approved iodine sources include calcium iodobehenate, cuprous iodide, 3,5-Diiodosalicyclic acid, ethylenediamine dihydroiodide, potassium iodide, sodium iodide, and thymol iodide (21 CFR §582.80).

In Europe, the use of iodine compounds in animal feeds is approved according to EC 1459-2005 (Van Paemel et al. 2010). The approved compounds include calcium iodate hexahydrate, calcium iodate anhydrous, sodium iodide, and potassium iodide. For all compounds, the maximum total contents in animal feeds is 4 mg/kg for horses, 5 mg/kg for dairy cows and laying hens, 20 mg/kg for fish, and 10 mg/kg for other species or categories of animals.

Iron

Ferrous sulfate is considered GRAS (21 CFR §184.1315). In accordance with 21 CFR §184.1(b)(1), ferrous sulfate can be used with no limitation other than current GMPs. Ferrous sulfate, listed as iron sulfate, is also considered GRAS. Other compounds are considered GRAS when added to feeds consistent with good feeding practice.
21 CFR §582.80 allows for the use of iron ammonia citrate, iron carbonate, iron chloride, iron gluconate, iron oxide iron phosphate, iron pyrophosphate, iron sulfate and reduced iron.

In Europe, iron compounds authorized for use in animal feeds under EC 2112/2003 and EC 479/2006 include ferrous carbonate, ferrous chloride tetrahydrate, ferrous chloride hexahydrate, ferrous fumarate, ferrous lactate trihydrate, ferric oxide, ferrous sulfate monohydrate, ferrous sulfate heptahydrate, ferrous chelate of amino acids hydrate and ferrous chelates of glycine hydrate (Van Paemel et al. 2010). The maximum allowed total iron content in complete feeds is 500 mg/kg for sheep, 1250 mg/kg for pet animals, 250 mg/kg for pigs up to one week before weaning, 750 mg/kg for other pigs, and 750 mg/kg for all other species.

Manganese

Manganese sulfate, but not manganese oxide, is considered GRAS (21 CFR §184.1461) in food for human consumption. The ingredient is used as a human nutrient supplement as defined in 21 CFR §170.3(o)(20). In accordance with 21 CFR §184.1(b)(1), manganese sulfate can be used in food for human consumption with no limitation other than GMPs.

According to 21 CFR §582.80, manganese sulfate, manganese acetate, manganese carbonate, manganese citrate (soluble), manganese chloride, manganese gluconate, manganese orthophosphate, manganese phosphate (dibasic), and manganese oxide are considered GRAS when added to animal feeds at levels consistent with good feeding practices.

In Europe, manganese compounds are authorized as feed additives under EC 1134/2003 and EC 479/2006 (Van Paemel et al. 2010). The approved compounds include manganous carbonate, manganous chloride tetrahydrate, manganous hydrogen phosphate trihydrate, manganous oxide, manganic oxide, manganous sulfate tetrahydrate, manganous sulfate monohydrate, manganese chelate of amino acids hydrate, manganomanganic oxide, and manganese chelate of glycine hydrate. The maximum approved content of manganese is animal feeds is a total of 150 mg/kg. For fish, this is reduced to 100 mg/kg.

Molybdenum

In the United States, sodium molybdate is allowed in animal feeds (AAFCO 2019).

In Europe, EU Council directive 70/524/EEC allows the use of ammonium molybdate and sodium molybdate in animal feeds at a maximum of total molybdenum dietary content of 2.5 mg/kg of complete feed (Van Paemel et al. 2010).

Selenium

In the United States, 21 CFR §573.920 allows for the use of selenium in the diets of chickens, swine, turkeys, sheep, cattle, and ducks. The permitted sources of selenium are sodium selenite, sodium selenate and selenium yeast. Sodium selenite and sodium selenate are equally effective, but sodium selenite is commonly used because of its lower cost (Saha et al. 2016). Selenium yeast is a dried, non-viable yeast of the species *Saccharomyces cerevisiae.* The yeast is cultivated in fed-batch fermentation, which provides incremental amounts of cane molasses and selenium salts in a manner that minimizes the detrimental effects of selenium salts on the growth rate of the yeast. This results in the incorporation of inorganic selenium into cellular organic material. Any residual inorganic selenium is removed by rigorous washing. The total amount of residual inorganic selenium cannot exceed two percent of the total selenium content in the final selenium yeast product (Saha et al. 2016).

Selenium compounds that can be used in the EU as additives under EU Council Directive 70/24/EEC and Commission Regulations EC 1750/2006, EC 634-2007, and EC 900/2009 include sodium selenite, sodium selenate, organic forms of selenium produced by *S. cerevisiae*, and selenomethionine produced by *S. cerevisiae*. The maximum allowed content of selenium in the complete feed is a total of 0.5 mg/kg (Van Paemel et al. 2010).

Zinc

Zinc oxide and zinc sulfate are considered GRAS when included in animal feeds consistent with good feeding practices (21 CFR §582.80). Other approved sources of zinc (when included in animal feeds consistent with good feeding practices) include, but are not limited to, zinc acetate, zinc carbonate, and zinc chloride.

In Europe, zinc compounds are authorized for use in animal feeds under EC 1134/2003, EC 479/2006, and EC 888/2009 (Van Paemel et al. 2010). The approved compounds include zinc lactate trihydrate, zinc acetate dihydrate, zinc carbonate, zinc chloride monohydrate, zinc oxide, zinc sulfate heptahydrate, zinc sulfate monohydrate, zinc chelate of amino acids hydrate, zinc chelate of glycine hydrate, and zinc chelate of hydroxyl analogue of methionine. For fattening chickens, the maximum total content of zinc in the feed from zinc chelate of hydroxyl analogue of methionine is 150 mg/kg. For the other zinc sources, the maximum allowed total content in the complete feed is 250 mg/kg for pet animals, 200 mg/kg for fish, 200 mg/kg for milk replacers, and 150 mg/kg for other species.

Calcium

Calcium carbonate is used as a source of calcium in animal feeds. In addition, calcium carbonate is the active ingredient in agricultural lime. Calcium carbonate is considered GRAS (21 CFR §184.1191) in foods for human consumption. In accordance with 21 CFR §184.1(b)(1), calcium carbonate can be used in food with no limitation other than good manufacturing practices. Calcium carbonate can be used in animal feed when used in accordance with good feeding practices. Additional calcium compounds that are considered GRAS for animal feeds include calcium carbonate (21 CFR §582.1192); calcium chloride (21 CFR §582.1193); calcium citrate (21 CFR §582.1195); calcium gluconate (21 CFR §582.1199); calcium hydroxide (21 CFR §582.1205); calcium lactate (21 CFR §582.1207); calcium oxide (21 CFR §582.1210); and calcium phosphate as mono-, di-, and tribasic forms (21 CFR §582.1217).

Magnesium

Magnesium sulfate is listed as GRAS (21 CFR §582.5443) and can be included in animal feeds in accordance with good feeding practice. Additional magnesium sources for animal feeds include magnesium carbonate

(21 CFR §582.1425), magnesium hydroxide (21 CFR §582.1428), magnesium oxide (21 CFR §582.1431 and 21 CFR §582.5431), magnesium phosphate (21 CFR §582.5434), and magnesium chloride (21 CFR §582.5446).

Phosphorus

Calcium phosphate as mono-, di-, and tribasic forms is considered GRAS when used in accordance with good feeding practices (21 CFR §582.1217).

Potassium

Sources of potassium considered GRAS when used according to good feeding practices include potassium bicarbonate (21 CFR §582.1613), potassium carbonate (21 CFR §582.1619), potassium citrate (21 CFR §582.1625), potassium hydroxide (21 CFR §582.1631), potassium chloride (21 CFR §582.5622), potassium glycerophospate (21 CFR §582.5628), potassium iodide (21 CFR §582.5634), and potassium sulfate (21 CFR §582.1643).

Sodium and chlorine

Salt was part of the original 1959 GRAS list and is currently listed at 21 CFR §182.1. Sodium is part of the mandatory elements for nutrition labeling.

Action of the Substance:

Animals obtain some of their mineral requirements through feed, water, and any consumed soil (Cheeke 2005). When this is insufficient to meet their nutrient requirements, supplementation of minerals is typically done through inclusion in the diet either as an individual substance or as part of a trace mineral premix (Cheeke 2005). The mineral compounds are then broken down in the digestive tract and the minerals are absorbed through the intestinal wall. The bioavailability of a mineral from a particular compound will vary depending on different factors, as described in the section on *Specific Uses of the Substance*.

A description of the action of each of the minerals in Table 1 follows.

Chromium

Metallic chromium has no biological activity. Trivalent chromium is part of the glucose tolerance factor, an essential activator of insulin-mediated reactions (Van Paemel et al. 2010). Chromium helps to maintain normal glucose metabolism and peripheral nerve function; without it, insulin cannot properly remove glucose from the blood after a meal.

While the NRC (2005) classified chromium as an essential nutrient, the EFSA (2009a) concluded that there is no evidence supporting the essentiality or non-essentiality of trivalent chromium as a trace mineral. They did, however, classify chromium as a nutritionally or pharmacologically beneficial element in humans (EFSA 2009a). Though the EFSA stated that no symptoms of chromium deficiency in farm animals have been identified under field conditions, other research has shown that chromium supplementation can improve the immune status of some farm animals (Lien et al. 2005; Rao et al. 2012; Uyanik et al. 2008). There has also be research showing that chromium supplementation can increase carcass weight and decrease abdominal fat in commercial meat chickens (Hossain et al. 1998), but not meat rabbits (Lambertini et al. 2014) or unstressed growing-finishing steers (Chang et al. 1992). Chromium supplementation can also be beneficial during heat stress situations for dairy cows (Al-Saiady et al. 2004).

Diets high in refined or simple sugars increase urinary chromium losses, and diets that produce propionate in the rumen would be expected to deplete chromium stores. Supplemental fat may induce insulin resistance or impair glucose tolerance. All these situations would increase an animal's chromium requirements (Jones 2014).

Cobalt

In ruminants, cobalt is required in the synthesis of vitamin B12 (Cheeke 2002), which is involved in the formation of red bloods and helps to create and regulate DNA. It is also crucial to the normal function of the brain and the nervous system. It plays a role in synthesizing fatty acids and in producing energy.

Vitamin B12 is also involved in the release of energy in the cell by helping the body absorb folic acid (Cheeke 2010). Metabolism in every cell in the body depends on vitamin B12.

Cobalt is primarily a trace mineral supplement of ruminants, horses, and rabbits which have large populations of microflora that can use the cobalt to synthesize vitamin B12 (EFSA 2009b). Most forages and feedstuffs fed to dairy and beef cattle are low in cobalt. Under grazing conditions, lambs are the most sensitive to cobalt deficiency, followed by mature sheep, calves, and mature cattle (McDowell 2003). Because the production of vitamin B12 would occur too far down the digestive tract to allow for substantial absorption by young ruminants, poultry, or swine, vitamin B12 is supplemented to these diets rather than cobalt (EFSA 2009b). There is no evidence that cobalt is needed for monogastrics when dietary vitamin B12 levels are adequate.

