PETITION TO INCLUDE CHOLINE AS ITS SALTS CHOLINE BITARTRATE & CHOLINE CHLORIDE AT 7CFR205.605 and 7CFR205.703

Item A. Categories for inclusion on the National List

- Non-agricultural, non-organic substances allowed in or on processed products labeled "*organic*" or "*made with organic (specified ingredients*)" **7 CFR 205.605(b)**
- Synthetic substances allowed for use in organic livestock production **7 CFR 205.603**

Item B. Information on the substance being petitioned

1. Common Name

Choline, as its water-soluble salt forms:

- **choline bitartrate** (2-hydroxyethyl)trimethylammonium bitartrate)
- **choline chloride** (2-hydroxyethyl)trimethylammonium chloride)

Balchem's choline is sold under the trade names Vitashure®, Vitacholine™, Memor-C™, and C-Salt™ to the food processing industry and as Reashure® to the feed industry.

2. Manufacturer's name, contact, telephone number

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3. Intended or current uses of the substances

Choline is used as a nutrient supplement (**21 CFR 170.3(o)(20)**) in its salt forms, choline bitartrate and choline chloride.

Although choline is not listed explicitly with the substances in **21 CFR 104.20(d)(3)** as an allowable synthetic vitamin or mineral, it has historically been informally considered an "accessory nutrient."

Choline bitartrate and choline chloride have been and are currently included in many commercialized infant formulas (**21 CFR107.100**) labeled *Organic*, as well as fortified *Organic* baby foods. These forms of choline have also been used in a variety of *Organic* and *Made with Organic* food products for the general market, including beverages and soy yogurt. These products were formulated with choline under the prevailing interpretation of the regulation, which is presently subject to clarification.

Choline bitartrate and choline chloride are intended to be used in organic handling as a source of the essential nutrient (1) choline in infant formula, foods, beverages, and dietary supplements.

Choline chloride, specifically, is also intended for use as a partial replacement and flavor enhancer for sodium chloride in sodium-reduced foods and beverages (2;3).

Applications include, but are not limited to, the following products (**21CFR170.3(n)**):

Baked goods and baking mixes
Beverages and beverage bases (nonalcoholic, including coffee and tea)
Breakfast cereals (ready-to-eat, instant, and cooked)
Milk and products of milk origin (cheese, yogurt, butter, frozen dairy desserts and mixes)
Dairy product analogs
Egg products and egg dishes made therefrom
Fats, oils, shortenings and dressings
Grain products and pastas
Meat products, including all meats and meat containing dishes
Poultry products, including all poultry and poultry-containing dishes
Fish products, including all fish and fish-containing dishes
Nuts and nut products, including whole or shelled tree nuts, peanuts, coconut, and nut and peanut spreads.
Plant protein products, reconstituted vegetable protein, and meat analogs and extenders made therefrom
Fresh and processed fruits and fruit juices
Fresh and processed vegetables and vegetable juices
Snack foods
Gravies and sauces
Soups and soup mixes
Condiments and relishes
Sweet sauces, toppings, and syrups
Jams and jellies
Seasonings and flavorings and blends thereof

Choline salts (most commonly choline chloride) are used in all species and categories of livestock as a feed additive. Its use in this manner is not restricted in doses or limited by special precautions.

4. Uses and mode of action

a. Crop, livestock and handling activities for which the substance will be used (rate and method of application).

Fortification of foods, usage in dietary supplements

Choline salts are used in foods and supplements, as indicated in section 3, to deliver nutritionally significant amounts of choline relative to the current dietary recommendations[1], according to Good Manufacturing Practice (GMP).

Choline is a required component of infant formula worldwide, with typical addition within the range of 7 to 50 mg/100 kcal (1.7 to 12 mg/100 kJ), as specified in standards of international authoritative bodies. Many commercial solid food preparations and "follow-up" formulas, intended for older infants, now also contain choline.

Replacement/flavor enhancement of sodium chloride

For choline chloride's use as a salt replacer, usage will be according to GMP. Typical usage level in practice will be replacement of 30-50% of the weight of sodium chloride with choline chloride.

Processing of feed Intended for livestock raised under Organic regulations

Choline is an important feed additive for cattle, swine, and poultry, primarily as choline chloride (4). The method of application of choline chloride is either in premixes, or directly in the feed or water provided to the animal. These ingredients have been and are currently allowable as livestock vitamins, with use according to the *quantum satis* principle (5).

Animal species / categories	ALL
Age group/ production stage	ALL
Proposed use	Added to feed, nutrient premixes, and/or water
Duration of administration	No limitations
Proposed withdrawal period	None

A choline requirement has been established by the National Research Council for almost all livestock animals, including fish, and those requirements are listed for the predominant livestock species in the table below. Although NRC has not specified a requirement for choline in ruminants, choline can be

[1] An adequate intake (AI) for choline of 7 mg/kg body weight/day was established by the Institute of Medicine in 1998. AI values for various age and gender groups are shown in the Appendix.

supplemented in a rumen-protected form and, as demonstrated in all other species, reduces the extent of hepatosteatosis (fatty liver).

Species	Stage	Choline supplementation, mg/kg feed (90% DM)	Choline requirements, mg/kg feed (90% DM)
Chickens (Broilers)	Starting, 0-8 weeks	500	1300
	Growing, 8-18 weeks	500	900
Chickens (Layers)		250	1310
	Breeding	300 - 600	1050
Turkeys	Starting, 0-8 weeks	800	1600
	Fattening, 8 weeks - end	500	1100
	Breeding	600	1000
Geese		varies	1500
Pheasants		varies	1430
Japanese Quail		varies	2000
Ducks	Market	900 - 1,100	1500
	Breeding	1,000 - 1,400	1700
Beef cattle		250-500	
Dairy cattle	Lactating	250-500	
Calves		200	1000
Pigs	Starting 3-20 kg	300 - 600	600
	Growing 20-50 kg	200 - 300	300
	Finishing 50 kg - end	150 - 250	300
	Gestating	150 - 500	1250
	Lactating	150 - 500	1000

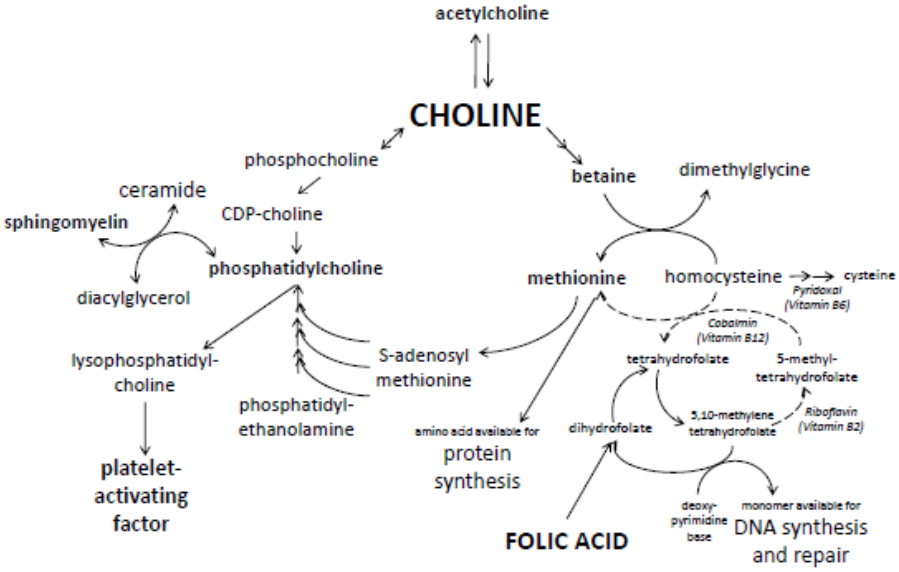
b. Mode of action

Choline's necessity for human and animal health is fundamental. Choline acts as a biochemical building block, an agent of cell-to-cell communication and transportation, and part of a regulatory system for gene expression. Its role in cell structure and function, phospholipid metabolism, cell signaling and epigenetic events underlie its contribution to the maintenance of cognitive, cardiovascular, and hepatic health. Some of choline's effects are direct, in that it is a biosynthetic precursor of numerous molecules that are important for diverse structural and functional purposes in the human body (6). By its participation in several common biochemical reactions, including phosphorylation, base exchange, oxidation, one-carbon transfer, and acetylation, it generates important numerous intermediates for key metabolic processes.

Choline is a precursor of:	**Cellular function** (6)	**Biological importance**
Phosphatidylcholine	Membrane phospholipid	Important primary structural component of the phospholipid membranes of all cells. PC functions in fat transport as a part of lipoproteins.
Sphingomyelin		Provides insulation along the length of a neuron. Precursor of molecules that function in intracellular signaling.
Phosphatidylinositol	Cell signaling	Directs cell membrane traffic. Controls the cell structure *via* the membrane and cytoskeleton.
Ceramide		Secondary messenger by its interaction with proteins. Role in processes of cell growth, aging, death.
Platelet-activating factor		Regulates the intercellular interactions that govern numerous diverse processes.
Betaine	Osmolyte Methyl donor	Controls water transport in and out of cells. Contributes to the 'methyl pool' toward maintenance of the balance of choline, folate and B-vitamins.
Acetylcholine	Neurotransmitter	Primary agent of neurotransmission in cholinergic neurons.

Other effects of choline are indirect, in that it impacts the balance of and need for many other partially compensatory metabolites to which it is closely related, via its influence on the activity of certain regulatory genes or the catalytic proteins they express. While choline exhibits nutritional synergies with vitamins involved in folate metabolism and the methionine cycle, such as B_6 and B_{12}, and nutrients such as omega-3 fatty acids, none of these substances can functionally replace it. Deficiency in these complementary nutrients elevates the need for choline in the diet (7;8).

Choline is considered an essential nutrient for humans (1) because the body does not produce quantities sufficient to sustain normal organ function. As biosynthesis is influenced by estrogen, individuals at a hormonal deficit (e.g. men and post-menopausal women) are most likely to become choline deficient with inadequate dietary intake (9). Certain previously unappreciated genetic variations, widespread in the general population, also result in increased choline need (9;10).



Choline is indispensible as a prenatal nutrient for mother and child. It is needed for the proper development of the fetus, particularly its central nervous system. The need for choline is extremely high in the first weeks and months of fetal and infant development, as billions of cells are growing, dividing and differentiating (11;12). Maternal choline intake has been shown to have lifelong repercussions; reliable availability of choline in the prenatal period contributes to physiological changes in neurons that are theorized to correspond to an improved capacity for messaging between cells (13;14). Adequate and/or enhanced maternal choline intake has been associated with long-lasting improvements in attention span, learning and memory in offspring of supplemented pregnancies (15-21). Furthermore, interventional studies in animals and epidemiological observations in humans suggest that maternal dietary choline intake may be as important as folate is in attenuating the risk of neural tube defects in offspring (22-25).