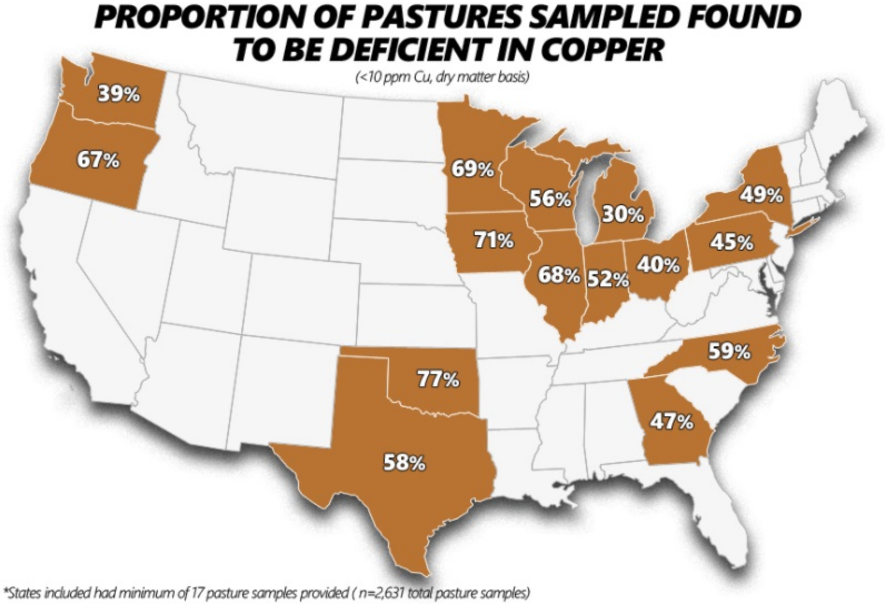
Copper

Biologically, copper is an important part of metalloenzymes—any enzymes containing tightly bound metal atoms (Cheeke 2005). The metal ions function as co-enzymes, imparting activity to the enzymes. For copper, these co-enzymes include ascorbic acid oxidases, cytochrome oxidase, catechol oxidase, and others. Copper is surpassed only by zinc in the number of enzymes which it activates. Copper is involved in maturation and stability of collagen and elastin, energy metabolism, the antioxidant defense system, and pigmentation. Copper is also involved in iron transport and metabolism, red blood cell formation, and immune function. Copper deficiencies can lead to achromotrichia (depigmentation), anemia, growth depression, bone disorders, demyelination of the spinal cord, fibrosis of the myocardium, and diarrhea. Copper toxicosis results in salivation, epigastric pain, nausea, vomiting, and diarrhea (Cheeke 2005).

Copper deficiencies can occur in plants grown in certain types of soils. As a result, copper deficiencies in cattle occur in many parts of the world (Underwood and Suttle 1999). An excess of molybdenum in the diet can lead to copper deficiencies in ruminants (Miltmore et al. 1970). High molybdenum levels were found in some hays in British Columbia, Canada, which could cause copper deficiencies. Scientists also found that copper concentrations in the hay were low in certain areas, which can result in copper deficiencies even in hay with lower molybdenum levels.

Agri-King analyzed 2,631 pasture samples sent in by clients in 15 states over a five-year period. The proportion of pastures that failed to meet the minimum requirement for copper are shown in Figure 1 below (Hafla 2018). The pastures were composed of grasses, legumes, grass/legume mixes, cereal grains, and brassicas. The samples represented all months of the year, but 92 percent were taken during common grazing months of April through October. Most of the samples were sent from the upper Midwest and Northeast.

Figure 1. Agri-King Analysis of Pastures Deficient in Copper



*States included had minimum of 17 pasture samples provided (n=2,631 total pasture samples)

Copper is not typically given to sheep as high-quality forages containing a mixture of grasses and legumes provide sufficient copper in most cases. It is important to note, however, that goats require substantially more copper than sheep, so a “one size fits all” approach to mineral supplements for goats and sheep should not be used (Wahlberg and Greiner 2006).

Copper availability for cereals in concentrated feeds is higher than the availability from forage (Cheeke 2005). High copper supplements in weaned pig diets have been shown to improve feed conversion and stimulate growth (Underwood and Suttle 1999) and has been shown to have a growth promoting effect in pigs (Cromwell et al. 1998) and broilers (Smith 1969; Jegede et al. 2011).

Iodine

Biologically, iodine is important for thyroid hormones (Cheeke 2005). The thyroid hormones thyroxine and triiodothyronine are important as regulators of energy metabolism and growth, as well as transmitters of nervous stimuli. They also play a role in brain development (Cheeke 2005).

Iodine deficiencies in beef cattle are rare (Nickel 2015). The Great Lakes region and the Northwest have the highest probability of iodine deficiency in cattle (Lanka 2015; Nickel 2015), and adjacent provinces in Canada are also likely to be deficient. Forages from all areas of the world are highly variable in iodine content and availability. Because no effective treatment for an iodine deficiency has yet been found, supplementing animal feeds with iodine is important (Lanka 2015).

Goitrogens may be present in some feedstuffs (Nickel 2015) and can cause an iodine deficiency. Goitrogens are dietary compounds that prevent the update of iodine from the digestive tract. Feeds that contain goitrogens include brassicas like turnips, rapeseed, or kale. Parts of white clover, carrots, linseed, cassava, sweet potatoes, lima beans, millets, peanuts, cottonseed, soybeans, and sugar beet pulp can also reduce iodine uptake (Nickel 2015). Some conditions— including foot rot, wooden tongue, lumpy jaw, and soft-tissue swellings around the neck and jawline— can be treated with iodine supplementation, though they are not necessarily the result of an iodine deficiency (Nickel 2015).

Iron

Iron is an important part of hemoglobin, which helps carry oxygen in the blood (Cheeke 2005). In addition, aerobic metabolism depends on iron because of its role as an electronic carrier in cytochromes in the Krebs Cycle. Aerobic metabolism is also dependent on iron for its role, in association with hemoglobin, in oxygen and carbon dioxide transport (Cheeke 2005). The body uses iron efficiently by recycling iron through the breakdown of old red blood cells (Gengelbach 2015)

Iron-deficient anemia is a common problem in piglets housed on concrete without access to soil (Gengelbach 2015) because of their rapid growth rate and the low concentration of iron in sows' milk. Iron-dextran injections are commonly given when piglets are 2–3 days old to protect them from anemia until weaning.

Many disease-causing microbes have high iron requirements (Gengelbach 2015). As a result, the body prevents iron from being available to the invading organisms during infection. In extreme cases, an animal can become temporarily anemic as the body attempts to make iron less available. Anemia can also occur during severe infestations of blood-sucking parasites or other causes of extreme blood loss (Gengelbach 2015).

Excess levels of dietary iron can be more problematic than deficiencies (Gengelbach 2015). Free iron is toxic to cells because iron ions can cause significant oxidative damage to cells. High dietary iron levels also interfere with the absorption of other minerals, especially copper and zinc (Gengelbach 2015).

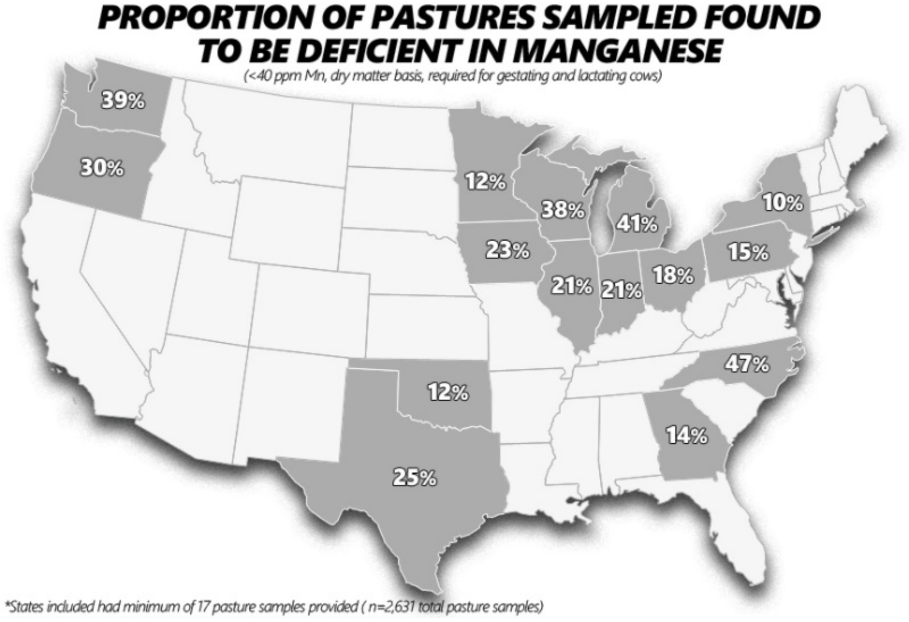
Manganese

Manganese is an essential element that is a constituent of multiple enzymes. It is a component of the organic matrix of bone (Cheeke 2005) and is essential for cartilage development. It is also involved in the metabolism of calcium and carbohydrates. Manganese is necessary for the utilization of biotin, vitamin B1, and vitamin C. Deficiency symptoms include impaired growth, skeletal abnormalities, depressed reproductive function, ataxia (incoordination) of the newborn, and defects of lipid and carbohydrate metabolism. Manganese deficiency as a practical problem is largely confined to avian species, where a deficiency results in perosis, a disorder characterized by leg deformity (Cheeke 2005).

There is a metabolic association between manganese and choline which affects fat metabolism in the liver (Coomer 2014). Manganese is involved in the biosynthesis of choline. A choline deficiency will limit the liver's ability to metabolize fats and use them for energy. As a result, fat may build up in the liver (referred to as fatty liver). This situation can occur in post-partum dairy cows since they are in a negative energy balance and rely on the liver to metabolize fat to meet their energy needs for milk production. Manganese deficiencies have been shown to result in sterility and reduced conception rates of cattle in both the United States and England (Coomer 2014).

Agri-King's analysis of 2,631 pasture samples sent in by clients in 15 states over a five-year period found a somewhat lower proportion of pastures deficient in manganese compared with the proportion deficient in copper, as shown in Figure 2 below (Hafla 2018).

Figure 2. Agri-King Analysis of Pastures Deficient in Manganese



*States included had minimum of 17 pasture samples provided (n=2,631 total pasture samples)

Molybdenum

Molybdenum is an essential element of three mammalian enzymes—xanthine oxidase, aldehyde oxidase, and sulfite oxidase (Cheeke 2005). Xanthine oxidase is important in the metabolism of purines (nucleotides in DNA) when they are no longer required. The enzyme converts xanthine to uric acid so that it can be excreted. Aldehyde oxidase breaks down aldehydes, which can be toxic to the body. In humans, it also helps the liver to breakdown alcohol and some drugs, including those used in cancer therapy. Sulfite oxidase is important in the metabolism of sulfur-containing amino acids, such as methionine. The enzyme converts sulfite to sulfate to help prevent a dangerous sulfite buildup. Sulfites are found naturally in foods and sometimes added as a preservative. A buildup of sulfites can trigger an allergic reaction that can result in diarrhea, skin problems, and even breathing difficulties (Cheeke 2005).

The requirement for molybdenum is closely associated with the copper requirement (Donaldson 2015). Molybdenum at high dietary levels can reduce copper absorption.

Soils vary widely in their molybdenum content and thus affect the amount found in forage crops (Donaldson 2015). Corn silage tends to have the lowest concentrations of molybdenum, with grass and alfalfa having intermediate levels, and pastures having a wide range of concentrations. Typically, only 10 percent of the molybdenum in plants is bioavailable, although this level increases as the pH of the soil increases. The dry matter of plants and grains typically contains 0.5 to 2.5 ppm molybdenum, which is usually sufficient for ruminants. For ruminants on high fiber diets with high copper:molybdenum ratios (greater than 4:1), most molybdenum is excreted in the manure (Donaldson 2015).

Non-ruminants and milk-fed calves metabolize molybdenum different than ruminants (Donaldson 2015). In monogastrics, molybdenum is absorbed very efficiently across the stomach and abomasum wall. The absorption occurs via an active, energy-dependent system shared with, and inhibited by, sulfate. Since very little sulfur leaves the rumen as sulfate, this antagonism is a feature only of non-ruminants (Donaldson 2015).

Selenium

Selenium is one of more than 30 distinctive selenoproteins (Cheeke 2005) and is involved in vitamin E metabolism. Selenium is an important part of glutathione peroxidase. Specifically, selenium reduces lipid hydroperoxides to their corresponding alcohols and reduces free hydrogen peroxide to water, which prevents these compounds from damaging body cells. Selenium is also important for an animal's immune status, growth, and reproduction. Selenium and vitamin E both help to protect animals from peroxidative damage, although their specific roles differ (Cheeke 2005).

Selenium occurs in the soil in varying concentrations in all parts of the world (Hafla 2015). Available selenium is taken up by many plants, including cereal grains and forages. Deficiency in grazing animals follows a geological pattern; the Pacific Northwest, the Great Lakes states, the Northeast, the Atlantic Seaboard, and Florida tend to have deficient selenium concentrations (Hafla 2015). The use of selenium is regulated by the FDA, with the maximum level of supplementation restricted to 0.30 mg/kg of total feed consumed.

Zinc

After iron, zinc is the second most abundant trace mineral in most vertebrates (Cheeke 2005). Zinc is an essential element that exerts most of its biological functions in association with proteins; it is an integral part of 300 known enzymes that catalyze more than 50 different biochemical functions. Zinc is also involved in transcription and translation of genetic material (Cheeke 2005).

Zinc is critical to immune system function, enzyme systems, and hoof health in cattle (Hafla 2018). When stressed, cattle deficient in zinc may have a greater incidence of illness, lower responses to treatment, and longer recovery times compared to cattle with adequate zinc status. Agri-King's analysis of 2,631 pasture samples sent in by clients over a five-year period found that only six percent of the pastures evaluated were found to be deficient in zinc (Hafla 2018). However, calves that are born with adequate zinc status may approach marginal deficiency by weaning due to rapid body growth and low zinc levels in milk. This can have negative impact on the effectiveness of vaccines and on the health and productivity of calves (Hafla 2018).

Calcium

Calcium is the most abundant mineral in the body and helps to build and maintain skeletal tissue in osteoblasts (bone-forming cells in which calcium phosphate is deposited) (Cheeke 2005). Calcium performs several other basic functions: maintaining the stability of fibrin, which allows blood to clot; transmitting nerve impulses; controlling the flow of fluid through cell membranes; and contracting and relaxing muscles.

Agri-King's analysis of 2,631 pasture samples sent in by clients over a five-year period found that most pastures provided adequate concentrations of calcium, phosphorus, potassium, and sulfur for mature cows, but that 30 percent of the pastures had low calcium:phosphorus ratios. When these ratios are below 1.5:1.0, water belly (urinary calculi) can occur (Hafla 2018).

Magnesium

Along with calcium, magnesium is required for the proper bone growth and maintenance (Cheeke 2005). Magnesium is required for the proper function of nerves, muscles, and many other parts of the body. It supports a healthy immune system, keeps the heart beat steady, and helps regulate blood glucose levels (Cheeke 2005). Magnesium is also needed for more than 300 biochemical reactions in the body.

Dietary magnesium deficiency in grazing animals is rare (Schauff 2014). Low blood magnesium typically occurs when diets are low in concentrates and grains and high in lush spring pastures. Cool season grasses grazed in early spring and wheat pastures in the fall pose the most potential risk for grass tetany due to magnesium deficiency.

Agri-King's analysis of 2,631 pasture samples sent in by clients over a five-year found that magnesium was deficient for lactating cows in 24 percent of the pastures tested (Hafla 2018).

Phosphorus

Phosphorus helps with the formation of bones and teeth (Cheeke 2005). It also plays an important role in how the body uses carbohydrates and fats and is involved in energy production. Phosphorus is needed for the body to make protein for the growth, maintenance, and repair of cells and tissue. Phosphorus also plays an important structural role in nucleic acid and cell membranes (Cheeke 2005).

Phosphorus deficiency is most common with animals consuming forages from soils that are deficient in phosphorus (Gengelbach 2014). Lactating dairy cows have a requirement for phosphorus that includes the amount needed for maintenance, the amount needed for growth and pregnancy, and the amount of phosphorus secreted in the milk (Gengelbach 2014). Phosphorus toxicity in grazing animals is rare because they are quite efficient in excreting excess phosphorus in the manure and saliva. See the section on *Calcium* for information on calcium:phosphorus levels in Agri-King's pasture sample analysis.

Since phosphorus is generally the most expensive macro-mineral added to animal diets, and considering the environmental concerns of excessive phosphorus in manure, adding phosphorus to animal diets must be done with caution (Gengelbach 2014).

Potassium

Potassium primarily serves as an electrolyte (Cheeke 2005). It becomes ionized in solution, which makes it capable of carrying an electrical charge and allows it to influence different body processes. It works in concert with sodium to exert its effects.

Potassium is the main electrolyte inside a cell and, along with sodium outside the cell, creates a phenomenon known as membrane potential, which allows an electrical current to pass from one cell to the next (Cheeke 2005). In doing so, it contracts muscle fibers, including those of the heart, and transmits nerve signals.

Information on potassium deficiency can be found in the section on potassium in *Specific Uses of the Substance*.

Sodium and chlorine

A certain amount of sodium chloride (salt) is required to facilitate important body functions. Basic sodium ions and acidic chloride ions are responsible for the acid-base equilibrium in the body. Sodium is the chief cation regulating blood pH, and muscle contractions rely on proper sodium concentrations. Sodium plays major roles in nerve impulse transmission and maintaining the heartbeat. In addition, sodium is required for the efficient absorption of amino acids and monosaccharides from the small intestine (Salt Institute, "Salt and trace minerals"). About half of the sodium in the body is in the soft tissues, with the other half present in the bones (Salt Institute, "Salt and trace minerals").

Sulfur

In ruminant animals, sulfur is essential for growth and production of wool and milk (Tisdale 1977). Sulfur can be found in many animal feed sources, including water. Sulfur supplements may keep animals healthy when no natural source can be found. Sheep and goats typically need more dietary sulfur than cattle because of the large amounts of sulfur needed to grow hair and wool. As a result, sulfur needs may increase during a wool-growing season. Increased sulfur intakes have also been shown to increase lamb survival rates and weight gain. In dairy cattle, sulfur supplementation improves the production of milk solids, milk fat, milk protein and milk casein. This results in improved cheese production (Tisdale 1977).

The conventional beef cattle industry commonly feeds distillers grains, which contain sulfur (Richter et al. 2012). However, the sulfur content of distillers grains can be very high and highly variable. Too much sulfur in the diet may harm ruminant performance and health. High dietary sulfur content can reduce animal performance, cause polioencephalomalacia (PEM) and can sometimes result in death (Richter et al. 2012).

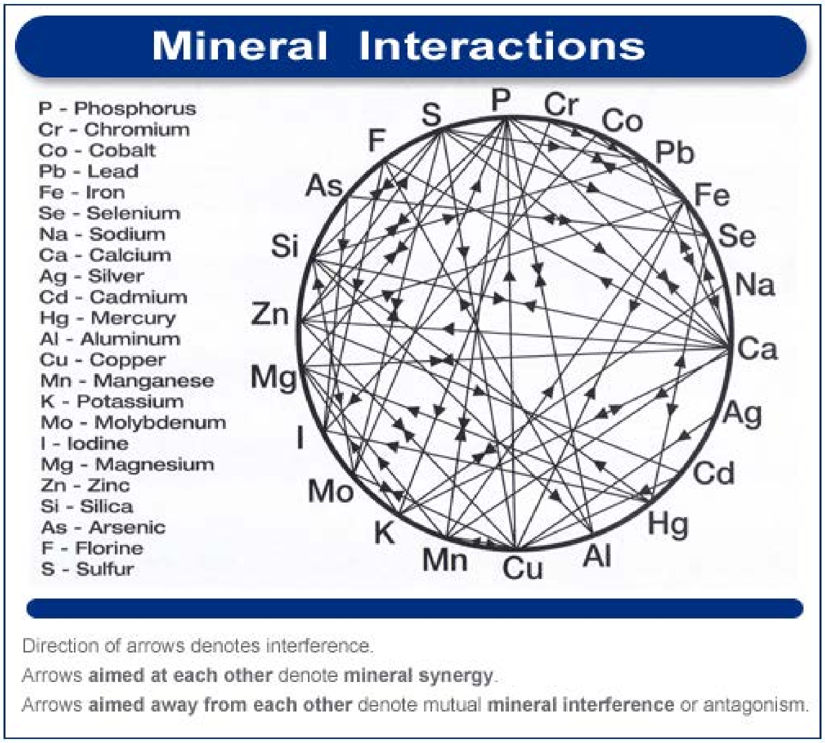
The use of urea as a nonprotein nitrogen supplement in conventional ruminant diets increased the need for sulfur supplementation. This is because the urea replaced the protein-rich feeds that were the usual source of sulfur. In addition, corn silage is often too low in sulfur (Bouchard and Conrad 1973). The others reported that a variety of sulfur sources have been shown to be effective, but sulfate sulfur is often used.

The metabolism of sulfur and nitrogen are closely related in ruminants (Kandylis 1984). These in turn are affected by the makeup of the microflora in the rumen. Sulfur adequate plants generally contain more sulfur amino acids than sulfur deficient plants. Due to seasonal changes and the use of different pasture species, sulfur intake of ruminants may drop to a level which causes a deficiency of sulfur for rumen microflora. Rumen microflora can reduce oxidized sulfur to form which can be incorporated into organic compounds. This allows ruminants the ability to obtain their sulfur supply through inorganic sources of sulfur (Kandylis 1984).

<u>**Combinations of the Substance**</u>

As illustrated in Figure 3 below, care must be taken to avoid unwanted mineral interactions in animal feeds (Coomer 2014). Specific minerals must be added in the correct amounts. For example, molybdenum reduces copper uptake and increases copper excretion. Low dietary zinc and iron and high calcium accentuates copper toxicity since iron and zinc compete with copper for binding sites during absorption. High manganese amounts increase iodine excretion and reduce iron absorption. Iron and cobalt slightly reduce manganese availability. High iron induces cobalt, copper, manganese, selenium, and zinc deficiency. Copper and iron are slightly antagonistic to zinc (Costigan 2003).

Figure 3. Mineral Interactions



Direction of arrows denotes interference.

Arrows **aimed at each other** denote **mineral synergy**.

Arrows **aimed away from each other** denote mutual **mineral interference** or antagonism.

Source: Coomer 2014

When producing a complete trace mineral product, other ingredients may be used as carriers to help minimize any interactions between the active ingredients (Avitech Animal Health 2007). A carrier neutralizes the electrostatic charges present in certain ingredients, is chemically inert, imparts good flowability, and sequesters water from other raw materials to reduce water activity and improve the stability of the premix. Carriers also provide density and particle shape and size compatible with the micro-ingredients used to prevent any material separation in the final premix product. Typical carriers used are either agricultural—wheat middlings, rice hulls, ground corn cobs, soybean meal, or lactose—or nonagricultural—calcium carbonate, dicalcium phosphate, monocalcium phosphate, zeolite, or fine dried salt. Agricultural carriers typically absorb moisture, whereas nonagricultural carriers increase premix density.

Commercial trace mineral premixes advertised online use a variety of different carriers. For example, one company includes "roughage products" and mineral oil (Catalyst poultry trace mineral premix). Their dairy mineral mix includes dehydrated alfalfa meal and mineral oil as well as natural and artificial flavors. Their beef, dairy, and cattle breeder mineral mixes include corn distillers' grains with solubles, cane molasses, and mineral oil as well as natural and artificial flavor. Another premix distributor offers an equine mineral premix including processed grain byproducts, dry molasses, mineral oil, and apple flavor.

Though most premixes sold online do not disclose product contents on labels, it is presumed that carriers are similar across brands. The USDA organic regulations at 7 CFR 205.237(a) require that "all agricultural ingredients included in the ingredients list, for such additives and supplements, shall have been produced and handled organically." Additionally, NOP Guidance 5030 (USDA 2013b) outlines review criteria for minor ingredients and carriers in livestock feed additives and supplements.

Status

Historic Use:

Industrial-scale production of animal feeds began in the late 19th century. Prior to the 19th century, only abstract ideas existed on the nature, origin, and function of the mineral constituents of plant and animal tissue (Underwood and Suttle 1999). During this time, traditional sources of animal feed included household food scraps and byproducts of the food processing industries. Through the second quarter of the 20th century, the understanding of the nutritional significance of minerals increased, which allowed producers to provide a balanced feed and move animals indoors, leading to the development of industrial animal agriculture.

Most of the advances in knowledge of essential minerals came from studying incidences of poor animal health or production due to mineral deficiencies, toxicities, or imbalances. For example, selenium was initially considered to be only of scientific interest, but it was later observed that selenium deficiency results in liver necrosis in rats and that selenium-responsive diseases were observed in farm animals in several countries (Underwood and Suttle 1999). In the final quarter of the 20th century, scientists applied molecular biology to studies of mineral metabolism and function (O'Dell and Sunde 1997).

Initially, various national authorities used different criteria to determine nutritional requirements, causing considerable confusion (Underwood and Suttle 1999). An attempt was made in 1983 to achieve an international consensus on mineral and other nutrient requirements for poultry (Blair et al. 1983). Since then, similar attempts have been made with other species. Some authorities now include a margin of safety in their requirements, while others simply estimate a minimum requirement. Safe allowances are essential for feed mills, but knowledge of the relevant variables is typically insufficient for precisely calculating a safety margin (Underwood and Suttle 1999).