Choline intake is also extremely important for mothers and infants postpartum, as infant brain development continues at a fast pace in the months after birth. In the first months of life, an infant will receive choline exclusively via breast milk or from infant formula, which is formulated to resemble the composition of breast milk (26-29). In breastfeeding, choline is transferred from maternal blood to breast milk by mammary epithelial cells against a significant concentration gradient (26;30-32), elevating the mother's choline need. Choline is a required ingredient in soy-based infant formulas, and is typically also added to those based on milk protein.

Choline continues to be necessary through the human lifespan for a variety of important purposes. Choline is thought to facilitate neurotransmission and cellular messaging by increasing availability and mobilization of neurotransmitters, secondary messengers and other bioactive metabolites (40). The level of choline in the brain is directly affected by its levels in plasma, which is significantly influenced by intake of the nutrient (12;33;34).

Choline contributes to the pool of methyl groups that can be used for biologically important one-carbon transfer reactions. Once oxidized, it remethylates homocysteine to S-adenosylmethionine, a methyl donor necessary for the synthesis of DNA and RNA, the myelin insulation for neurons, and other biological materials (35;36). By this mechanism, choline intake has also been shown to reduce levels of plasma homocysteine (37) a metabolically-generated amino acid (38-41) currently debated as a biomarker, by-product, risk-factor or active agent (42) of biochemical change. Accumulated homocysteine is widely believed to be associated with numerous health conditions (43), including age-related cognitive decline, cardiovascular occlusion (44;45), and negative outcomes in pregnancy, such as low birth weight, pre-eclampsia, placental abruption and recurrent pregnancy loss (46-49).

Choline is an important component of the structure of very low density lipoproteins, the cellular packaging system designed to remove excess lipid material from the liver (50-52). Deprivation of dietary choline is manifest as a decrease in plasma choline, a subsequent increase in plasma homocysteine, accumulation of fat in vacuoles of liver cells (steatosis), and damage to liver cell membranes (9). As deprivation devolves into dietary deficiency, cell suicide is activated in lymphocytes (53), damage is sustained by muscle cells, and organ dysfunction begins (54). Dietary administration of choline easily reverses these processes and symptoms of deficiency (55). In fact, the current dietary recommendations for choline are based on the daily dosage necessary to prevent these abnormalities in most individuals, i.e. 7 mg/kg body weight/day (1).

Dietary choline is equally critical for growth and required optimal nutrition and health of livestock species (56;57), by many of the same biochemical mechanisms that operate in humans (57;58). Choline is needed for conversion to phosphatidylcholine, to build and maintain cell structure, especially important in growing animals such as broilers. It is essential for fat metabolism in the liver, where it hastens removal of fat and decreases its deposition. In all animal species tested, fatty liver occurs when there is a deficiency in choline (56). Choline provides methyl groups for biosynthesis of methionine, and is needed as a raw material for acetylcholine, important in brain development and neurotransmission in both the central and the peripheral nervous systems. As with humans, most animals can produce some amount of choline in the body, but not all that is necessary. In the case of the growing chick, for example, there is an absolute requirement for dietary choline as sufficient amounts are not able to be synthesized until up to 13 weeks of age (58). In the case of the turkey, it has been shown that the amount of choline required to prevent the leg disorder perosis was greater than that required to sustain normal growth (58).

5. Source of the substance and detailed description of the manufacturing processes

Balchem Corporation is a basic manufacturer of water-soluble choline salts, producing grades appropriate for domestic and international food and feed industries. The Corporation maintains manufacturing facilities for these ingredients in the United States, Canada and Europe. Facilities manufacturing food-grade choline salts have programs for Hazard Analysis & Critical Control Points (HACCP) in place.

The choline salts are first chemically synthesized in water (or other solvent) using pure chemical feedstocks, including amine-based compounds, and acids. The resultant solutions are then filtered to remove extraneous matter. This step is followed by removal of solvent, and a final drying step, yielding a powder-granular product. A conditioning aid may be added to facilitate powder flow. Material then goes through quality checks, is packaged, and released for shipment.

Balchem choline salts do not contain unlabeled synthetic or non-synthetic substances. Neither the ingredient nor any component used in its manufacture is derived from genetic engineering, treated with ionizing radiation, or produced using sewage sludge.

Current monographs exist for choline bitartrate and choline chloride in the United States Pharmacopeia (USP 32) and Food Chemicals Codex (FCC VII). Monographs are included in the Appendix. Balchem Corporation produces choline chloride and choline bitartrate to these standards for use in foods and dietary supplements. Conditioned products are USP/FCC-grade prior to conditioning.

Product specifications for these, as well as Balchem's feed-grade choline salts, are provided in the Appendix.

CBI-deleted

Flow diagrams for the choline salt synthetic processes are shown below:

CBI

CBI

6. *Summary of previous reviews of the petitioned substance by State or private certification programs, or other programs*

a. Choline for Food Uses:

The petitioned substance is generally recognized as safe (GRAS) when used as a nutrient according to Good Manufacturing Practices (GMPs) (**21 CFR 182.8250**, **21 CFR 182.8252**) (59).

Choline has received "independent assessment and recognition as supplementing the human diet or providing support for optimal health"[2]. In 1998, the Food and Nutrition Board of the Institute of Medicine developed dietary reference intake (DRI) values for choline for age/life stage groups based on then-current understanding of choline metabolism and available data on intake of the nutrient by the US population (1). Adequate Intake values for various age and gender groups are shown in the Appendix.

Minimum and maximum levels of choline in infant formula were recommended in the Assessment of Nutrient Requirements for Infant Formulas conducted by the Life Sciences Research Office (60).

Choline bitartrate and choline chloride are listed in several standards of the FAO/WHO Joint Expert Committee on Food Additives (JECFA), including:

- *Advisory Lists of Nutrient Compounds for Use in Foods for Special Dietary Uses Intended for Infants and Young Children* CAC/GL 10-1979[3]
- *Codex Class Name and the International Numbering System for Food Additives* CAC/GL 36-1989[4]
- *Standard for Infant Formula and Formulas for Special Medical Purposes Intended for Infants* STAN 72-1981[5]
- *Standard for Special Dietary Foods with Low-Sodium Content (Including Salt Substitutes)* STAN 53-1981[6]
- *Specifications for Flavourings*[7]

Choline salts are allowable in infant formula in Canada, listed under Division 25 (B.25.054(1)(a)(vii)) of the Food and Drug Regulations. Choline salts are allowable in organic counterparts of these food products by virtue of their necessity by legal requirement, according to Organic Production Systems General Principles and Management Standards (CAN/CGSB-32.310-2006) and Organic Production Systems Permitted Substances List (CAN/CGSB-32.311-2006).

Choline salts are an acceptable form of choline in infant formula and infant food in European Union, according to Commission Directive 2006/141/EC, Commission Directive 2006/125/EC. They are also allowed in the category of "foods for particular nutritional uses" (Commission Regulation 953/2009,

[2] NOSB Handling Committee Discussion Document – The Use of Nutrient Supplementation in Organic Foods, September 2, 2010
[3] http://www.codexalimentarius.net/download/standards/300/cxg_010e.pdf
[4] http://www.inchem.org/documents/jecfa/jeceval/jec_412.htm;
http://www.codexalimentarius.net/download/standards/7/CXG_036e.pdf
[5] http://www.codexalimentarius.net/download/standards/288/CXS_072e.pdf
[6] http://www.codexalimentarius.net/download/standards/287/CXS_053e.pdf
[7] http://www.fao.org/ag/agn/jecfa-flav/details.html?flavId=7004

Commission Directive 2009/39/EC). Choline salts are allowable in organic counterparts of these food products by virtue of their necessity by legal requirement, according to European Commission Regulation 889/2008.

b. Choline for Feed Uses:

Choline bitartrate and choline chloride are GRAS for use as a nutrient/dietary supplement in animal feed (**21 CFR 582.5250, 21 CFR 582.5252)**.

The Organic Materials Research Institute (OMRI) has considered choline chloride (IFN 7-02-228) as allowable for use as a nutrient/dietary supplement in animal feed with *quantum satis* restrictions (4). The listing is including in the Appendix.

In 2006, Pennsylvania Certified Organic determined that Balchem's Reassure [*sic*] Choline was allowable for organic production as a feed additive/supplement. A letter is included in the Appendix.

Choline chloride is included in the European Union feed additive register (EC Regulation 1831/2003)[8].

[8] http://ec.europa.eu/food/food/animalnutrition/feedadditives/comm_register_feed_additives_1831-03.pdf

7. Information regarding EPA, FDA and State regulatory registrations

The petitioned substance is generally recognized as safe (GRAS) when used as a nutrient according to Good Manufacturing Practices (GMPs) (**21 CFR 182.8250**, **21 CFR 182.8252**) (59).

The nutrient is a requisite component of infant formula (**21 CFR1 07.100(a)**).

Nutrient Content Claims based on current published authoritative statements from federal scientific bodies are permitted for choline under the provisions of the Food and Drug Administration Modernization Act of 1997 (FDAMA). They are as summarized in the table in the Appendix. All are based on a Daily Consumption Value of 550 mg/day. None of these claims may be used in products intended for consumers under 4 years of age.

Choline chloride is listed as a flavor ingredient (#4500) on the GRAS list of the Flavor and Extracts Manufacturers Association (FEMA)[9].

In September 2010, Balchem Corporation submitted a *Notification of New Technology* to the United States Department of Agriculture's Office of Policy and Program Development, Risk Innovations and Management Division, describing the use of choline chloride as a direct replacement for sodium chloride and an enhancer of salty flavor in foods under USDA's jurisdiction. USDA has expressed 'no objection' to the use of choline chloride for this non-nutritive purpose, in processed, ready-to-eat, fresh and frozen meat and poultry products (excluding eggs), with or without standards of identity or composition, at levels not to exceed 1200 parts per million (ppm) in the finished application. The March 2011 USDA response letter is included in the Appendix.

The Environmental Protection Agency established an exemption[10] from the requirement of a tolerance for residues of choline chloride applied pre-harvest on all raw agricultural commodities when applied or used as an inert component of a solvent. It is considered safe under section 408(q) of the Federal Food Drug and Cosmetic Act (**40 CFR 180.920**). Full detail, including an analysis of toxicological data, is included in the Appendix.

[9] http://www.femaflavor.org/GRAS%2024.pdf
[10] http://edocket.access.gpo.gov/2010/E9-31280.htm

8. *Chemical Abstracts Service Number (CAS #) of the substance, Product Labels, etc.*

Choline Chloride: CAS # 67-48-1
Choline Bitartrate: CAS # 87-67-2

Balchem Corporation's choline product numbers are as follows:

Product	**Conditioning agent/flow-aid**	**Product number**	**Grade**
Choline chloride	None	F6522120	Food
C-Salt™ (choline chloride 98%)	Magnesium stearate	F6526120	Food
Choline bitartrate, 20M conditioned	Silica	F6502120	Food
Choline bitartrate, 40M conditioned	Silica	F6472120	Food
Choline bitartrate, 40-80M conditioned	Silica	F6672118	Food
Choline bitartrate, conditioned regular	Silica	F6512120	Food
Choline bitartrate, regular	None	F6492120	Food
70% choline chloride – aqueous	Water	F3060030	Feed
75% choline chloride – aqueous	Water	F3090030	Feed
60% choline chloride on carrier	Corn cob, beet pulp	F3070230	Feed
70% choline chloride on carrier	Corn cob, beet pulp	F3080230	Feed
50% choline chloride on carrier	Silica	F3040030	Feed
Reashure®	Soybean oil, corn cob	F3428016	Feed

Facsimiles of labels of all Balchem choline products appear in the Appendix.