Forages do not satisfy the mineral requirements of grazing cattle (McDowell 1992). Mineral deficiencies and imbalances in grazing ruminants have been reported in almost all regions of the world (McDowell 1996), with the minerals most likely to be lacking including calcium, phosphorus, sodium, cobalt, copper, iodine, selenium, and zinc. Under specific conditions, magnesium, potassium, iron, and manganese may also be deficient, or there may be an excess of molybdenum and selenium.

Historically, the North American animal feed industry has used the inorganic sources of minerals previously discussed. More recently, organic forms have become available. This would include the various chelates and complex forms. One of the limiting factors to the use of chelated minerals has been high cost (USDA 2002). At the time of the review, chelated minerals cost 10 to 15 times more per milligram of mineral supplied, compared to inorganic sources.

Organic Foods Production Act, USDA Final Rule:

Section 2111(c)(1)(C)(3) of the Organic Food Production Act of 1990 (OFPA) states that producers "shall not use …. Synthetic trace elements used to stimulate growth or production of such livestock." Specific trace minerals are not identified.

According to USDA organic regulation 7 CFR Part §205.237(a),

> "the producer of an organic livestock operation must provide livestock with a total feed ration composed of agricultural products, including pasture and forage, that are organically produced and handled by operations certified to the NOP, except as provided in 7 CFR §205.236(a)(2)(i), except that, synthetic substances under 7 CFR §205.603 may be used as feed additives and feed supplements, *provided* that all agricultural ingredients included in the ingredients list, for such additives and supplements, shall have been produced and handled organically."

7 CFR §205.603(d)(2) states that, as feed additives, trace minerals can be used for enrichment or fortification when FDA-approved. NOP Guidance 5030 clarifies that in organic production, the protein used to produce metal proteinates must not come from slaughter-derived byproducts (USDA, 2013b).

International

Canadian General Standards Board (CGSB) Permitted Substance List

CAN/CGSB-32.310, §6.44(c) specifically restricts feeding supplements or additives beyond those required for adequate nutrition and health maintenance for the species at each specific stage of life.

CAN/CGSB-32.311, Table 5.3 includes "Minerals, trace minerals, elements" as substances permitted for use in organic livestock production in Canada and allows for "non-synthetic chelated or sulphated minerals" including oyster shell, calcium chloride, and magnesium oxide. Synthetic nutrient minerals may be used if non-synthetic sources are not commercially available. This annotation does not list all the specific minerals allowed; a note in CAN/CGSB-3211*2018, 5.1.2 references Feeds Regulations 1983 as the regulatory document to use when assessing mineral supplements to be used in livestock feed. It is important to note that chromium and molybdenum are not included in this regulation.

Feeds Regulations 1983 also defines a range of nutrient guarantees for complete feeds for use in the exemption of feeds from registration.

CODEX Alimentarius Commission, Guidelines for the Production, Processing, Labelling and Marketing of Organically Produced Foods (GL 32-1999)

The CODEX recommends that "feedstuffs of mineral origin, trace elements, vitamins, or provitamins can only be used if they are of natural origin. In case of shortage of these substances, or in exceptional circumstances, chemically well-defined analogic substances may be used."

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

Trace minerals, referred to as "trace elements," are permitted as per article 14 which states that "Livestock should be fed on grass, fodder, and feedingstuffs produced in accordance with the rules of organic farms …In addition, in order to provide for basic nutritional requirements of livestock, certain minerals, trace elements, and vitamins may need to be used under well-defined conditions."

Annex VI lists all trace elements approved for inclusion in animal feeds, with the disclaimer that the additives must have been approved under Regulations (EC) No 1831/2003. Chromium is not included in this list.

Japan Agricultural Standard (JAS) for Organic Production

The Japan Agricultural Standards (JAS) for Organic Production defines feed additives as "Those specified by Article 2.3 of the Law Concerning Safety and Quality of Feeds (Law No. 35 1953)." JAS allows for "feed additives" as ingredients in livestock feed "which are natural substances, or those derived from natural substances without chemical treat. In case of a difficulty to obtain those feed additives, the use of similar agents to describe food additives are permitted only for supplementing nutrition and effective compounds in feeds."

Japanese standards for organic feed also allow the following macro-nutrients – "Limestone, shellfish fossils, shells, dolomite, phosphate rock, and diatomaceous earth (all referred to as 'limestones') and those derived from limestones without chemical treatments. This does not include any chemically synthesized substances from calcium carbonate, magnesium carbonate, dicalcium carbonate, tricalcium carbonate, magnesium carbonate, dicalcium phosphate, tricalcium phosphate, and silicic acid."

IFOAM – Organics International
The IFOAM standards indicate that "organic animal management provides animals with vitamins, trace elements and supplements only from natural sources unless they are not available in sufficient quantity and/ or quality."

IFOAM standards also state that "Synthetic vitamins, mineral and supplements may be used when natural sources are not available in sufficient quantity and quality.

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?

Yes, the substances all contain minerals, and some contain copper or sulfur compounds.

(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?

As petitioned, the substance is not a synthetic inert ingredient and its compliance is not limited to EPA assignment as a substance of toxicological concern. With that said, some trace minerals are assigned 2004 EPA List 4 status and when used as an inert with an active pesticide, could be allowed by other paragraphs in the National Organic Program standard.

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)).

Descriptions of the common processes used to manufacture materials included in Table 1 above are included below.

This level of detail is not provided for the class of substances called metal amino acid chelates since the processes used to manufacture those materials are largely the same. Metal amino acid chelates are the products resulting from the reaction of a metal ion form a soluble metal salt with amino acids (AAFCO 2019). A chelate is defined as a compound having a ring structure that usually contains a metal ion held by coordinate bonds as shown in the image below. The organic molecule holds the mineral like a claw. As such, it acts as a fence to protect the mineral from adverse interactions with other substances. The chelated minerals are transported across the intestinal wall.

Source: Novotech Nutraceuticals

As described in the Proteinated and Chelated Mineral Complexes TAP review (USDA 2002), chelation refers to a bond forming between a mineral ion and a ligand carrier (protein or amino acid and chelating agent). Chelates are generated by reacting a mineral salt with enzymatically prepared mixture of amino acids and peptides. The reaction is carried out under controlled conditions. The procedures involved in the manufacture of chelated minerals is company-specific and proprietary.

Metal amino acid complexes are the products resulting from complexing a soluble salt with one or more amino used as a commercial feed ingredient where the specific metal and amino acid(s) must be declared. A metal proteinate is the product from the chelation of a soluble salt with amino acids and/or partially hydrolyzed protein. A metal methionine hydroxy analogue chelate is the product resulting from the reaction of a metal salt with 2-hydroxy-4-methyllthiobutanoic acid. Similarly, a metal propionate is the product resulting from the reaction of a metal salt with propionic acid.

Chromium

Although chromium is found combined with various other minerals, chromite is the mined source used for commercial production (IARC 1990). Ferrochrome (an alloy of iron and chromium) is produced by mixing chromite with a reductant such as coke, coal, charcoal or quartz in a high temperature submerged arc furnace or direct current arc furnace.

To produce pure chromium, the iron must be separated from the chromium present in the mined ore. In the United States, there are two processes that can be used (IARC 1990). The most commonly used process is the electrolyte method, which involves a chromium-containing electrolyte prepared by dissolving a high-carbon ferrochromium in a solution of sulfuric acid and chromium potassium sulfate. This solution is then subjected to electrolysis (i.e., passing an electric current through the electrolyte solution). The other method is an aluminothermic reduction (i.e., an exothermic chemical reaction using aluminum as the reducing agent at high temperature). In this method, chromic oxide is reduced with finely divided aluminum (IARC 1990).

Chromium propionate is produced by the reaction of chromium salt with propionic acid (21 CFR §573.304). Chromium picolinate is the product resulting from the reaction of chromium chloride with picolinate. Chromium yeast is produced by feeding live yeast cells on chromium chloride (EFSA 2009e). In doing so, the chromium is incorporated and integrated into the cell walls of the yeast, making it part of the proteins. The yeast is then killed.

Cobalt

Cobalt is primarily produced as a byproduct of the mining and processing of copper and nickel ores and to a lesser extent of silver, zinc, iron, lead, and gold ores. The three main processes for leaching cobalt from these ores, or ore concentrations (e.g., oxide or sulfide ore concentrate), are acid sulfate leaching, acid chloride leaching, and ammoniacal solution leaching.

Cobalt acetate ($Co(CH_3CO_2)_2$) is manufactured by combining cobalt carbonate ($CoCO_3$) with acetic acid (CH_3COOH) with subsequent crystallization. It can also be produced commercially from cobaltous hydroxide or carbonate and an excess of dilute acetic acid (Toxicology Data Network 2019).

Cobalt carbonate ($CoCO_3$) is produced by heating solutions of cobaltous sulfate ($CoSO_4$) and sodium carbonate (Na2CO_3) (Toxicology Data Network 2019). Cobalt chloride is produced by dissolution of cobalt raw materials such as cobalt metal, cobalt oxide, or cobalt hydroxide in hydrochloric acid. The cobalt chloride produced can then be precipitated with ammonium bicarbonate to form cobalt gluconate (EFSA 2012d). Cobalt glucoheptonate is a combination of a cobalt salt with glucoheptonic acid, a carbohydrate acid that is heptonic acid with hydroxyl groups (OH) at six of the seven carbons (C). Cobalt oxide is usually prepared by heating the cobaltic hydroxide that is precipitated from cobalt-containing solutions by sodium hypochlorides. Cobalt sulfate is formed by the action of sulfuric acid on cobaltous oxide (Toxicology Data Network 2019).

Copper

Copper is a metal that occurs naturally in rocks, soil, water, and air. Pure copper metal is generally produced from a multi-stage process that begins with mining and concentrating low-grade ores containing copper sulfide minerals, followed by smelting and electrolyte refining to produce a pure copper cathode.

Copper acetate is produced by the action of acetic acid on copper oxide (CuO) or copper carbonate (CuCO3). Copper carbonate is produced by adding sodium carbonate to copper sulfate solution, filtering and drying. Copper chloride is produced by the reaction of metallic copper with chlorine at 752–932°F (400–500°C). Tribasic copper chloride is produced by the reaction of cuprous oxide with copper with air oxidation. It can also be produced by mixing copper oxide ores with sodium chloride (Toxicology Data Network 2019). Copper citrate can be made by reacting copper oxide or hydroxide with citric acid. Copper gluconate is produced by the reaction of gluconic acid solutions with basic copper (II) carbonates or copper (II) hydroxide. Copper hydroxide is produced by the reaction of copper salt solution and sodium hydroxide (Toxicology Data Network 2019).

Cuprous iodide can be produced by the interaction of solutions of potassium iodide with copper sulfate. Copper (II) salt solutions can also be reacted with alkali iodides to precipitate copper (I) iodide. Additionally, cuprous iodide can be manufactured pyrometallurgically (any process that uses high temperatures to transform either metals or their ores) by the reaction of hot copper with iodine vapor (Toxicology Data Network 2019).

Copper orthophosphate can be produced by the reaction of copper (II) sulfate with soluble alkali phosphates. For example, reacting copper sulfate and diammonium hydrogen phosphate (PubChem).

Copper oxide can be produced by several methods. One involves ignition of copper carbonate or copper nitrate. It can also be produced by oxidation of copper turnings at 1472°F (800°C) in air or oxygen. Copper (II) hydroxide can be converted to copper oxide by heating. Copper oxide can be produced pyrometallurgically by heating copper metal at 1472°F in air. Molten copper is oxidized to copper oxide when sprayed into an oxygen containing gas (Toxicology Data Network 2019).

Copper pyrophosphate is produced by the action of dilute sulfuric acid on copper or copper oxide (often as oxide ores) in large quantities, followed by evaporation and crystallization (PubChem 2019). Copper sulfate pentahydrate can be prepared by the reaction of basic copper (II) compound with sulfuric acid solution. According to 21 CFR §184.1261, copper sulfate is prepared by the reaction of sulfuric acid with cupric oxide or with copper metal.

Iodine

Iodine is found naturally in the ocean; some sea fish and water plants will store it in their tissues (EFSA 2005). Tons of iodine escape from oceans every year as iodide in sea spray. Iodine is also removed from the ocean as iodide, hydrochloric acid, and methyl iodide produced by marine organisms. Much of it is deposited on land where it may become part of the biocycle (EFSA 2005). Iodine is also found naturally in air, water, and soil.

According to 21 CFR 184.1206, calcium iodate ($Ca(IO_3)_2 \bullet H_2O$) does not occur naturally, but can be prepared by passing chlorine through a hot solution of lime ($CaCO_3$) in which iodine has been dissolved.

According to 21 CFR §184.1635, potassium iodate does not occur naturally, but can be prepared by reacting iodine with potassium hydroxide.

The Toxicology Data Network references a manufacturing procedure for calcium iodobehenate included in an old version of the Merck Index, but the most recent Index (O'Neil 2013) does not include the compound. No other reference could be found to explain the method of manufacture for calcium iodobehenate. Iodobehenate can also not be found in the manual.

Cuprous iodide can be produced by the interaction of solutions of potassium iodide with copper sulfate. Copper (II) salt solutions can also be reacted with alkali iodides to precipitate copper (I) iodide. Additionally, cuprous iodide can be manufactured pyrometallurgically (any process that uses high temperatures to transform either metals or their ores) by the reaction of hot copper with iodine vapor (Toxicology Data Network 2019).

Diiodosalicylic acid can by synthesized through many different routes. According to MOLBase—an integrated platform for chemical e-commerce—there are 15 different routes for manufacturing diiodosalcylic acid (2019). For example, combining ethanol, iodine and salicylic acid results in the production of 5-iodosalicylic acid, 2-hydroxy3-iodobenzoic acid and 3,5-diiodosalicylic acid. In addition, ethanol plus 2-hydroxy-iodobenzoic acid and iodine results in the production of 3,5-diiodosalicylic acid. There are 13 similar routes.

Ethylenediamine is manufactured from ethylene dichloride and ammonia (O'Neil 2013). The form used for animals is the dihydrochloride form. The Merck Index does not indicate how it is produced, but it is presumably from a combination of ethylene dihydrochloride and ammonia.

There are 28 possible synthesis routes for potassium iodide (MOLBase 2019). For example, potassium iodate can be broken down to iodine and potassium iodide. Similarly, dipotassium oxalate can be mixed with iodoethane to produce potassium iodide. There are 26 more synthesis routes. MOLBase also indicates that there are 28 possible routes to produce sodium iodide (2019).

Thymol is a natural derivate of cymene, which is isomeric of carvacrol found in the oil of thyme. Thymol iodide is made by treating a solution of thymol in a solution of sodium hydroxide with iodine-potassium iodide solution (Toxicology Data Network 2019).

Iron

Industrial iron production starts with iron ores (which typically have the formula Fe_2O_3), also known as hematite. The ore is reduced to the metal in a treatment with carbon, which typically occurs in a blast furnace at temperatures of about 3632°F (2000°C). Carbon is provided in the form of coke, a solid carbonaceous residue derived from the destructive distillation of coal.

The term "ferric" refers to the iron in an oxidation state of +3 and is denoted as iron (III). The term "ferrous," on the other hand, refers to iron in the oxidation state of +2 and is denoted as iron (II). Iron (III) is usually the more stable form of iron.

Ferric ammonium citrate is prepared by the addition of ferric hydroxide ((Fe(OH)3) to an aqueous solution of citric acid and ammonia (PubChem 2019). Ferric chloride can be produced industrially by reaction of dry chlorine with scrap iron at 932–1292°F (500–700°C) (Toxicology Data Network 2019 and The Chemical Company 2019). Ferric formate is the iron salt of formic acid (AAFCO 2019) and can be prepared through precipitating a mixture of iron (II) chloride, ammonium chloride, urea, nitric acid, formic acid, and water (Goode and Kenner 1965).

Ferric phosphate is produced by adding a solution of sodium phosphate to a solution of ferric chloride. The product is then filtered and dried (PubChem 2019). The technical report on ferric phosphate for use in crop production (as a slug control) indicates that ferric phosphate occurs naturally in the soil, but to obtain the concentrations needed for use as a molluscide it must be synthetically produced. To produce ferric phosphate, an aqueous iron sulfate solution is mixed with an aqueous disodium phosphate solution in a stainless steel boiler. The mixture is heated to 122–158°F (50-70°C), where ferric phosphate will then precipitate out. The precipitated ferric phosphate is filtered from the solution, washed with distilled water, and dried with hot air (USDA 2010).

The Merck Index references a 1932 source for the manufacturing procedure for ferric pyrophosphate (O'Neil 2013), which appears to be no longer available. All other information sources reference the same article.

Ferric sodium pyrophosphate is made from disodium ethylenediaminetetraacetic acid and ferric nitrate (O'Neil 2013). Ethylenediamine is produced from dichloride and ammonia. There is no indication how the disodium ethylenediaminetetraacetic acid is made.

Ferric sulfate can be produced by treating ferrous sulfate with boiling concentrated sulfuric acid or by evaporating a mixture of ferrous oxide and sulfuric acid. It can also be produced by adding sulfuric acid to ferric hydroxide (PubChem 2019). On a large scale, it is produced by treating sulfuric acid with a hot solution of ferrous sulfate and an oxidizing agent such as chlorine, nitric acid, or hydrogen peroxide.

Ferrous carbonate occurs naturally as the mineral siderite in open pit mines (Costigan 2003). According to 21 CFR §184.1307b, ferrous carbonate is an odorless, white solid that can also be prepared by treating solutions of iron (II) salts with alkali carbonate salts.

Ferrous chloride is produced by the action of hydrochloric acid on an excess of iron, with subsequent crystallization (PubChem 2019). According to the Merck Index (O'Neil 2013), ferrous fumarate is produced according to U.S. Patent 2848366, where anhydrous ferrous fumarate is prepared by slowly mixing hot solutions of sodium fumarate and ferrous sulfate. The resulting ferrous fumarate precipitates out (Erisch and Lemp 1958).

Ferrous gluconate can be prepared from barium gluconate and iron sulfate. It can also be prepared by heating ferrous carbonate with the proper quantity of gluconic acid in aqueous solution. Ferrous lactate is produced by the interaction of calcium lactate with ferrous sulfate or by direct action of lactic acid on iron fillings. Ferrous oxide is produced from ores and minerals by washing, drying, grinding, blending, and calcining. It can also be prepared by heating oxalate, but the resulting product will contain some ferric oxide as well (PubChem).

The Merck Index (O'Neil 2013) indicates that the preparation of ferrous phosphate first involves the preparation of the octahydrate form, but does not provide details of the procedure. It does state that ferrous phosphate, octahydrate is a grayish-blue powder or monoclinic crystals. It is practically insoluble in water but is soluble in mineral salts. It must be protected from light. Due to unavoidable oxidation, most of the commercial ferrous phosphate also contains ferric phosphate.

According to 21 CFR §184.1315, ferrous sulfate heptahydrate, the form typically used as an animal supplement, is prepared by the action of sulfuric acid on iron. It occurs as pale, bluish-green crystals or granules. When heated, it produces ferrous sulfate monohydrate with varying amounts of ferrous sulfate tetrahydrate. Dried ferrous sulfate occurs as a grayish-white to buff-colored powder.

According to 21 CFR §573.580, iron choline citrate complex is made by reacting approximately equimolar quantities of ferric hydroxide, choline, and citric acid.

Manganese

Manganese is often found in minerals in combination with iron. To produce ferromanganese, the manganese ore is mixed with iron ore and carbon and then reduced in either a blast furnace or in an electric arc furnace. Pure manganese is produced by leaching the manganese ore with sulfuric acid and a subsequent electrowinning process—passing a current from an inert anode through a liquid leach-solution containing the metal so that the metal is extracted as it is deposited in an electroplating process onto the cathode.

Manganese acetate is produced by the action of acetic acid on manganese hydroxide, tetrahydrate (Toxicology Data Network 2019).

Manganese carbonate is produced as a precipitate from the addition of sodium carbonate to a solution of manganese salt or by hydrometallurgical treatment of manganiferous iron ore. It is produced commercially from manganese sulfate by precipitation with alkali-metal carbonates or hydrogen carbonates. If the presence of alkali-metal ions in the final product are not desired, ammonium hydrogen carbonate can be used as the precipitating agent. The precipitated manganese carbonate is then filtered, washed and dried at 230–248°F (110–120°C). Manganese carbonate can also be extracted from mines where it occurs in quartz granite as in the mines of Butte, Montana. Processing of the mined extract requires washing to remove the clay followed by crushing the low-grade ores and beneficiation with sulfuric acid and sulfur dioxide leach, or by nitric oxide or nitric oxide leach (Toxicology Data Network 2019).

Manganese chloride is produced when manganese metal or ferromanganese is chlorinated at 1292–1832°F (700–1000°C). Manganese chloride can also be produced industrially by the reaction of aqueous hydrochloric acid with manganese (IV) oxide ore, manganese (II) oxide or manganese carbonate (Toxicology Data Network 2019). According to EFSA (2016b), manganous chloride tetrahydrate is produced by reacting elemental manganese with hydrochloric acid (37 percent). The solution is concentrated by evaporation and the resulting manganese chloride crystals are isolated, dried and packaged.

Manganese citrate is produced by the action of citric acid on manganese hydroxide (Toxicology Data Network 2019). Manganese gluconate is typically produced by reacting manganese carbonate with gluconic acid in aqueous medium and then crystallizing the product to form a slightly pink powder (DrugBank). A 1997 patent from China suggested that manganese gluconate could be produced by fermenting *Aspergillus niger* strain IFFI2230 with glucose.

The Merck Index does not list the compound manganese glycerophosphate (O'Neil 2013) and no other source for the manufacturing procedure could be found. The Merck Index also does not list the compound manganese hypophosphate but does list manganese hypophosphite (CAS 10043-84-2), $H_4MnO_4P_2$. It does not describe the manufacturing procedure, and no other source for the information could be found. Manganese phosphate is also not listed in the Merck Index, and no other reference for its manufacturing procedure could be found.

Manganese oxide is produced by the reduction of dioxide in hydrogen or by heating the carbonate with the exclusion of air (Toxicology Data Network 2019).

According to 21 CFR §184.1461, manganese sulfate is produced by reacting manganese compounds with sulfuric acid. It is also obtained as a byproduct in the manufacture of hydroquinone. A second method for producing manganese sulfate monohydrate was described in EFSA (2016b) and first involved the production of manganous oxide from manganese dioxide by calcination. Sulfuric acid is added to produce manganous sulfate. The content of iron and cadmium is reduced by chemical and physical processes. The resulting manganous sulfate solution is heated, and the dried product is packed and labelled.

Molybdenum

Molybdenum does not occur naturally as a free metal on earth. The main commercial source is molybdenite (MoS_2). In molybdenite processing, the ore is first roasted in air at 1292°F (700°C). The oxidized ore is then usually extracted with aqueous ammonia to give ammonium molybdate. Copper can be an impurity in molybdenite which is less soluble in ammonia than molybdenum. To remove the copper, the solution is precipitated in hydrogen sulfide. Ammonia molybdate converts to ammonium dimolybdate which is then isolated as a solid. Heating this solid gives molybdenum trioxide. The crude trioxide is then further purified by sublimation at 2012°F (1100°C). Metallic molybdenum is then produced by reduction of the oxide with hydrogen.

Sodium molybdate is produced as a dihydrate by evaporating an aqueous solution of molybdenum trioxide and sodium hydroxide. Heating the dihydrate at 212°F (100°C) converts it to the anhydrous salt (The Chemical Book 2019).

Selenium

Selenium is found in metal sulfide ores such as copper, nickel, or lead, where it partially replaces sulfur. Commercial selenium is produced as a byproduct of refining these ores, most commonly copper.

According to the Merck Index (O'Neil 2013), sodium selenate is the naturally occurring from of selenium found in alkaline soils and water.

Sodium selenite is produced by evaporating an aqueous solution of selenious acid with sodium hydroxide at 60-100°C. It is also produced by heating a mixture of sodium chloride and selenium oxide or by neutralizing selenious acid with sodium carbonate and crystallizing (Toxicology Data Network 2019).