9. Physical properties and chemical mode of action (interactions with other materials, toxicity & environmental persistence, environmental impacts from use/manufacture, effects on human health, soil microorganisms, crops and livestock).

Much of this information, relative to a specific evaluation of choline chloride, was summarized in an evaluation by EPA, referenced in the Appendix. A Screening Information Data Set (SIDS) report for choline chloride is available from the International Programme on Chemical Safety (INCHEM)[11].

Choline is extremely thermostable, particularly to food and feed processing operations (e.g. extrusion, retort, ultra high temperature sterilization). Choline salts are, in general, very hygroscopic, with choline chloride being more deliquescent than choline bitartrate. These ingredients are frequently conditioned with inert material (indicated in Section 8), such as silica, magnesium stearate, or vegetable carrier (corn cob) to improve flow characteristics and handling qualities. Bulk choline salts react with strong acids and bases, and may cause corrosion or discoloration of iron, mild steel and galvanized steel.

A summary of peer-reviewed studies on the pharmacological, genetic toxicological (61;62) and mutagenic (63) studies of choline chloride is available from the National Institute of Environmental Health Sciences[12], and was summarized in the evaluation by EPA, referenced in the Appendix. Choline chloride is readily biodegradable, and bio- or geoaccumulation is not expected.

The safety of choline bitartrate and choline chloride as nutritional ingredients has been well established by a GRAS evaluation (59). The benefits of choline in the human and animal diet have been discussed at length in Section 4.b. Dietary choline is important in that it provides nutrient pools that can attenuate the need to catabolize and recycle other choline-containing molecules, including membrane phospholipids (12;64-66), during periods of high metabolic activity. Oral administration of water-soluble choline readily affects serum choline levels (34;67-69). When, in the course of digestion, choline reaches the upper small intestine, it is transported by a carrier (70) in a concentration-regulated mechanism, and subsequently enters the portal circulation (69), where it can be picked up by the liver via the portal vein (69). The liver uses choline in the construction of phospholipid membranes needed to package lipids and export them to adipose tissue for storage. Choline is converted in an irreversible oxidation process into the osmolyte betaine, primarily in the liver and in the kidney, where it regulates influx and efflux of water in cells. Free choline crosses the blood-brain-barrier (12;71;72) so that it is available at neuron terminals for conversion to acetylcholine(12;73), necessary for neurotransmission in the central nervous system (65). Acetylcholine synthesis and use is significant elsewhere in the body, as well. It occurs in the non-neural cholinergic system present in other cells, tissues and organs, including the epithelium, endothelium, and mesothelium, mesenchyme, and immune cells (74), and may be significant in mediating cellular inflammation. Excess choline is converted to trimethylamine by the action of intestinal flora (75).

[11] http://www.inchem.org/documents/sids/sids/67481.pdf
http://www.inchem.org/documents/icsc/icsc/eics0853.htm
[12] http://ntp.niehs.nih.gov/?objectid=BCE40402-123F-7908-7BA487AA2C7B08A2

The Institute of Medicine has established Upper Limits (UL) of choline exposure (1) based on studies in human subjects. ULs are based on observations of the onset of hypotension and fishy body odor, and are calculated by dividing the lowest-observed-adverse-effect level (LOAEL) by an uncertainty factor of 2. ULs and estimates of choline intake are shown in a table in the Appendix. Current intake of choline in the US is below the nutrient's AI, and well below its UL.

Choline salts are not known to have inherent antimicrobial effects. Limited studies have been conducted in certain food applications *e.g*. references (76;77). Pure choline salts are not likely to sustain microbial growth as a sole nutrient source. A statement on microbial stability of the bulk ingredient is included in the Appendix.

Benefits for the well-being of livestock have been previously presented. Choline is absorbed at the small intestine. Excess choline beyond essential need is oxidized and hence allows animals to tolerate high intakes of choline with no adverse effects (56).

10. Safety Information

Material Safety Data sheets for all Balchem choline ingredients are included in the Appendix.

A substance report on choline chloride is available from the National Institute of Environmental Health Studies[13].

[13] http://ntp.niehs.nih.gov/go/TS-10846-G

11. Research reviews and bibliographies

Listed below are the references cited in this petition. Reference (1) represents a comprehensive view of choline's necessity for human health.

Reference List

(1) Institute of Medicine. Choline. In: Food and Nutrition Board NAoS, editor. Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin and Choline.Washington, DC: National Academy Press; 1998. p. 390-422.

(2) Fielding S, Locke KW, Kershman A, inventors; Interneuron Pharmaceuticals, assignee. Choline containing compositions as salt substitutes and enhancers and a method of preparation. United States patent 5,206,049. 1993 Apr 27.

(3) Locke KW, Fielding S. Enhancement of salt intake by choline chloride. Physiol Behav 1994;55(6):1039-46.

(4) AAFCO (Association of American Feed Controls Officials I. Official Feed Definitions. In: AAFCO (Association of American Feed Controls Officials I, editor. 2009 Official Publication. 2009. p. 427.

(5) Organic Materials Review Institute (OMRI). OMRI Generic Materials List: A directory of substances allowed and prohibited in organic production and handling. 2009.

(6) Zeisel SH, Blusztajn JK. Choline and human nutrition. Annu Rev Nutr 1994;14:269-96.

(7) Kim Y-I, Miller JW, daCosta KA, Nadeau MR, Smith D, Selhub J et al. Severe folate deficiency causes secondary depletion of choline and phosphocholine in rat liver. J Nutr 1994;124:2197-203.

(8) Selhub J, Seyoum E, Pomfret EA, Zeisel SH. Effects of choline deficiency and methotrexate treatment upon liver folate content and distribution. Cancer Res 1991;51:16-21.

(9) Fischer LM, daCosta KA, Kwock L, Stewart PW, Lu TS, Stabler SP et al. Sex and menopausal status influence human dietary requirements for the nutrient choline. Am J Clin Nutr 2007;85:1275-85.

(10) Kohlmeier M, daCosta KA, Fischer LM, Zeisel SH. Genetic variation of folate-mediated one-carbon transfer pathway predicts susceptibility to choline deficiency in humans. PNAS 2005;102(44):16025-30.

(11) Wurtman RJ. Synapse formation and cognitive brain development: effect of docosahexaenoic acid and other dietary constitutents. Metab Clin Expt 2008;57 Suppl 2:S6-S10.

(12) Wurtman RJ, Cansev M, Ulus IH. Choline and its products acetylcholine and phosphatidylcholine. In: Tettamani G, Goracci G, editors. Handbook of Neurochemistry and Molecular Neurobiology: Neural Lipids. 3 ed. New York: Springer; 2009. p. 443-500.

(13) Meck WH, Williams CL. Metabolic imprinting of choline by its availability during gestation: implications for memory and attentional processing across the lifespan. Neurosci Biobehav Rev 2003;27:385-99.

(14) Zeisel SH. Importance of methyl donors during reproduction. Am J Clin Nutr 2009;89S:673S-7S.

(15) McCann JC, Hudes M, Ames BN. An overview of evidence for a causal relationship between dietary availability of choline during development and cognitive function in offspring. Neurosci Behav Rev 2006;30:696-712.

(16) Meck WH, Smith RA, Williams CL. Pre- and postnatal choline supplementation produced long-term facilitation of spatial memory. Dev Psychobiol 1988;21:339-53.

(17) Meck WH, Smith RA, Williams CL. Organizational changes in cholinergic activity and enhanced visuospatial memory as a function of choline administered prenatally or postnatally or both. Behav Neurosci 1989;103:1234-41.

(18) Meck WH, Williams CL. Characterization of the facilitative effects of perinatal choline supplementation on timing and temporal memory. Neuroreport 1997;8:2831-5.

(19) Meck WH, Williams CL. Perinatal choline supplementation increases the threshold for chunking in spatial memory. Neuroreport 1997;8:3053-9.

(20) Meck WH, Williams CL. Choline supplementation during prenatal development reduces proactive interference in spatial memory. Dev Brain Res 1999;118:51-9.

(21) Williams CL, Meck WH, Heyer DD, Loy R. Hypertrophy of basal forebrain neurons and enhanced visuospatial memory in perinatally choline-supplemented rats. Brain Res 1998;794:225-38.

(22) Fisher MC, Zeisel SH, Mar MH, Sadler TW. Perturbations in choline metabolism cause neural tube defects in mouse embryos *in vitro*. FASEB J 2002 February 25.

(23) Shaw GM, Carmichael SM, Yang W, Selvin S, Schaffer DM. Periconceptual dietary intake of choline and betaine and neural tube defects in offspring. Am J Epidemiol 2004;160:102-9.

(24) Shaw GM, Carmichael SM, Laurent C, Rasmussen SA. Maternal nutrient intakes and risk of orofacial clefts. Epidemiology 2006;17:285-91.

(25) Shaw GM, Finnell RH, Blom HJ, Carmichael SM, Vollset S, Yang W et al. Choline and risk of neural tube defects in a folate-fortified population. Epidemiology 2009;20:714-9.

(26) Holmes-McNary MQ, Cheng WL, Mar MH, Fussell S, Zeisel SH. Choline and choline esters in human and rat milk and in infant formulas. Am J Clin Nutr 1996;64:572-6.

(27) Zeisel SH, Char D, Sheard NF. Choline, phosphatidylcholine and sphingomyelin in human and bovine milk and infant formulas. J Nutr 1986;116:50-8.

(28) Zeisel SH. Choline and choline esters as required nutrients during pregnancy and lactation. In: Zeisel SH, Szuhaj BF, editors. Choline, Phospholipids, Health and Disease.Champaign, IL: AOCS Press; 1998. p. 131-42.

(29) Zeisel SH. Choline and phosphatidylcholine are important components of an infant's diet. In: Huang YS, Sinclair SJ, editors. Lipids in Infant Nutrition.Champaign, IL: AOCS Press; 1998. p. 192-212.

(30) Ilcol YO, Urncu G, Ulus IH. Free and phospholipid-bound choline concentrations in serum during pregnancy, after delivery, and in newborns. Arch Phys Biochem 2002;110(5):393-9.

(31) Ilcol YO, Ozbek R, Hamurtekin E, Ulus IH. Choline status in newborns, infants, children, breast-feeding women, breast-fed infants and human breast milk. J Nutr Biochem 2005;16:489-99.

(32) Chao CK, Pomfret EA, Zeisel SH. Uptake of choline by rat mammary-gland epithelial cells. Biochem J 1988;254:33-8.