Selenium-enriched yeast are produced by fermenting *Saccharomyces cerevisiae* in a selenium-rich media (Toxicology Data Network 2019). Almost all of the selenium structurally substitutes for the sulfur in the amino acid methionine to form selenomethionine, which is structurally similar to methionine and is taken up nonspecifically to become part of yeast protein. The selenomethionine is isolated from the yeast product by hydrolysis of the yeast protein.

Zinc

Zinc is normally found in association with base metals such as copper and lead in ores. Other sources of zinc include smithsonite (zinc carbonate) and wurtzite (zinc sulfide). Sphalerite (ZnS) is a form of zinc sulfite that is heavily mined, as its concentration of zinc is 60–62 percent.

Zinc acetate is produced by the action of acetic acid on zinc oxide. It can also be an anhydrous salt from zinc nitrate and acetic anhydride (Toxicology Data Network 2019). Zinc carbonate is produced by grinding the mineral smithsoite or by the action of sodium bicarbonate on a solution of zinc salt (Toxicology Data Network 2019).

The Merck Index (O'Neil 2013) does not include zinc chloride diammine complex. It does include zinc chloride but does not indicate a manufacturing procedures. Diammine is a complex with two ammonia ligands. Metals such as zinc and copper form extremely stable ammoniacal complexes producing a buffering system during leaching. This keeps the pH very close to neutrality (Limpo and Luis 1993).

$$Zn(NH_3)_2^{2+}\_ + 2\ Cl^- \leftrightarrow Zn(NH_3)_2Cl_2$$

Zinc gluconate is not listed in the Merck Index (O'Neil, 2013) and no other source could be found with regards to its manufacture.

Although zinc oxide occurs naturally as the mineral zincite, most zinc oxide is produced synthetically. Zincite usually contains manganese and other impurities that give it a yellow to red color.

The French method for synthesizing zinc oxide involves melting metallic zinc in a graphite crucible at a temperature of about 1832°F/1000°C. The zinc vaporizes and reacts with the air to form zinc oxide. Zinc oxide particles are transported into a cooling duct and collected. The American method is similar but starts with zinc ores or smelter byproducts. With the lower purity of the source material, the final product is of lower quality (Toxicology Data Network 2019).

According to the Toxicology Data Network, there are three methods to produce zinc stearate. The first generates waste water and includes a double decomposition method. The other methods include direct transformation method and the fusion process. The insoluble metallic stearates can be produced by reacting a selected grade of stearic acid with a caustic solution (usually sodium hydroxide) in an aqueous system. This produces a solution containing the soluble sodium salt of stearic acid. The insoluble metallic stearate precipitates out when a solution containing the desired metal is added to the sodium stearate solution. The insoluble stearate is then washed free of the water-soluble impurities, dried, milled, and packaged. Additionally, an aqueous solution of zinc sulfate can be added to sodium stearate to precipitate zinc stearate. The zinc stearate is then washed with water and dried. Zinc stearate can also be produced from stearic acid and zinc chloride (Toxicology Data Network 2019).

Zinc sulfate production involves mixing a zinc-containing material (e.g., metal, minerals, ores) with sulfuric acid (Toxicology Data Network 2019). In addition, zinc oxide reacts with sulfuric acid to produce zinc sulfate.

<u>Evaluation Question #3:</u> 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)).

Commercial forms of many of the trace mineral compounds added to animal feeds are typically produced via chemical synthesis and are described in detail in *Evaluation Question #2*.

<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)).

When used as petitioned, trace minerals from unconsumed feed have the potential to be transferred to ground or surface waters. While trace minerals are essential dietary components for animal feeds, some are considered heavy metals with strong toxic potential (Goldhaber 2003). When included in animal feeds above required amounts, trace elements accumulate in urine and feces (Brugger and Windisch 2015). The environmental risks include impairment of plant production, accumulation in edible animal products, and contamination of the water supply. In addition, there is a correlation between increased trace mineral loads and antimicrobial resistance; as a result, trace minerals have upper limits for inclusion (Brugger and Windisch 2015).

Not all the trace minerals supplemented to feed in inorganic forms are 100 percent available. As a result, excesses are excreted in the urine and feces. While organic forms of trace minerals have been on the market for more than 30 years, it is only in the past few years that their use has become popular. This is mainly due to the environmental concerns about accumulation of minerals from inorganic sources, as well as the possible contamination of inorganic salts with heavy metals such as cadmium (Leeson 2015).

<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)).

The European Food Safety Authority (EFSA) published several reports related to the safety of metal amino acid chelates and complexes. In early studies they were not able to assess the safety of calcium amino acid chelate, copper amino acid chelates, magnesium amino acid chelate, manganese amino acid chelate, and zinc amino acid chelated as food supplements because of insufficient information in the supporting dossiers provided to them (EFSA 2009f). Similarly, they were not able to assess the safety of potassium amino acid chelate and iron amino acid chelate supplements (EFSA 2009g).

In later reports, however, sufficient information was provided to allow them to assess the safety of several metal complexes and chelates:

- **Copper**: EFSA (2013d) also concluded that cupric chelate of amino acids hydrate is safe for all animal species up to the maximum permitted level of total copper content in a complete feed. ESA (2015c) concluded that the use of cupric_chelate of amino acids, hydrate and cupric chelate of glycine, hydrate, were safe for use in feed for all animal species when used up to the maximum permitted levels for total copper.

- **Iron**: EFSA (2013e) concluded that iron chelate of amino acids, hydrate is considered safe for all animal species when used up to the maximum permitted content of total iron in a complete feed. EFSA (2016a) concluded that ferrous chelate of amino acids, hydrate and ferrous chelate of glycine, hydrate were safe for inclusion in animal feeds up to the maximum allowed levels of total iron in the complete feed.
- **Manganese**: EFSA (2013f) concluded that manganese chelates of amino acids, hydrate is considered safe for all animal species when used up to the maximum permitted content of total manganese in a complete feed. EFSA (2016b) concluded that manganese chelate of amino acids, hydrate and manganese chelate of glycine, hydrate could be safely added to animal feeds up to the maximum total manganese levels allowed in complete feeds.
- **Zinc**: EFSA (2012c) found that zinc from zinc chelate of amino acids hydrate would not exert additional or different adverse effects when added to feed than those from approved inorganic sources. EFSA (2013c) evaluated methionine-zinc as a source of methionine for ruminants and as a zinc source for all species. The concluded that the additive is safe for all animal species since its use in supplementing feed is first limited by the regulatory maximum content of zinc. EFSA (2015b) concluded that the use of zinc chelate of amino acids, hydrate and zinc chelate of glycine, hydrate in animal feed was safe when used at maximum permitted levels of total zinc in the complete feed.

Chromium

Chromium is released into the environment by natural resources, mainly through dust from rocks and volcanic activity (Goldhaber 2003). Chromium occurs in different forms, including trivalent and hexavalent forms. Trivalent chromium is ubiquitous in nature, occurring in the air, water, soil, and in biological materials. Algae appear to be the most sensitive organism to short-term chromium exposure. The toxicity of trivalent chromium appears to be quite low compared to the hexavalent forms (Goldhaber 2003). The U.S. Environmental Protection Agency (EPA) classifies materials as hazardous waste if they contain leachable chromium (40 CFR §261.5) unless it can be shown that the leachable chromium is not in the hexavalent form (40 CFR §261.94).

Hexavalent chromium is believed to be synthetic and does not occur naturally in the environment (Goldhaber 2003). Hexavalent chromium most commonly occurs in industrial processes and can be present in drinking water resulting from man-made contamination. Environmental exposure to the synthetic form can also occur through metal industries, burning oil and coal, and waste incineration.

Chromium compounds are stable in the trivalent state and occur naturally in ores such as ferrochromite ($FeCr_2O_4$). Trivalent chromium in soil is mostly present as insoluble carbonate and oxide of chromium (III) and thus will not be mobile in soil. The solubility of chromium (III) in soil and its mobility may increase with the formation of soluble complexes with organic matter in soil, with lower soil pH potentially facilitating complexation. Chromium has low mobility for translocation from roots to the above-ground parts of the plants (Goldhaber 2003).

Dietary chromium is poorly absorbed when consumed by animals and is mostly excreted in manure. It is possible that chromium (III) is genotoxic (i.e., damages DNA and causes mutations in cells) in rats and mice; the EFSA recommends avoiding additional exposure to consumers resulting from the use of supplemental chromium in animal nutrition (2009a). The conclusion of the report by Van Paemel et al. (2010), however, was that the use of chromium supplements in animal feeds has not been shown to be a risk to soil or to the aquatic environment. Other publications have reported genotoxic effects from some chromium (III) compounds in vitro, raising questions about the safety of these supplements in animal feeds. Eastmond et al. (2008) reviewed evidence published since 1990 to assess the risks associated with chromium (III) as feed additives and concluded that the nutritional benefits outweigh the theoretical risk of genotoxic effects in vivo at normal or modestly elevated levels.

In aquatic ecosystems, MiningWatch Canada (2012) concluded that chromium bioaccumulates in algae, aquatic plants, invertebrates, and fish, but the uptake, accumulation, and effects of chromium depend on the species organism size, sex and developmental state, presence of other contaminants, water temperature, pH, alkalinity, and salinity. They acknowledge, however, that there is very little information on chromium uptake and effects in freshwater species. Surprisingly, they also reported that chromium III in water can be more toxic to fish than chromium IV. It decreases reproductive success, can cause death at relatively lose doses, and deposits on the gills. It is important to note, however, that most of the studies looking at the effect of chromium on aquatic ecosystems have been conducted in the laboratory and not observed on wild populations in the field. No studies could be identified where contamination resulted from chromite or ferrochrome industries.

Cobalt

Cobalt occurs naturally in seawater and in some surface water and groundwater at low levels (Smith and Carson 1979). Transmission methods of synthetic sources of cobalt into the environment include the disposal of cobalt-containing wastewater and atmospheric deposition from activities such as burning fossil fuels and smelting and refining metals. Cobalt is naturally released into the atmosphere by windblown soil, seawater spray, volcanic eruptions, and forest fires.

A literature review by Van Paemel et al. (2010) concluded that there are no indications that the presence of cobalt in animal feeds has an environmental impact. However, no cobalt sources are approved for use in the European Union in the manufacture of food supplements. In a recent EFSA opinion (2009b), the panel concluded that, given the genotoxicity and carcinogenicity of cobalt (II) hexahydrate, the use of cobalt (II) chloride hexahydrate should be considered a safety concern. However, FEEDAP concluded that the potential for cobalt supplementation to diets for ruminants, horses, and rabbits should be maintained (EFSA 2009c).

Copper

The Scientific Committee for Animal Nutrition (SCAN) did not identify any environmental risks associated with the use of copper in pig and ruminant diets when supplemented at levels authorized under Council Directive 70/524/ECC (SCAN 2003a). This was confirmed by Van Paemel et al. (2010). Very high levels of copper, however, can cause acute toxicity; human deaths have been reported from deliberate ingestion of large quantities of copper sulfate (Goldhaber 2003). The EFSA evaluated the use of cupric acetate, cupric carbonate, cupric chloride, cupric oxide, and cupric sulfate and found that these sources of copper are safe for all animal species when included in diets up to the maximum permitted levels of total copper. They use of the copper compounds in drinking water, however, was considered unsafe for ovines and certain breeds of dogs and cats. For the other animal species, the simultaneous use of the copper compounds in food and water should be avoided (EFSA 2015c).

Iodine

Iodine in animal feeds can enter the environment via direct excretion of feces and urine on pasture or by spreading the waste on land. FEEDAP calculated the maximum increase in soil iodine from manure from the targeted animals and concluded it would be below the background concentration (EFSA 2005). They concluded, therefore, that iodine supplementation of animal feed does not pose an environmental risk. Van Paemel et al. (2010) also concluded that the use of iodine supplementation in animal feeds is not expected to pose an environmental risk.

Toxicity from excess iodine results in goiter, hypothyroidism, or hyperthyroidism in humans (Goldhaber 2003) and is primarily caused by the overconsumption of iodine supplements.

Iron

Based on the high background concentration of iron and sulfur in soil and water, the EFSA concluded that the supplementation of feed with ferrous sulfate heptahydrate is not expected to pose an environmental risk (2014a). This was confirmed for ferrous sulfate, as well as six other iron supplements, in the EFSA report (2016a). Van Paemel et al. (2010) also concluded that there were no indications of environmental consequences related to the use of iron as a feed supplement.

Acute toxicity resulting from accidental ingestion of large doses of iron has been reported (Goldhaber 2003).

Manganese

In an assessment of five manganese compounds (i.e., manganous chloride, tetrahydrate; manganous sulfate, monohydrate; manganous oxide; manganese chelates of amino acids, hydrate; manganese chelates of glycine, hydrate), it was concluded that the use of these compounds in animal nutrition for all animal species is not expected to pose a risk to the environment (EFSA 2016b).

Molybdenum

Van Paemel et al. (2010) reported that there is no information available on the environmental consequences of using molybdenum as a feed supplement. Molybdenum toxicity in humans was reported to be associated with an increased incidence of gout-like syndromes, although the methodology used in the study has been questioned (Goldhaber 2003).

Selenium

Van Paemel et al. (2010) concluded that, at recommended inclusion levels, the use of selenium supplementation is not considered an environmental risk. The EFSA concluded that the use of selenium-enriched yeast in animal feed did not pose an additional risk to the environment compared to other sources of selenium for which is substituted (2011). Selenium-enriched yeast, however, is more biologically available, and the bio-transfer of selenium to milk and the fetus is substantially higher than sodium selenite (EFSA 2011). In addition, selenium retention in the meat of animals receiving selenium-enriched yeast is substantially higher (EFSA 2011). Saha et al. (2016) reported that, with selenium-enriched yeast, lower levels of selenium can be included in the feed and reduce the excretion of selenium in the manure.

Selenium toxicity has been reported in humans who ingested large quantities of selenium tablets (Goldhaber 2003).

Zinc

Van Paemel et al. (2010) concluded that zinc supplementation in animal diets has not been shown to be an environmental risk. In an assessment of seven zinc compounds, including zinc oxide and zinc sulfate, the EFSA also concluded that the use of the compounds did not pose an immediate concern for soil zinc levels. They did express concern, however, of the potential for drainage and runoff of zinc to surface water and felt that acidic sandy soils would be the most vulnerable. They concluded that further refinement of the assessment of zinc-based additives in livestock feeds needs to be considered and additional data is required (2015b).

<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)).

As indicated in the answer to *Evaluation Question* #2, there are many different methods involved in the manufacture of the different trace minerals. Many methods involve the reactions of caustic chemicals and care must be taken in the manufacturing process, especially with regards to human exposure to chemicals used. Care must also be taken to prevent human exposure when producing trace mineral premixes involving the various individual trace minerals. Once the premixes are prepared, care must be taken in the feed mill to prevent human exposure. For many of the compounds, respiratory, skin and eye irritations are possible. Proper disposal procedures must be followed for each of the compounds to prevent environmental contamination. Many of these are identified in detail by the Toxicology Data Network.

Many of the manufacturing methods described in *Evaluation Question #2* begin with mined minerals. Extraction methods used to manufacture these mined minerals present environmental contamination concerns. For example, according to MiningWatch Canada (2012), chromite mining—the first step in obtaining chromium compounds for use in feeds—produces waste rock, tailings, and tailings water. Dry milling (grinding) of chromite ore is known to convert chromium III to the more toxic chromium IV and efforts are put in place to avoid producing and spreading chromium IV during mining activities. Ferrochrome production can create air pollution (nitrogen oxides, carbon dioxides, and sulfur oxides), dust, slag (waste produced during ferrochrome separation from other ore elements), and process water. These materials have the potential to be contaminated with chromium and other heavy metals.

It is important that the trace minerals be included in animal feeds at the appropriate amounts and according to requirements that change during the rapid growth and development of animals during their production cycles (López-Alonso 2012). It is difficult to establish requirements for trace minerals in the same way that they are determined for energy, protein, or amino acids. Most estimates of trace mineral requirements are based on minimum levels required to overcome a deficiency symptom and not necessarily to promote productivity. Many different authorities around the world (e.g., INRA in France, ACR in the United Kingdom, FEDNA in Spain) have developed mineral requirements to ensure there are no deficiency symptoms, but they rarely agree. In the United States, recommendations for trace minerals include a safety margin to take into account the presence of any antagonists (López-Alonso 2012). For example, in ruminants, copper uptake is inhibited by molybdenum, sulfur, and (to a lesser extent) iron. High levels of copper are required in the presence of zinc. In addition, animals under stress require higher levels of copper and zinc. The mineral content of the feedstuffs being used in the complete feed must also be considered.

In recent years, there has been increased environmental concern related to animal feeding operations. As a result, maximum total levels of inclusion in a complete feed have been set for most of the trace minerals. When used at levels below these maximums, no environmental concerns have been reported with the use of trace minerals in animal feeds (see the various EFSA reports for specific minerals).

When included in animal feeds above required levels, trace elements accumulate in high levels in urine and feces (Brugger and Windisch 2015). The effects of environmental contamination by trace minerals is discussed in detail in *Evaluation Question #5* above.

Regarding macro-minerals, excess phosphorus in animal diets can lead to excess excretion in the manure. Phosphorus buildup in the soil can lead to contamination of surface water and lead to eutrophication, or excessive richness of nutrients. Eutrophication restricts water use for fisheries and recreation due to an increased growth of algae and aquatic weeds. Oxygen shortages for fish can result in death and decomposition (Nixon 1995).

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)).

Because trace minerals interact with each other, care must be used in formulating trace mineral premixes. Several macro-minerals also interact with trace minerals and adversely affect their bioavailability. These interactions are solely of concern for the animals being fed and do not have any adverse health effects on the environment or human health.

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, zinc, manganese, iron, and molybdenum are trace minerals essential to plant growth, but are toxic to plants at high concentrations (He et al. 2005). Cobalt and selenium are not essential to plant growth but are required by animals and human beings. Chromium can have toxic effects on living organisms and is often considered a contaminant. Soil microorganisms are the first living organisms affected by high levels of metal contamination (He et al. 2005).

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)).

The sustainability of any animal production system depends on management practices to minimize the potential environmental impacts of the animal manure. With the use of trace minerals in livestock feeds, manure application has emerged as an important source of certain minerals in soils (Sheppard and Sanipelli 2013). Poultry litter and other animal manure can provide nitrogen, phosphorus, and trace minerals for crop production. Land application of such organic fertilizers can lead to the accumulation of trace minerals in soils, primarily near the soil surface (Toor et al. 2007). A single application of poultry litter would lead to copper and zinc soil levels below the EPA's annual application limits for biosolids (Toor et al. 2007). Repeated applications, however, could result in high soil loading of trace minerals above the environmental thresholds (Toor et al. 2007). Applications of poultry litter to silt loam and sandy loam soils result in increased soil copper and zinc levels (Toor and Haggard 2009). These have the potential to serve as a non-point source of trace mineral pollution through leaching and runoff (Nolan et al. 2004). Benke et al. (2008) reported similar findings with repeated application of cattle manures.

Benke et al. (2008) evaluated the levels of trace elements in soil as a result of long-term cattle manure application and concluded that repeated applications of manure lead to elevated amounts of trace elements in the soil. The main concern with these elevated amounts involved zinc levels, as other studies have linked high levels of zinc with certain types of cancers and human illness.

Crop or pasture application of manure from animals fed supplemental selenium may not result in increased plant selenium content. Ingested selenium is converted to a chemically reduced form (selenide) in the digestive tract and is excreted in manure, most of which is not available for plant uptake (Saha et al. 2016).

The EFSA concluded that while zinc sulfate monohydrate did not pose a direct environmental concern for agricultural soils, more research was needed to exclude any risk related to drainage and the runoff of zinc to surface water (2012a).

The EFSA also concluded that calcium iodate anhydrous is a safe source of iodine when added to animal feed up to current maximum allowed levels except for horses and dogs, for which they concluded the current maximum levels were too high. They also hypothesized that the iodine content of food of animal origin could represent a substantial risk to consumers (primarily from milk consumption and, to a limited degree, from eggs). They recommended a reduction in the authorized maximum iodine concentrations for dairy cows and laying hens (2013a).

EPA regulations (40 CFR Part 503) set ceiling concentrations for each trace mineral that may not be exceeded if sewage sludge is to be applied to the land. Since the behavior and effects of land application of trace minerals in animal manures are essentially the same as application of sewage sludge, it would be prudent to adopt similar guidelines for manure application. The European Union already has restrictions on the levels of trace minerals that can be used in animal feeds, and the FDA is utilizing similar measures for some of the trace minerals discussed in this report. For example, 21 CFR §573.304 specifically addresses chromium propionate, which can be used with a restriction of 0.2 ppm of total chromium in the complete feed. 21 CFR §573.920 restricts the level of total selenium that can be include in animal feeds depending on the animal species.

Soil inherits trace minerals from its parent materials, but only a small portion of these trace minerals are bioavailable (He et al. 2005). Human activity is another main source of trace minerals in soils. Repeated use of metal-enriched chemicals or fertilizers may cause contamination at a large scale. Organic materials, such as farm manures or composts, typically contain higher concentrations of trace elements than most agricultural soils (He et al. 2005).

Cobalt salts, such as cobalt acetate, are poisonous.

<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)).

The human health effects related to the use of trace minerals include:

Chromium (III): Allergenicity and potential genotoxicity (EFSA 2009c).

Cobalt: Respiratory irritation, inflammation of the nasopharynx, decreased pulmonary function, wheezing, asthma, pneumonia, and fibrous growths (EPA 2010).7y

Copper: Anorexia, nausea, and perspiration in workers who grind and sieve copper dust (Suciu et al. 1981).

Iodine: Skin and eye irritation. No specific studies on irritation, dermal sensitization, or inhalation toxicity were found for potassium iodate, but it would be prudent to consider them as an irritant to eyes, skin, and the respiratory tract (EFSA 2013a). Both calcium and potassium iodate have high dusting potential, so both should be considered hazardous when inhaled. A coating of the additive may be beneficial (EFSA 2012a).

Iron: Ferrous sulfates and ferric chloride hexahydrate are corrosive upon contact with mucosae and irritants to skin and respiratory tract. Ferrous fumarate, ferrous carbonate, ferrous chelate of glycine, hydrate, and ferrous chelate of amino acids are considered irritants to skin, eyes, and mucous membranes. Ferrous fumarate and ferrous carbonate pose a risk to users by inhalation due to the levels of nickel present (EFSA 2016a).

Manganese: The handling of manganese oxide and manganous sulfate monohydrate poses a risk to users (EFSA 2013b). Inhalation exposure can be a risk. Manganous oxide is considered a potential skin and eye irritant as well as a dermal sensitizer. Manganous sulfate monohydrate is an eye irritant but is not irritating to the skin and is not likely to be a dermal sensitizer.

Molybdenum: Very little is known about specific effects of molybdenum compounds on human health (EFSA 2009d).

Selenium: Highly toxic by inhalation, ingestion, and skin contact (IPCS 1987). Acute inhalation of selenium dioxide can provoke pulmonary edema. Inhalation of elemental selenium causes irritation to the mucous membranes in the nose and throat resulting in coughing, nose bleeds, and loss of olfaction. Heavy exposure results in dyspnea (labored breathing), bronchial spasm, bronchitis, and chemical pneumonia (EFSA 2015a).

Zinc: The pathologies and symptoms caused by zinc inhalation depend on the zinc compound involved. Zinc sulfate monohydrate has been shown to have high dusting potential and to cause severe irritation of the eyes (EFSA 2012a).

Based on the information above, the hazards associated with the use of the macro-minerals are primarily associated with dust irritation of the skin and eyes.

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)).

As discussed in *Specific Uses of the Substance*, livestock, poultry, and companion animals obtain most of their minerals from the feeds and forages they consume. Mineral concentrations in plants and their seeds depend on plant genotype, soil environment, climate, and stage of maturity (Suttle 2010b). Most of the trace minerals identified in this report have low availability from plant sources, making it impossible to meet requirements from typical feedstuffs included in animal feed. For grazing animals, pasture material is insufficient to meet all their trace minerals. As a result, supplementation of feeds with trace minerals is required, although the amounts will vary with animal species, age, stage of production, and current feed sources.

Some trace minerals can be manufactured using natural (nonsynthetic) methods. Although selenium and other mineral-rich yeasts are manufactured from naturally occurring biological processes, the mineral source used may be produced through synthetic means.