(33) Babb SM, Ke Y, Lange N, Kaufman MJ, Renshaw PF, Cohen BM. Oral choline increased choline metabolites in human brain. Pscyh Res Neuroimag 2004;130:1-9.

(34) Hirsch MJ, Growdon JH, Wurtman RJ. Relations between dietary choline or lecithin intake, serum choline levels, and various metabolic indices. Metabolism 1978;27(8):953-60.

(35) Lokk J. Association of vitamin B12, folate, homocysteine and cognition in the elderly. Scand J Nutr 2003;47(3):132-8.

(36) Ulrey CL, Liu L, Andrews LG, Tollefsbol TO. The impact of metabolism on DNA methylation. Hum Molec Genetics 2005;14(Review Issue 1):R139-R147.

(37) Dudman NP, Wilcken DE, Wang J, Lynch JF, Macey D, Lundberg P. Disordered methionine/homocysteine metabolism in premature vascular disease: Its occurrence, cofactor therapy and enzymology. Arteriocler Thrombosis 1993;13:1253-60.

(38) Cho E, Zeisel SH, Jacques PF, Selhub J, Dougherty L, Colditz GA. Dietary choline and betaine assessed by food-frequency questionnaire in relation to plasma total homocysteine concentration in the Framingham Offspring Study. Am J Clin Nutr 2006;83:905-11.

(39) McCully KS. Homocysteine and vascular disease: The rold of folate, choline and lipoproteins in homocysteine metabolism. In: Zeisel SH, Szuhaj BF, editors. Choline, Phospholipids, Health and Disease.Champaign, IL: AOCS Press; 1998. p. 117-30.

(40) Olthof MR, Brink EJ, Katan MB, Verhoef P. Choline supplemented as phosphatidylcholine decreases fasting and postmethionine-loading plasma homocysteine concentrations in healthy men. Am J Clin Nutr 2005;82:111-7.

(41) Verhoef P, de Groot LCPGM. Dietary determinants of plasma homocysteine concentrations. Seminars in Vascular Medicine 2005;5(2):110-23.

(42) Hustad S, Midttun O, Schneede J, Vollset S, Grotmol T, Ueland PM. The methylenetetrahydrofolate reductase 677 C->T polymorphism as a modulator of a B vitamin network with major effects on homocysteine metabolism. Am J Hum Genet 2007;80:846-55.

(43) James SJ, Melnyk S, Pogribna M, Pogribny I, Caudill MA. Elevation in S-adenosylmethionine and DNA hypomethylation: Potential epigenetic mechanism for homocysteine-related pathology. J Nutr 2002;132:2361S-6S.

(44) Malinow MR. Plasma homocysteine and arterial occlusive diseases: a mini-review. Clin Chem 1995;41(1):173-6.

(45) Malinow MR. Plasma homocysteine: a risk factor for arterial occlusive diseases. J Nutr 1996;126(4):1238S-43S.

(46) Molloy AM, Mills JL, Cox C, Daly SF, Conley M, Brody LC et al. Choline and homocysteine interrelations in umbilical cord and maternal plasma at delivery. Am J Clin Nutr 2005;82:836-42.

(47) Velzing-Aarts FV, Holm PI, Fokkema MR, van der Dijs FP, Ueland PM, Muskiet FA. Plasma choline and betaine and their relation to plasma homocysteine in normal pregnancy. Am J Clin Nutr 2005;81:1383-9.

(48) Vollset S, Refsum H, Irgens L, Emblem BM, Tverdal A, Gjessing HK et al. Plasma total homocysteine, pregnancy complications and adverse pregnancy outcomes: the Hordaland Homocysteine study. Am J Clin Nutr 2000;71:962-8.

(49) Zeisel SH. Choline, homocysteine and pregnancy. Am J Clin Nutr 2005;82:719-20.

(50) Gibbons GF, Wiggins D, Brown AM, Hebbachi AM. Synthesis and function of hepatic very-low-density lipoprotein. Biochem Soc Trans 2004;32(1):59-64.

(51) Yao Z, Vance DE. The active synthesis of phosphatidylcholine is required for very low density lipoprotein secretion from rat hepatocytes. J Biol Chem 1988;263(6):2998-3004.

(52) Yao Z, Vance DE. Head group specificity in the requirement of phosphatidylcholine biosynthesis for vrey low density lipoprotein secretion from cultured hepatocytes. J Biol Chem 1989;264(19):11373-80.

(53) daCosta KA, Niculescu M, Craciunescu CN, Fischer LM, Zeisel SH. Choline deficiency increases lymphocyte apoptosis and DNA damage in humans. Am J Clin Nutr 2006;84:88-94.

(54) daCosta KA, Badea M, Fischer LM, Zeisel SH. Elevated serum creatine phosphokinase in choline-deficient humans: mechanistic studies in C2C12 mouse myoblasts. Am J Clin Nutr 2004;80:163-70.

(55) Waite KA, Cabilio NR, Vance DE. Choline deficiency-induced liver damage is reversible in *Pemt*$^{-/-}$ mice. J Nutr 2002;132:68-71.

(56) Garrow TA. Choline. In: Zempleni J, Rucker RB, McCormick DB, Suttie JW, editors. Handbook of Vitamins. 4 ed. Boca Raton, FL: CRC Press; 2007. p. 459-87.

(57) McDowell LR. Vitamins in Animal and Human Nutrition. Ames, IA: Iowa State University Press; 2000.

(58) Combs GF. The Vitamins: Fundamental Aspects in Nutrition and Health. 3 ed. Burlington, MA: Elsevier Academic Press; 2008.

(59) LSRO, FASEB. Evaluation of the Health Aspects of Choline Chloride and Choline Bitartrate as Food Ingredients. Washington, DC: Department of Health, Education and Welfare; 1975. Report No.: SCOGS-42.

(60) LSRO F. Assessment of Nutrient Requirements for Infant Formulas. J Nutr 1998;128(11S):2126S-7S.

(61) Galloway S, Bloom A, Resnick M, Margolin B, Nakamura F, Archer P et al. Development of a standard protocol for in vitro cytogenetic testing with Chinese hamster ovary cells: Comparison of results for 22 compounds in two laboratories. Environ Mutagen 1985;7:1-52.

(62) Haworth S, Lawlor T, Mortelmans K, Speck W, Zeiger E. Salmonella mutagenicity test results for 250 chemicals. Environ Mutagen 1983;5(Suppl. 1):3-142.

(63) Mutagenicity evaluation of choline chloride FCC 000067-48-1 FDA 75-69. Kensington, MD; 1977. Report No.: FDA/BF-77/87.

(64) Blusztajn JK, Wurtman RJ. Choline and cholinergic neurons. Science 1983;221:614-20.

(65) Blusztajn JK, Liscovitch M, Richardson UI. Synthesis of acetylcholine from choline derived from phosphatidylcholine in a human neuronal cell line. PNAS 1987;84:5474-7.

(66) Leventer SM, Rowell PP. Investigation of the rate-limiting step in the synthesis of acetylcholine by the human placenta. Placenta 2005 May;5(3):261-70.

(67) Cohen EL, Wurtman RJ. Brain acetylcholine: Increase after systemic choline administration. Life Sci 1975;16(16):1095-102.

(68) Cohen EL, Wurtman RJ. Brain acetylcholine: Control by dietary choline. Science 1976;191(4227):561-2.

(69) Zeisel SH. Dietary choline:Biochemistry, physiology, and pharmacology. Annu Rev Nutr 1981;1:95-121.

(70) Kamath AV, Darling IM, Morris ME. Choline uptake in human intestinal Caco-2 cells is carrier-mediated. J Nutr 2003;133:2607-11.

(71) Sweiry JH, Yudilevich DL. Characterization of choline transport at maternal and fetal interfaces of the perfused guinea-pig placenta. J Physiol 1985;366:251-66.

(72) Zeisel SH. Dietary influences on neurotransmission. Adv Pediatr 1986;33:23-48.

(73) Lockman PR, Allen DD. The transport of choline. Drug Dev Indust Pharm 2002;28(7):749-71.

(74) Wessler I, Kirkpatrick CJ. Acetylcholine beyond neurons: the non-neuronal cholinergic system in humans. Brit J Pharmacolog 2008;154:1558-71.

(75) de la Huerga J, Popper H. Factors influencing cholineabsorption in the intestinal tract. J Clin Investig 1952;31(6):598-603.

(76) Castellani AG. Inhibiting effects of amino acids and related compounds upon the growth of enterotoxic micrococci in cream pastry. Applied Micro 1953;1:195-9.

(77) Engle JS, Lipps PE, Graham TL, Boehm MJ. Effects of choline, betaine and wheat floral extracts on growth of *Fusarium graminearum*. Plant Dis 2004;88:175-80.

(78) Jensen HH, Batres-Marquez SP, Carriquiry A, Schallnake KL. Choline in the diets of the U.S. population: NHANES 2003-2004. FASEB J. 21, lb219. 2007.

(79) Fischer LM, Scearce J, Mar MH, Patel JR, Blanchard RT, Macintosh BA et al. *Ad libitum* choline intake in healthy individuals meets or exceeds the proposed adequate intake level. J Nutr 2005;135:826-9.

(80) Keast DR. Food sources of choline in the diets of older U.S. adults: NHANES 1999-2004. 2007 Apr 27; Washington, DC 2007.

(81) Zeisel SH, daCosta KA. Choline: an essential nutrient for public health. Nutr Rev 2009;67(11):615-23.

(82) Fischer LM, daCosta KA, Kwock L, Galanko JA, Zeisel SH. Dietary choline requirements of women: effects of estrogen and genetic variation. Am J Clin Nutr 2010;92(5):1113-9.

(83) Christensen KE, Wu Q, Wang X, Deng L, Caudill MA, Rozen R. Steatosis in mice is associated with gender, folate intake and expression of genes of one-carbon metabolism. J Nutr 2010;140(10):1736-41.

(84) Craciunescu CN, Johnson AR, Zeisel SH. Dietary choline reverses some, but not all, effects of folate deficiency on neurogenesis and apoptosis in the fetal mouse brain. J Nutr 2010;doi: 10.3945/jn.110.122044.

(85) Jacob RA, Jenden DJ, Allman-Farinelli MA, Swendseid ME. Folate nutriture alters choline status of women and men fed low choline diets. J Nutr 1999;129:712-7.

(86) Niculescu M, Zeisel SH. Diet, methyl donors and DNA methylation: Interactions between dietary folate, methionine and choline. J Nutr 2002;132:2333S-5S.

12. Petition justification statement

Use in processed foods - Fortification

Accessory nutrients are a category for which scientific knowledge is emerging, and for which (*optional*) dietary use is thought to serve a purpose of enhancement of health and well-being. An essential nutrient, however, is one that is *necessary* to sustain normal organ and system function, but is produced in insufficient quantity by endogenous synthesis. Though choline may not be strictly biochemically categorized as a vitamin, its nutritional importance in the diet for many species must be emphasized. Minimally, choline should be considered an *essential*, rather than *accessory* nutrient, by current working definitions[14], and Balchem Corporation advocates clarification of this designation in the National List.