Mined sources of macro-minerals are manufactured using natural (and therefore nonsynthetic) production methods. Many macro-minerals are manufactured from mined sources.

Kelp is a rich source of minerals and vitamins reported to contain 46 minerals, 16 amino acids, and 11 vitamins. The level of iodine, which can be a concern, is negligible in a batch of kelp fed at recommended levels. However, kelp grown in polluted water can contain unacceptable levels of contaminants (Shuttleworth 2012).

<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)).

Cattle on pastures receive small quantities of minerals from soil and water, but the plants they feed on provide their main dietary source of trace minerals (McDowell 1996). The fraction of minerals in the soil that are taken up by plants is influenced by soil characteristics, plant species, stage of maturity, yield, pasture management, and climate. Plant trace mineral content is a dynamic process of nutrient uptake and transport as well as dry matter accumulation. The form of the mineral in soil will affect its uptake. For example, total soil trace mineral content may exceed the demand of a single crop by more than a thousand-fold, but the available fraction may be insufficient. This results in crop nutrient deficiencies despite the high soil trace mineral content (Graham 1984).

Mineral deficiencies or imbalances in grazing cattle have been reported worldwide (McDowell 1996). The main trace minerals of concern for grazing ruminants are cobalt, copper, iodine, selenium, and zinc, but iron and manganese may be needed in other areas. The typical method employed worldwide to meet these trace mineral requirements is the use of free-choice dietary mineral blocks. These blocks should contain area-specific needed minerals, however, as in some areas providing excess copper or selenium could be detrimental to grazing ruminants (McDowell 1996).

Most incidences of mineral deficiencies in grazing ruminants are region-specific and directly related to soil characteristics. Trace element fertilization has been shown to be effective in increasing trace mineral content of crops (McDowell 1996). With the use of commercial, non-trace mineral fertilizer (nitrogen-phosphorus-potassium), trace mineral deficiencies in grasses have become more common on conventionally managed pastures. The use of organic fertilizer would, presumably, not be associated with this problem, although there are few reports on this topic.

The choice of forage crop is important for providing recommended levels of trace minerals. For example, copper concentrations are shown to be highest in herbs and weeds, slightly lower in legumes, and lower still in grasses (MacPherson 2008). Similarly, cobalt levels are reported to be higher in legumes than in grasses grown in soils with low cobalt amounts, but there are no differences when both are grown in soils high in cobalt (MacPherson 2008). Grasses are typically higher in selenium than white clover (MacPherson 2008). In addition, Lindström et al. (2014) showed that increasing the proportion of red clover versus timothy in pastures had the potential to increase the overall trace mineral content of the forage, but differences in soil properties between sites needed to be taken into consideration.

The part of the plant consumed, and the plant's state of maturity also affect trace mineral levels. Cobalt levels in grasses are typically highest in the leaves, followed by flowering heads and stems. Iodine levels are also higher in leaves than in stems. There is not much data available on selenium levels in different parts of plants and in plants of different states of maturity (MacPherson 2008).

Soil type and condition are also important for trace mineral levels, as the level of any trace mineral in the plant depends on the level in the soil. Forages grown on poorly drained soils can have up to seven times more cobalt than similar forages grown on well-drained soils, whereas soils derived from red sandstone, granite, and limestone parent material are inherently low in cobalt. Livestock grazing on naturally higher pH soils will have a greater incidence of cobalt deficiencies. Iodine concentration is lowest in sandy soils and river clays low in organic material and are highest in peat soils and soils with younger marine clay (MacPherson 2008).

Climatic conditions and seasons when plant material is eaten/gathered can affect mineral levels; for example, silage cut in the late spring has been reported to have higher cobalt than hay cut in midsummer (MacPherson 2008).

Feeding animals cereals and grains is typically associated with trace mineral deficiencies (Miner et al. 2018) as cereals are relatively low in trace elements (Welch et al. 1997). Corn is a major cereal crop and the main energy source used in the diets of non-ruminant diets, but the phytate in both corn and soybeans are a potent inhibitor of zinc and other mineral absorption (Cheeke 2005). The addition of phytase, a feed enzyme which breaks down phytate, could increase the availability of trace minerals in phytate-rich crops. Research suggests that phytase supplementation could reduce zinc excretion by 20 percent (EFSA 2014b). Similar findings on the benefits of phytase supplementation on zinc availability were also reported by Świątkiewicz et al. (2001). Breeding efforts to increase the trace mineral content of corn and other grains through genetic or agronomic biofortification can increase trace mineral levels to an extent, but there is limited potential for improvement in iron and zinc levels (Miner et al. 2018).

Research has been conflicting regarding nitrogen fertilization's effect on the trace mineral content of crops. Some have indicated no impact, and others have reported increased content of trace minerals, assuming the levels in the soil are not limiting (Miner et al. 2018). Copper and manganese levels in stover increased substantially with nitrogen fertilizer whereas copper and manganese levels in grain did not; this suggests that nitrogen fertilization could alleviate deficiencies for silage but not for grains. Reports on cobalt levels ranged from no effect of nitrogen fertilization, to reduced content, to increased content. Nitrogen fertilizer increases the levels of cyanogenetic glucosides in some plants, resulting in a higher need for iodine, while decreasing iodine content in the forage (MacPherson 2008).

Most minerals in plant materials, especially phosphorus, are tied up with phytate complexes. As a result, phosphorus supplementation is used. To reduce the need for phosphorus supplementation, the feed enzyme phytase can be added to animal diets to improve the availability of the phytate phosphorus. Best management practices are required to minimize the runoff of manure-borne phosphorus (Sharpley et al. 2004).

Report Authorship

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All individuals are in compliance with Federal Acquisition Regulations (FAR) Subpart 3.11—Preventing Personal Conflicts of Interest for Contractor Employees Performing Acquisition Functions.

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Appendix A
Regulatory Citations for Livestock Trace Minerals

Mineral	Compound	AAFCO	FDA
Chromium	Chromium tripropionate	57.166	21 CFR 573.304
	Chromium picolinate	57.155	n/a
	Chromium-enriched yeast	n/a	Baker's yeast: 21 CFR 184.1983
Cobalt	Cobalt acetate	57.58	21 CFR 582.80
	Cobalt carbonate	57.59	21 CFR 582.80
	Cobalt chloride	57.60	21 CFR 582.80
	Cobalt glucoheptonate	57.148	n/a
	Cobalt gluconate	57.147	n/a
	Cobalt oxide	57.61	21 CFR 582.80
	Cobalt sulfate	57.62	21 CFR 582.80
	Cobalt amino acid chelate	57.142	n/a
	Cobalt amino acid complex	57.150	n/a
	Cobalt choline citrate complex	57.123	n/a
	Cobalt polysaccharide complex	57.29	n/a
	Cobalt proteinate	57.29	n/a
Copper	Copper acetate, monohydrate	57.153	n/a
	Copper carbonate	57.63	21 CFR 582.80
	Copper chloride, basic	57.64	21 CFR 582.8
	Copper citrate	57.158	n/a
	Copper gluconate	57.65	21 CFR 582.80 21 CFR 582.5260
	Copper hydroxide	57.66	21 CFR 582.80
	Copper orthophosphate	57.67	21 CFR 582.80
	Copper oxide	57.68	21 CFR 582.80
	Copper pyrophosphate	Section 100 – referring to 21 CFR 582.80	21 CFR 582.80
	Copper sulfate	57.69	21 CFR 582.80
	Cuprous iodide	57.70	21 CFR 582.80
	Tribasic copper chloride	57.64	21 CFR 582.80
	Copper amino acid chelate, monohydrate	57.142	n/a
	Copper amino acid complex	57.150	n/a
	Copper choline citrate complex	57.122	n/a
	Copper lysine complex	57.151	n/a
	Copper polysaccharide complex	57.29	n/a
	Copper proteinate	57.23	n/a
Iodine	Calcium iodate	57.54	21 CFR 582.80
	Calcium iodobehenate	57.55	21 CFR 582.80
	Cuprous iodide	57.70	21 CFR 582.80
	Diiodosalicylic acid	57.72	21 CFR 582.80
	Ethylenediamine Dihydriodide	57.75	21 CFR 582.80 Sec 651.100
	Potassium iodate	57.103	21 CFR 582.80

	Potassium iodide	57.104	21 CFR 582.80
	Sodium iodate	57.107	21 CFR 582.80
	Sodium iodide	57.108	21 CFR 582.80
	Thymol iodide	57.112	21 CFR 582.80
Iron	Ferric ammonium citrate	57.76	21 CFR 582.80
	Ferric chloride	57.78	21 CFR 582.80
	Ferric formate	57.127	n/a
	Ferric phosphate	57.81	21 CFR 582.5301
	Ferric pyrophosphate	57.82	21 CFR 582.5304
	Ferric sodium pyrophosphate	Section 100 – referring to 21 CFR 582.5306	21 CFR 582.5306
	Ferric sulfate	57.129	21 CFR 582.80
	Ferrous carbonate	57.77	21 CFR 582.80
	Ferrous chloride	57.128	21 CFR 582.80
	Ferrous fumarate	57.164	n/a
	Ferrous gluconate	57.79	21 CFR 582.80
	Ferrous lactate	n/a	21 CFR 582.5311
	Ferrous phosphate	57.81	21 CFR 582.80
	Ferrous sulfate	57.83	21 CFR 582.80 21 CFR 582.5315
	Ferrous oxide	57.80	21 CFR 582.80
	Ferric choline citrate	90.26	21 CFR 573.580
	Ferric choline citrate complex	57.121	21 CFR 573.580
	Ferric methionine complex	57.151	n/a
	Ferrous glycine complex	57.139	21 CFR 582.80
	Iron amino acid chelate	57.142	n/a
	Iron amino acid complex	57.150	n/a
	Iron polysaccharide complex	57.29	n/a
	Iron proteinate	57.23	n/a
	Iron yeast		n/a
Manganese	Manganese acetate	57.89	21 CFR 582.80
	Manganese carbonate	57.90	21 CFR 582.80
	Manganese chloride	57.91	21 CFR 582.80 21 CFR 582.5449
	Manganese citrate	57.92	21 CFR 582.80 21 CFR 582.5449
	Manganese gluconate	57.93	21 CFR 582.5452
	Manganese glycerophosphate	Section 100 – referring to 21 CFR 582.5455	21 CFR 582.5455
	Manganese hypophosphite	Section 100 – referring to 21 CFR 582.5458	21 CFR 582.5458
	Manganese orthophosphate	57.94	21 CFR 582.80
	Manganese oxide	57.97	21 CFR 582.80
	Manganese phosphate	57.95	21 CFR 582.80
	Manganese sulfate	57.96	21 CFR 582.80 21 CFR 582.5461
	Manganese amino acid complex	57.150	n/a
	Manganese amino acid complex	57.142	n/a

	Manganese methionine complex	57.151	n/a
	Manganese polysaccharide complex	57.29	n/a
	Manganese proteinate	57.23	n/a
Molybdenum	Sodium molybdate	57.145	n/a
Selenium *(restricted use under 21 CFR 573.920)*	Sodium selenate	57.120	21 CFR 573.920
	Sodium selenite	57.119	21 CFR 573.920
	Selenium yeast	57.163	21 CFR 573.920
	Selenomethionine	n/a	21 CFR 573.920
Zinc	Zinc acetate	57.114	21 CFR 582.80
	Zinc carbonate	57.115	21 CFR 582.5985
	Zinc chloride	57.116	21 CFR 582.80 21 CFR 582.5985
	Zinc chloride diammine complex	57.143	n/a
	Zinc gluconate	Section 100 – referring to 21 CFR 582.5988	21 CFR 582.5988
	Zinc oxide	57.117	21 CFR 582.80 21 CFR 582.5991
	Zinc stearate	Section 100 – referring to 21 CFR 582.5994	21 CFR 582.5994
	Zinc sulfate	57.118	21 CFR 582.80 21 CFR 582.5997
	Zinc amino acid chelate	57.142	n/a
	Zinc amino acid complex	57.150	n/a
	Zinc lysine complex	57.151	n/a
	Zinc methionine complex	57.151	n/a
	Zinc polysaccharide complex	57.29	n/a
	Zinc proteinate	57.23	n/a