Recent population studies suggest that a significant portion of the US population does not consume dietary choline at current recommended levels (78), contrary to earlier data from certain smaller-scale investigations (79). Individuals opting to minimize their intake of foods high in fat and cholesterol may be unwittingly eliminating good natural sources of choline (*e.g.* egg yolks, liver, etc.) in their diets, though, exacerbating the shortfall of this important nutrient. Fewer than 10% of Americans currently achieve their target choline intake (78), and the choline shortfall is more apparent in certain ethnic groups (80) and specific subpopulations. For example, there is evidence that approximately 90 percent of pregnant women in the U.S. have usual intakes below the choline AI level (78). Dietary intake is especially critical to individuals with common loss-of-function variations (81) in their genes for choline metabolism (55;82), B-vitamin metabolism (9;10) and one-carbon transfer(7;10;83-86). Choline nutriture is an absolute necessity for infants, for reasons previously discussed. The nutrient remains extremely important as children begin to complement their liquid nutrition with solid foods. Fortified foods and beverages are useful vehicles to deliver choline to these consumers, as the most common nutrient-dense natural sources may not be practical or palatable additions to a child's diet. Several widely-available solid infant/toddler food preparations and "follow-up" formulas, intended for older infants, now also contain this nutrient to meet these needs. Dietary supplements, choline-rich meal-replacement products, and discretionary fortification of foods and beverages, are appropriate ways to deliver necessary choline to consumers. Eliminating from the diet the option of organic foods that are fortified with choline would certainly not improve these current inadequate dietary trends, and it would limit consumer choice.

Use in processed foods – Salt replacement/enhancement

Control of dietary sodium intake has been identified as an important objective in improving American public health and nutrition, as indicated in the recent USDA *Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans, 2010*[15]. Most segments of the American population consume sodium in excess of tolerable upper limits (UL) via their dietary choices. Processed foods are

[14] [DRAFT] Overview of Accessory/Voluntary Nutrients – Prepared for the USDA National Organic Program and the National Organic Standards Board, February 5, 2010. Accessed on 9/20/10 at:
http://www.ams.usda.gov/AMSv1.0/getfile?dDocName=STELPRDC5084069
15 http://www.cnpp.usda.gov/DGAs2010-DGACReport.htm

widely known to be a major source of sodium, primarily in the form of sodium chloride. The unique non-nutritive functionality of choline chloride as a partial replacement for (and flavor enhancer of) sodium chloride provides a new option in reformulation of processed foods to reduce their sodium content. Choline chloride represents a functional alternative to salt replacers such as potassium chloride, monosodium glutamate, and autolyzed yeast, which are not currently listed as allowable in the National Organic Program.

Use in livestock feed

Although almost all animals can produce choline in the body, dietary choline is required for optimal nutrition (56)). Despite the naturally-occurring choline content of livestock diets, most growing animals require some level of supplemental choline specific to species, age and life stage. Choline salts help to bring bioavailable choline content up to recommended levels. The need to supplement organic feed with choline (as choline chloride or choline bitartrate) may be further elevated for organic production, as these methods prohibit the use of naturally choline-rich mammalian slaughter by-products (*e.g.* poultry meal).

Water-soluble choline salts choline chloride and choline bitartrate are very easily added to virtually any processed food or feed product, liquid, tablet or capsule. They have a long history of safe use and a minimal environmental impact in manufacture and use. Choline chloride and choline bitartrate deliver a greater bioavailable cation content (74 and 40%, respectively) than do naturally-occuring forms (e.g. phosphatidylcholine, soybean meal, etc.), and they exhibit excellent stability and high bioavailability in virtually all applications.

13. Confidential Business Information Statement

The process flow diagrams describing Balchem Corporation's synthesis of choline salts are considered a trade secret.

APPENDIX

Appendix Section 1.

Adequate Intake and Upper Limits for dietary choline

1. Dietary Reference Intakes and Upper Limits for choline as designated by the Institute of Medicine.

Choline intakes were measured in the National Health and Nutrition Examination Survey (NHANES) study.

Age	Dietary Reference Intake (mg)[1]		Upper limit (mg)[1]	Mean Actual Intake (mg)[35]	
	Male	Female		Male	Female
1-3y	200		1000	224	
4-8y	250		1000	244	
9-13y	375	375	2000	275	237
14-18y	550	400	3000	337	232
19-50y	550	425	3500	415	264
51-70	550	425		372	276
≥71	550	425		327	253

Appendix Section 2.

Current USP and FCC monographs for choline bitartrate and choline chloride

Choline Bitartrate

USP Image 3D Image

$C_9H_{19}NO_7$ 253.25

2-Hydroxyethanaminium,-*N*,*N*,*N*-trimethyl-, [*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate (1:1).
(2-Hydroxyethyl)trimethylammonium-L-(+)-tartrate salt (1:1) [87-67-2].

» Choline Bitartrate contains not less than 99.0 percent and not more than 100.5 percent of $C_9H_{19}NO_7$, calculated on the anhydrous basis.

Packaging and storage— Preserve in well-closed containers.

USP REFERENCE STANDARDS ⟨ 11 ⟩—

USP Choline Bitartrate RS

USP Choline Chloride RS

Identification—

A: *Infrared Absorption* ⟨ 197K ⟩.

B: Dissolve 1 g of Choline Bitartrate with 20 mL of water, and add 2 mL of potassium chloride solution (1 in 4). A white precipitate of potassium bitartrate is formed.

SPECIFIC ROTATION ⟨ 781S ⟩: between +17.5° and +18.5°.

Test solution: 400 mg per mL, in water.

pH ⟨ 791 ⟩: between 3.0 and 4.0, in a solution (1 in 10).

WATER, *Method I* ⟨ 921 ⟩: not more than 0.5%.

RESIDUE ON IGNITION ⟨ 281 ⟩: not more than 0.1%.

ARSENIC, *Method I* ⟨ 211 ⟩— Proceed as directed in the test for *Arsenic* under *Choline Chloride:* the limit is 2 µg per g.

LEAD ⟨ 251 ⟩— Proceed as directed in the test for *Lead* under *Choline Chloride:* not more than 0.3 µg per g is found.

HEAVY METALS, *Method II* ⟨ 231 ⟩: 10 µg per g.

Limit of total amines— Proceed as directed in the test for *Limit of total amines* under *Choline Chloride:* not more than 10 µg per g.

Test solution— Transfer 10.0 g of Choline Bitartrate to a beaker containing a plastic-coated stirring bar, add 70 mL of sodium hydroxide TS and 130 mL of water, and stir until dissolved.

Chromatographic purity—

Buffer solution, Mobile phase, Standard solution, and *Chromatographic system*— Proceed as directed in the test for *Chromatographic purity* under *Choline Chloride*.

Test solution— Transfer about 500 mg of Choline Bitartrate, accurately weighed, to a centrifuge tube; add 2.0 mL of water; and swirl to dissolve. Add 0.5 mL of potassium chloride solution (7.5 in 25), centrifuge, and transfer 1.0 mL of the supernatant to a 24-mL screw-capped vial. Dry at 120° for 2 hours. Add 400 mg of 3,5-dinitrobenzoyl chloride and 10 mL of acetonitrile, and mix. Cap the vial, and heat at 55° for 2 hours. Cool to room temperature, add 5 mL of water, and allow to stand for 5 minutes. Quantitatively transfer this solution to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Pipet 2.0 mL of the solution to a 25-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Procedure— Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure all the peak responses. Calculate the percentage of each impurity in the portion of Choline Bitartrate taken by the formula:

$$(253.25/139.62)62{,}500(C/W)(r_i / r_S)$$

in which 253.25 and 139.62 are the molecular weights of choline bitartrate and choline chloride, respectively; C is the concentration of *USP Choline Chloride RS*, in mg per mL, in the *Standard solution; W* is the weight, in mg, of Choline Bitartrate taken to prepare the *Test solution;* r_i is the peak response for each impurity, other than that of the choline bitartrate derivative and 3,5-dinitrobenzoic acid; and r_S is the peak response for the choline chloride derivative in the *Standard solution:* not more than 0.3% of any individual impurity is found; and not more than 2.0% of total impurities is found.

RESIDUAL SOLVENTS ⟨467⟩**:** meets the requirements, except that the limit for 1,4-dioxane is 10 µg per g.

Assay— Transfer about 200 mg of Choline Bitartrate, accurately weighed, to a conical flask, and dissolve with 50 mL of glacial acetic acid. Titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically (see *Titrimetry* ⟨541⟩). Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 25.32 mg of $C_9H_{19}NO_7$.

Auxiliary Information— Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
Monograph	Huy T. Dinh, M.S. Scientific Liaison 1-301-816-8594	(DS2010) Monographs - Dietary Supplements
Reference Standards	RS Technical Services 1-301-816-8129 rstech@usp.org	

USP34–NF29 Page 1107

Pharmacopeial Forum: Volume No. 30(3) Page 950

Choline Bitartrate

First Published: Prior to FCC 6

(2-Hydroxyethyl)trimethylammonium-L-(+)-tartrate Salt

$C_9H_{19}NO_7$

Formula wt 253.25

INS: 1001(v)

CAS: [87-67-2]

DESCRIPTION

Choline Bitartrate occurs as a white, hygroscopic, crystalline powder. It is freely soluble in water, slightly soluble in alcohol, and insoluble in ether and in chloroform.

Function: Nutrient

Packaging and Storage: Store in tight containers.

IDENTIFICATION

Change to read:

- **A.** ▲**INFRARED ABSORPTION,** ▲*FCC 7* *Spectrophotometric Identification Tests,* Appendix IIIC

  ▲**Reference standard:** USP Choline Bitartrate RS

  Sample and standard preparation: *K*

  Acceptance criteria: The spectrum of the sample exhibits maxima at the same wavelengths as those in the spectrum of the *Reference standard.* ▲*FCC 7*

- **B. PROCEDURE**

  Sample: 500 mg

  Analysis: Dissolve the *Sample* in 2 mL of iodine TS. A red-brown precipitate forms immediately. Add 5 mL of 1 N sodium hydroxide. The precipitate dissolves, and the solution becomes clear yellow. Heat the solution.

  Acceptance criteria: A pale yellow precipitate forms following the heating step.

- **C. PROCEDURE**

  Sample solution: 10 mg/mL

  Analysis: Add 1 mL of the *Sample solution* and 2 mL of a 20 mg/mL solution of potassium ferrocyanide to 2 mL of cobaltous chloride TS.

Acceptance criteria: An emerald green color develops immediately.

ASSAY

- **PROCEDURE**

Sample: 500 mg

Analysis: Transfer the *Sample* into a 250-mL Erlenmeyer flask. Add 50 mL of glacial acetic acid and warm on a steam bath until dissolution is complete. Cool, add 2 drops of crystal violet TS, and titrate with 0.1 N perchloric acid in glacial acetic acid to a green endpoint. [**CAUTION**— Handle perchloric acid in an appropriate fume hood.] Perform a blank determination (see *General Provisions*), and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 25.36 mg of $C_9H_{19}NO_7$.

Acceptance criteria: NLT 98.0% of $C_9H_{19}NO_7$, calculated on the anhydrous basis

IMPURITIES

Inorganic Impurities

- **LEAD**, *Lead Limit Test, Flame Atomic Absorption Spectrophotometric Method*, Appendix IIIB

Sample: 5 g

Acceptance criteria: NMT 2 mg/kg

Organic Impurities

- **1,4-DIOXANE**, Appendix IIIB

Acceptance criteria: Passes test

SPECIFIC TESTS

- **OPTICAL (SPECIFIC) ROTATION**, Appendix IIB

Sample solution: 400 mg/mL

Acceptance criteria: $[\alpha]_D^{25}$ between 17.5° and 18.5°

- **RESIDUE ON IGNITION (SULFATED ASH)**, Appendix IIC

Sample: 2 g

Acceptance criteria: NMT 0.1%

- **WATER**, *Water Determination*, Appendix IIB

Sample solution: 2 g of sample in 50 mL of methanol.

[NOTE— Alternatively, the *Water Determination* can be made by drying the sample in a vacuum desiccator over phosphorus pentoxide for 4 h.]

Acceptance criteria: NMT 0.5%

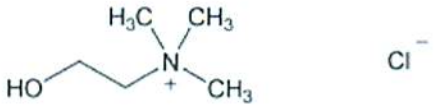
Auxiliary Information— Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee

Monograph	Jeffrey Moore, Ph.D. Scientific Liaison 1-301-816-8288	(FI2010) Monographs - Food Ingredients

FCC Seventh Edition Page 211

Choline Chloride



USP Image 3D Image

$C_5H_{14}ClNO$ 139.62

(2-Hydroxyethyl)trimethylammonium chloride.

2-Hydroxy-*N*,*N*,*N*,-trimethylethanaminium chloride [67-48-1].

» Choline Chloride contains not less than 99.0 percent and not more than 100.5 percent of $C_5H_{14}ClNO$, calculated on the anhydrous basis.

Packaging and storage— Preserve in well-closed containers.

USP REFERENCE STANDARDS ⟨ 11 ⟩—

USP Choline Chloride RS

Identification—

A: *Infrared Absorption* ⟨ 197K ⟩.

B: A solution (1 in 20) meets the requirements of the tests for *Chloride* ⟨ 191 ⟩.

pH ⟨ 791 ⟩**:** between 4.0 and 7.0, in a solution (1 in 10).

WATER, *Method I* ⟨ 921 ⟩**:** not more than 0.5%.

RESIDUE ON IGNITION ⟨ 281 ⟩**:** not more than 0.05%.

ARSENIC, *Method I* ⟨ 211 ⟩— Add 30 mL of water and 5 mL of hydrochloric acid to dissolve the sample: the limit is 2 µg per g.

LEAD ⟨ 251 ⟩— [NOTE—Use methylene chloride in place of chloroform to prepare the *Dithizone Extraction Solution* and *Standard Dithizone Solution.*]

Ammonium hydroxide–sodium hydroxide solution— Transfer 8.4 g of sodium hydroxide solution (1 in 2) to a plastic bottle, add 100 mL of ammonium hydroxide, and mix.

Standard solution— Transfer 1.0 mL of the *Diluted Standard Lead Solution* to a separatory funnel containing 25.0 mL of water.

Test solution— Dissolve 3.00 g in a separatory funnel containing 25.0 mL of water.

Procedure— Separately add 6.0 mL of *Ammonium Citrate Solution* and 3.0 mL of *Potassium Cyanide Solution* to the *Standard solution* and the *Test solution.* Extract each of the resulting

solutions three times with 5.0-mL portions of *Dithizone Extraction Solution*, shaking for 60 seconds and draining off each extract into another separator. Shake the combined dithizone solutions for 30 seconds with 20.0 mL of nitric acid (1 in 100), and discard the methylene chloride layer. Add 6.0 mL of *Ammonia Cyanide Solution*, 2 mL of *Ammonium hydroxide–sodium hydroxide solution*, and 10 mL of *Standard Dithizone Solution*, and shake for 45 seconds. Allow the phases to separate, and measure the absorbance of the lower layer at 510 nm with a suitable spectrophotometer. The absorbance of the *Test solution* is not more than the absorbance of the *Standard solution:* not more than 0.3 µg per g is found.

HEAVY METALS, *Method II* ⟨231⟩: 0.001%.

Limit of total amines—

Standard solution— Dissolve an accurately weighed quantity of trimethylamine hydrochloride in water, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of 500 µg per mL.

Test solution— Transfer 10.0 g of Choline Chloride to a beaker containing a plastic-coated stirring bar, add 170 mL of water and 30.0 mL of sodium hydroxide TS, and stir until dissolved.

System suitability solution— Dissolve an accurately weighed quantity of trimethylamine hydrochloride in water, and dilute quantitatively, and stepwise if necessary, to obtain a solution containing 10 µg of trimethylamine hydrochloride per mL. Transfer 10.0 mL of this solution to a beaker containing a plastic-coated stirring bar, add 170 mL of water and 30.0 mL of sodium hydroxide TS, and stir until dissolved.

Electrode system— Use a gas-sensing, ammonia-specific indicating electrode with internal reference connected to a pH meter capable of measuring potentials with a minimum reproducibility of ±0.1 mV (see *pH* ⟨791⟩).

Standard response line— Transfer 30.0 mL of sodium hydroxide TS to a suitable beaker, and add enough water to give a total volume of 200 mL. Add a plastic-coated stirring bar, insert the electrode into the solution, and record the potential, in mV. Continue stirring, and at 5-minute intervals add 0.200, 0.600, 1.00, and 2.00 mL of *Standard solution*, and record the potential after each addition. Plot the logarithms of the cumulative trimethylamine concentrations (0.50, 1.50, 2.50, and 5.00 µg per mL) versus potential, in mV, and determine the slope *(S)* of the *Standard response line* for the electrode.

System suitability— Proceed with the *System suitability solution* as directed for *Test solution* in the *Procedure,* and measure the potentials: the trimethylamine equivalent is between 8.5 and 11.5 mg per L.

Procedure— Rinse the electrode, insert it into the *Test solution,* stir, and record the potential, in mV. Add 0.100 mL of the *Standard solution,* and record the potential. Add another 0.100 mL of the *Standard solution,* and record the potential. [NOTE—If the total change after the second addition of the *Standard solution* is less than 10 mV, add a third aliquot of 0.200 mL.] Calculate the quantity, in µg per g, of total amines in the portion of Choline Chloride taken by the formula:

$$500V_A / (F - 1)W$$

in which V_A is the total volume of the *Standard solution* added to the *Test solution; W* is the weight, in g, of Choline Chloride taken to prepare the *Test solution;* and the correction factor, *F,* is calculated by the formula:

$$\text{antilog } [(mV_F - mV_0) / S]$$

in which mV_F is the final reading, in mV, after the additions of the *Standard solution;* mV_0 is the initial reading, in mV, of the *Test solution;* and *S* is the slope of the *Standard response line* for the electrode: not more than 0.001% is found.

Chromatographic purity—

Buffer solution— Dissolve 7.1 g of anhydrous dibasic sodium phosphate in 1 L of water. Adjust with phosphoric acid to a pH of 2.5.

Mobile phase— Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (70:30).

Standard solution— Transfer an accurately weighed amount, not more than 100 mg, of *USP Choline Chloride RS* to a 24-mL screw-capped vial, and add 400 mg of 3,5-dinitrobenzoyl chloride and 10 mL of acetonitrile. Cap the vial, heat to 55°, and continue heating for 2 hours. Cool to room temperature, and add 5 mL of water. Allow to stand for 5 minutes. Quantitatively transfer the solution to a 25-mL volumetric flask, dilute with acetonitrile to volume, and mix. Dilute a volume of this solution with *Mobile phase* to obtain a solution having a known concentration of 2.0 µg of *USP Choline Chloride RS* per mL.

Test solution— Transfer about 110 mg of Choline Chloride, accurately weighed, to a 24-mL screw-capped vial. Dry at 120° for 2 hours. Add 400 mg of 3,5-dinitrobenzoyl chloride and 10 mL of acetonitrile. Cap the vial, heat to 55°, and continue heating for 2 hours. Cool to room temperature, and add 5 mL of water. Allow to stand for 5 minutes. Quantitatively transfer the solution to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Pipet 2.0 mL of the solution to a 25-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see **CHROMATOGRAPHY** ⟨621⟩)— The liquid chromatograph is

equipped with a 208-nm detector and a 4.6-mm × 25-cm column that contains packing L7. The column temperature is maintained at 30°. The flow rate is about 1.0 mL per minute. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the capacity factor, *k′,* is not less than 2; and the relative standard deviation determined from the choline chloride derivative peak is not more than 5%.

Procedure— Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure all the peak responses. Calculate the percentage of each impurity in the portion of Choline Chloride taken by the formula:

$$62{,}500(C/W)(r_i / r_S)$$

in which *C* is the concentration, in mg per mL, of *USP Choline Chloride RS* in the *Standard solution; W* is the weight, in mg, of Choline Chloride taken to prepare the *Test solution;* r_i is the peak response for each impurity, other than that for the choline chloride derivative and 3,5-dinitrobenzoic acid obtained from the *Test solution;* and r_S is the peak response for the choline chloride derivative obtained from the *Standard solution:* not more than 0.3% of any individual impurity is found; and not more than 2.0% of total impurities is found.

RESIDUAL SOLVENTS ⟨467⟩: meets the requirements, except that the limit for 1,4-dioxane is 10 µg per g.

Assay— Transfer an accurately weighed quantity of Choline Chloride, about 120 mg, to a conical flask, dissolve in 35 mL of water, and add 3 drops of acetic acid. Titrate with 0.1 N silver nitrate VS, determining the endpoint potentiometrically (see *Titrimetry* ⟨541⟩). Perform a blank determination, and make any necessary correction. Each mL of 0.1 N silver nitrate is equivalent to 13.96 mg of $C_5H_{14}ClNO$.

Auxiliary Information— Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
Monograph	Huy T. Dinh, M.S. Scientific Liaison 1-301-816-8594	(DS2010) Monographs - Dietary Supplements
Reference Standards	RS Technical Services 1-301-816-8129 rstech@usp.org	

USP34–NF29 Page 1108

Pharmacopeial Forum: Volume No. 31(1) Page 84

Chromatographic Column—

CHOLINE CHLORIDE

Chromatographic columns text is not derived from, and not part of, USP 34 or NF 29.

Choline Chloride

First Published: Prior to FCC 6

(2-Hydroxyethyl)trimethylammonium Chloride

$C_5H_{14}ClNO$

Formula wt 139.65

INS: 1001(iii)

CAS: [67-48-1]

DESCRIPTION

Choline Chloride occurs as colorless or white crystals or as a crystalline powder. It is hygroscopic, and is very soluble in water and in alcohol.

Function: Nutrient

Packaging and Storage: Store in tight containers.

IDENTIFICATION

- **A. CHLORIDE,** Appendix IIIA

  Sample solution: 50 mg/mL

  Acceptance criteria: Passes tests

Change to read:

- **B.**

  ▲**INFRARED ABSORPTION,** *Spectrophotometric Identification Tests,* Appendix IIIC

  Reference standard: USP Choline Chloride RS

Sample and standard preparation: *K*

Acceptance criteria: The spectrum of the sample exhibits maxima at the same wavelengths as those in the spectrum of the *Reference standard*. ▲ FCC 7

- **C. PROCEDURE**

Sample: 500 mg

Analysis: Dissolve the *Sample* in 2 mL of iodine TS. A red-brown precipitate forms immediately. Add 5 mL of 1 N sodium hydroxide. The precipitate dissolves, and the solution becomes clear yellow. Heat the solution.

Acceptance criteria: A pale yellow precipitate forms following the heating step.

- **D. PROCEDURE**

Sample solution: 10 mg/mL

Analysis: Add 1 mL of the *Sample solution* and 2 mL of a 20 mg/mL solution of potassium ferrocyanide to 2 mL of cobaltous chloride TS.

Acceptance criteria: An emerald green color develops immediately.

ASSAY

- **PROCEDURE**

Sample: 300 mg

Analysis: Transfer the *Sample* into a 250-mL Erlenmeyer flask. Add 50 mL of glacial acetic acid and warm on a steam bath until dissolution is complete. Cool, add 10 mL of mercuric acetate and 2 drops of crystal violet TS, and titrate with 0.1 N perchloric acid in glacial acetic acid to a green endpoint. [**CAUTION**— Handle perchloric acid in an appropriate fume hood.] Perform a blank determination (see *General Provisions*), and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 13.96 mg of $C_5H_{14}ClNO$.

Acceptance criteria: 98.0%–100.5% of $C_5H_{14}ClNO$, calculated on the anhydrous basis

IMPURITIES

Inorganic Impurities

- **LEAD**, *Lead Limit Test, Flame Atomic Absorption Spectrophotometric Method*, Appendix IIIB

Sample: 5 g

Acceptance criteria: NMT 2 mg/kg

- **WATER**, *Water Determination*, Appendix IIB

[NOTE— Alternatively, the *Water Determination* can be made by drying the sample in a vacuum desiccator over phosphorus pentoxide for 4 h.]

Acceptance criteria: NMT 0.5%

Organic Impurities

- **1,4-DIOXANE**, Appendix IIIB

  Acceptance criteria: Passes test

SPECIFIC TESTS

- **RESIDUE ON IGNITION (SULFATED ASH)**, Appendix IIC

  Sample: 4 g

  Acceptance criteria: NMT 0.05%

Auxiliary Information— Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
Monograph	Jeffrey Moore, Ph.D. Scientific Liaison 1-301-816-8288	(FI2010) Monographs - Food Ingredients

FCC Seventh Edition Page 212

Appendix Section 3.

All specifications for choline products manufactured by Balchem Corporation for the food and feed industries

Product Specification Sheet

Choline Chloride

USP FCC

Product code USA product code: F6522120

Formula $C_5H_{14}ClNO$

Synonyms 2-Hydroxy-*N,N,N*-trimethylethanaminium chloride

CAS N°: 6**7-48-1** Trimethyl (2-hydroxyethyl) ammonium chloride

Appearance White, crystalline solid, hygroscopic

Quality

Determination	Specification	Reference
Appearance	passes test	
Assay	99.0 % w/w minimum	USP
Identification test*	passes test B	USP
Infrared spectrum*	passes test	USP
pH (10% solution)	4-7	USP
Water	0.5 % w/w maximum	USP
Residue on ignition	0.05 % w/w maximum	USP
Arsenic*	2 mg/kg maximum	USP
Lead*	0.3 mg/kg maximum	USP
Heavy metals as Lead*	10 mg/kg maximum	USP
Chromatographic purity*	passes test	USP
Residual solvents*	passes test	USP
1,4-Dioxane*	10 mg/kg maximum	USP
Total amines as TMA	10 mg/kg maximum	USP
Total plate count**	100 cfu/g maximum	AOAC
Yeast and molds**	30 cfu/g maximum	AOAC
*Escherichia coli***	negative/10g	AOAC
*Salmonella***	negative/25g	AOAC
Total coliform**	negative/10g	AOAC
*Enterobacteriaceae***	negative/10g	AOAC
*Cronobacter spp***	negative/10g	AOAC
Sulphite Reducing *Clostridia***	negative/1g	AOAC
*Staphylococcus aureus***	negative/10g	AOAC
Bacillus cereus spores**	negative/10g	AOAC
*Listeria monocytogenes***	negative/25g	AOAC

*Analysis regularly performed from selected lots in compliance with Balchem's documented quality control program.

**Microbiological testing is done quarterly on representative samples.

LO-ODOR ™ TECHNOLOGY

52 Sunrise Park Road • New Hampton, New York 10958 • Tel. 845.326.5675 • Fax 845.326.5717 • www.balchem.com

Product Specification Sheet

Retest date	1 year from date of manufacture
Physical Properties	See MSDS sheet
Applications	Nutritional additive
Packaging	Net weight = 25 Kg (55.115 lbs), in a 12-gallon fiber drum, with two polyethylene liners. Desiccant Bag placed between liners. Drum dimensions: 22.75"H x 12.5" D = 1.6 cft. Gross weight = 26.3 kg (57 lbs) Heat treated wooden pallets are ISPM 15 compliant measuring 40" x 48" x 4" Full pallet qty is 24 drums, 600 kg. Pallets are wrapped with 80 gauge stretch film.
Health and safety	See MSDS sheet
Regulatory info United States	Balchem manufactures according to Good Manufacturing Practices, GMPs as defined in 21 CFR, part 110. Choline Chloride is Generally Regarded As Safe (GRAS) when used according to 21 CFR 182.8252
Europe	Choline Chloride is currently acceptable for use in foods for particular nutritional uses, as described in: Directive 2009/39/EC Commission Regulation No. 953/2009
Contacts	Balchem Corporation 52 Sunrise Park Road, New Hampton, NY 10958 Phone +1 845 326 5675 Fax 845-326-5717 Email:nutrients@balchem.com
Note	These conditions can be subject to amendments
Certifications	Halal certified by IFANCA, the Islamic Food and Nutrition Council of America Kosher certified by Orthodox Union, the Union of Orthodox Jewish Congregations of America
Version	Jan 2011 Revision 02

VitaCholine™

LO-ODOR ™ TECHNOLOGY

C-Salt™

F6526120

PRODUCT SPECIFICATIONS:

Appearance	White crystalline solid
Water, %	0 – 1 %
Assay (anhydrous choline chloride), %	97 – 99 %

TYPICAL PROPERTIES:

Composition	Choline Chloride (21CFR182.8252), Magnesium Stearate (21CFR184.1440, E470b)
Characteristics	Slight amine-like odor. Hygroscopic. Occasional soft clumps.
Choline cation content	72-74%

INGREDIENT STATEMENT: *Choline Chloride, Magnesium Stearate*

C-Salt™ is Kosher and non-GMO.

PACKAGING:

Drums:

- 25 kilograms in a 12-gallon fiber drum, with two polyethylene liners
- 12.5" x 22.75" = 1.6 cft.
- Net Weight = 25 kilos (55.115 pounds)
- Gross Weight = 26.3 kilos (57 pounds)

Pallet/Skid:

- 12 drums per pallet
- 26" (H) x 48" (L) x 40" (W) = 28.89 cft.
- Net Weight = 300 kilos (661.38 pounds)
- Pallets are wrapped with 80 gauge stretch film

FOR CONSULTATION OR NEEDS ANALYSIS:

Balchem Corporation
52 Sunrise Park Road
New Hampton, NY 10958
Phone: 845.355.5302
Fax: 845.326.5717
e-mail: foodinfo@balchem.com
www.balchem.com

Product Specification Sheet

Choline Bitartrate Conditioned 20 Mesh

USP FCC (prior to conditioning)

Product code USA product code: F6502120

Formula $C_9H_{19}NO_7$

Synonyms
(2-Hydroxyethyl) trimethylammonium bitartrate
Choline hydrogen tartrate
(L+)-choline bitartrate

CAS N°: **87-67-2** (*choline bitartrate from natural L(+)-tartaric acid*)

Appearance White, crystalline solid, hygroscopic powder, free from foreign materials

Quality

Determination	Specification	Reference
Appearance	pass test	
Assay (after conditioning)	98.0 % w/w minimum	USP
Assay (prior to conditioning)	99.0 % w/w minimum	
Identification test*	pass test B	USP
Infrared spectrum*	pass test	USP
Specific rotation*	between +17.5° and +18.5°	USP
pH (10% solution)	3-4	USP
Water	0.5 % w/w maximum	USP
Residue on ignition (prior to conditioning)	0.1% w/w maximum	USP
Arsenic*	2 mg/kg maximum	USP
Lead*	0.3 mg/kg maximum	USP
Heavy metals as Lead*	10 mg/kg maximum	USP
Chromatographic purity*	pass test	USP
Residual solvents*	pass test	USP
1,4-Dioxane*	10 mg/kg maximum	USP
Silicon dioxide (conditioning agent)	0.5-1.0 % w/w	USP
Total amines as TMA	10 mg/kg maximum	USP
Particle size 20 mesh	2% w/w maximum	VGM
Total plate count**	100 cfu/g maximum	AOAC
Yeast and molds**	30 cfu/g maximum	AOAC
*Escherichia coli***	negative/10g	AOAC
*Salmonella***	negative/25g	AOAC
Total coliform**	negative/10g	AOAC
*Enterobacteriaceae***	negative/10g	AOAC
*Cronobacter spp***	negative/10g	AOAC
*Staphylococcus aureus***	negative/10g	AOAC
Bacillus cereus spores**	negative/10g	AOAC
*Listeria monocytogenes***	negative/25g	AOAC

*Analysis regularly performed from selected lots in compliance with Balchem's documented quality control program.
**Microbiological testing is done quarterly on representative samples.

LO-ODOR ™ TECHNOLOGY

52 Sunrise Park Road • New Hampton, New York 10958 • Tel. 845.326.5675 • Fax 845.326.5717 • www.balchem.com

Product Specification Sheet

Retest date	3 years from date of manufacture
Physical Properties	See MSDS sheet
Applications	Nutritional additive
Packaging	Net weight = 25 Kg (55.115 lbs), in a 12-gallon fiber drum, with two polyethylene liners. Drum dimensions: 22.75"H x 12.5" D = 1.6 cft. Gross weight = 26.3 kg (57 lbs) Heat treated wooden pallets are ISPM 15 compliant measuring 40" x 48" x 4" Full pallet qty is 24 drums, 600 kg. Pallets are wrapped with 80 gauge stretch film.
Health and safety	See MSDS sheet
Regulatory info United States	Balchem manufactures according to Good Manufacturing Practices, GMPs as defined in 21 CFR, part 110. Choline Bitartrate is Generally Regarded As Safe (GRAS) when used according to 21 CFR 182.8250
Europe	Choline Bitartrate is currently acceptable for use in foods for particular nutritional uses, as described in: Directive 2009/39/EC Commission Regulation No. 953/2009
Contacts	Balchem Corporation 52 Sunrise Park Road, New Hampton, NY 10958 Phone +1 845 326 5675 Fax 845-326-5717 Email:nutrients@balchem.com
Note	These conditions can be subject to amendments
Certifications	Halal certified by IFANCA, the Islamic Food and Nutrition Council of America Kosher certified by Orthodox Union, the Union of Orthodox Jewish Congregations of America
Version	Jan 2011 Revision 02

VitaCholine™

LO-ODOR ™ TECHNOLOGY

Product Specification Sheet

Choline Bitartrate Conditioned 40 Mesh

USP FCC (prior to conditioning)

Product code USA product code: F6472120

Formula $C_9H_{19}NO_7$

Synonyms
(2-Hydroxyethyl) trimethylammonium bitartrate
Choline hydrogen tartrate
(L+)-choline bitartrate

CAS N°: **87-67-2** (*choline bitartrate from natural L(+)-tartaric acid*)

Appearance White, crystalline solid, hygroscopic powder, free from foreign materials

Quality

Determination	Specification	Reference
Appearance	passes test	
Assay (prior to conditioning)	99.0 % w/w minimum	USP
Assay (after conditioning)	97.0 % w/w minimum	
Identification test*	passes test B	USP
Infrared spectrum*	passes test	USP
Specific rotation*	between +17.5° and +18.5°	USP
pH (10% solution)	3-4	USP
Water	0.5 % w/w maximum	USP
Residue on ignition (prior to conditioning)	0.1% w/w maximum	USP
Arsenic*	2 mg/kg maximum	USP
Lead*	0.3 mg/kg maximum	USP
Heavy metals as Lead*	10 mg/kg maximum	USP
Chromatographic purity*	passes test	USP
Residual solvents*	passes test	USP
1,4-Dioxane*	10 mg/kg maximum	USP
Silicon dioxide (conditioning agent)	1.3-1.9 % w/w	USP
Total amines as TMA	10 mg/kg maximum	USP
Particle size 40 mesh	2% w/w maximum	VGM
Total plate count**	100 cfu/g maximum	AOAC
Yeast and molds**	30 cfu/g maximum	AOAC
*Escherichia coli***	negative/10g	AOAC
*Salmonella***	negative/25g	AOAC
Total coliform**	negative/10g	AOAC
*Enterobacteriaceae***	negative/10g	AOAC
*Cronobacter spp***	negative/10g	AOAC
*Staphylococcus aureus***	negative/10g	AOAC
Bacillus cereus spores**	negative/10g	AOAC
*Listeria monocytogenes***	negative/25g	AOAC

*Analysis regularly performed from selected lots in compliance with Balchem's documented quality control program.
**Microbiological testing is done quarterly on representative samples.

LO-ODOR ™ TECHNOLOGY

52 Sunrise Park Road • New Hampton, New York 10958 • Tel. 845.326.5675 • Fax 845.326.5717 • www.balchem.com

Product Specification Sheet

Retest date	3 years from date of manufacture
Physical Properties	See MSDS sheet
Applications	Nutritional additive
Packaging	Net weight = 25 Kg (55.115 lbs), in a 12-gallon fiber drum, with two polyethylene liners. Drum dimensions: 22.75"H x 12.5" D = 1.6 cft. Gross weight = 26.3 kg (57 lbs) Heat treated wooden pallets are ISPM 15 compliant measuring 40" x 48" x 4" Full pallet qty is 24 drums, 600 kg. Pallets are wrapped with 80 gauge stretch film.
Health and safety	See MSDS sheet
Regulatory info United States	Balchem manufactures according to Good Manufacturing Practices, GMPs as defined in 21 CFR, part 110. Choline Bitartrate is Generally Regarded As Safe (GRAS) when used according to 21 CFR 182.8250
Europe	Choline Bitartrate is currently acceptable for use in foods for particular nutritional uses, as described in: Directive 2009/39/EC Commission Regulation No. 953/2009
Contacts	Balchem Corporation 52 Sunrise Park Road, New Hampton, NY 10958 Phone +1 845 326 5675 Fax 845-326-5717 Email:nutrients@balchem.com
Note	These conditions can be subject to amendments
Certifications	Halal certified by IFANCA, the Islamic Food and Nutrition Council of America Kosher certified by Orthodox Union, the Union of Orthodox Jewish Congregations of America
Version	Feb 2011 Revision 01

VitaCholine™

LO-ODOR ™ TECHNOLOGY

BALCHEM

Product Specification Sheet

CHOLINE BITARTRATE Conditioned

USP FCC based on current edition (prior to conditioning)

Product code EU product code: 5400543 USA product code: F6672118

Formula $C_9H_{19}NO_7$

Synonyms
(2-Hydroxyethyl) trimethylammonium bitartrate
Choline hydrogen tartrate
(L+)-choline bitartrate

CAS N°: **87-67-2** (*choline bitartrate from natural L(+)-tartaric acid*)

Appearance White, crystalline, hygroscopic powder, free from foreign materials

Quality

Determination	Specification	Reference
Appearance	pass test	
Assay after conditioning	98.0 % w/w minimum	USP/SAM 723.01
Assay prior to conditioning	99.0 % w/w minimum	USP/SAM 723.05
Identification test*	pass test B	USP
Infrared spectrum*	pass test	USP
Specific rotation*	between +17.5° and +18.5°	USP
pH (10% solution)	3-4	USP
Water	0.5 % w/w maximum	USP
Residue on ignition (prior to conditioning)	0.1% w/w maximum	USP/SAM 260.05
Arsenic*	2 mg/kg maximum	USP/ICP
Lead*	0.3 mg/kg maximum	USP/ICP
Heavy metals as Lead*	10 mg/kg maximum	USP
Chromatographic purity*	pass test	USP
Residual solvents	pass test	USP
1,4-Dioxane*	10 mg/kg maximum	USP
Silicon dioxide E551 (conditioning agent)	0.5-1.0 % w/w	USP/SAM 260.05
Total amines as TMA	10 mg/kg maximum	USP/SAM 839.03
Melting point (prior to conditioning)	147-152°C	SAM F83.9
Particle size 80 mesh*	10% w/w maximum	SAM 721.06
Particle size 40 mesh*	2% w/w maximum	SAM 721.06
Total plate count**	100 cfu/g maximum	ISO
Yeast and moulds**	30 cfu/g maximum	ISO
*Escherichia coli***	negative/10g	ISO
*Salmonella***	negative/25g	ISO
Total coliform**	negative/10g	ISO
*Enterobacteriaceae***	negative/10g	ISO
Cronobacter spp.**	negative/10g	ISO
*Staphylococcus aureus***	negative/10g	ISO
Bacillus cereus spores**	negative/10g	ISO
*Listeria monocytogenes***	negative/25g	ISO

*Analysis regularly performed from selected lots in compliance with Balchem's documented quality control program.
**Microbiological testing is done quarterly on representative samples.

LO-ODOR ™ TECHNOLOGY

Via del Porto snc • 28040 Marano Ticino (NO) - Italy • Tel. +39 0321 9791 • Fax +39 0321 979246 • www.balchem.com

Product Specification Sheet

Retest date	3 years from date of manufacture
Physical Properties	a_w = 0.52 See MSDS sheet
Application	Nutritional additive
Packaging	Packaging Unit Dimensions (l*w*h) = 365x365x268 mm Net weight = 25 Kg, Gross weight = 26 kg Units per pallet = 45 Pallet Dimensions (l*w) = 114x114 cm
Health and safety	See MSDS sheet
Regulatory info	Choline Bitartrate is manufactured in Balchem Italia (Marano Ticino, Italy) in compliance with: – Regulation 178/2002/EC - General requirements of food law. – Regulation 852/2004/EC - Hygiene of foodstuffs. – Commission Directive 2008/84/EC - Purity criteria on food additives. – Commission Regulation 1881/2006/EC - Maximum levels for certain contaminants in foodstuffs. – Commission Regulation 1441/2007/EC – Microbiological criteria for foodstuffs. Choline Bitartrate meets purity requirements for special food applications: – Commission Directive 2006/141/EC - Infant formulae and follow-on formulae. – Commission Directive 2006/125/EC - Processed cereal-based foods and baby foods for infants and young children. – Commission Regulation 953/2009/EC - Substances that may be added for specific nutritional purposes in foods for particular nutritional uses.
Contacts	Balchem Corporation 52 Sunrise Park Road, New Hampton, NY 10958 Phone +1 845 326 5675 Email:nutrients@balchem.com Balchem Italia Via del Porto snc, 28040 Marano Ticino (NO) - Italy Phone +39 0321 9791; Fax +39 0321 979249 Email:HUM-Italy@balchem.com
Note	These conditions can be subject to amendments
Certifications	ISO 22000:2005, ISO 9001:2008 and ISO 14001:2004 Management System Kosher (EuroK) and Halal (HFCE) product certifications
Version	January 2011

LO-ODOR ™ TECHNOLOGY

Product Specification Sheet

Choline Bitartrate Conditioned Regular

USP FCC (prior to conditioning)

Product code USA product code: F6512120

Formula $C_9H_{19}NO_7$

Synonyms
(2-Hydroxyethyl) trimethylammonium bitartrate
Choline hydrogen tartrate
(L+)-choline bitartrate

CAS N°: **87-67-2** (*choline bitartrate from natural L(+)-tartaric acid*)

Appearance White, crystalline solid, hygroscopic powder, free from foreign materials

Quality

Determination	Specification	Reference
Appearance	pass test	
Assay (after conditioning)	98.0 % w/w minimum	
Assay (prior to conditioning)	99.0 % w/w minimum	USP
Identification test*	pass test B	USP
Infrared spectrum*	pass test	USP
Specific rotation*	between +17.5° and +18.5°	USP
pH (10% solution)	3-4	USP
Water	0.5 % w/w maximum	USP
Residue on ignition (prior to conditioning)	0.1% w/w maximum	USP
Arsenic*	2 mg/kg maximum	USP
Lead*	0.3 mg/kg maximum	USP
Heavy metals as Lead*	10 mg/kg maximum	USP
Chromatographic purity*	pass test	USP
Residual solvents*	pass test	USP
1,4-Dioxane*	10 mg/kg maximum	USP
Silicon dioxide (conditioning agent)	0.5-1.0 % w/w	USP
Total amines as TMA	10 mg/kg maximum	USP
Total plate count**	100 cfu/g maximum	AOAC
Yeast and molds**	30 cfu/g maximum	AOAC
*Escherichia coli***	negative/10g	AOAC
*Salmonella***	negative/25g	AOAC
Total coliform**	negative/10g	AOAC
*Enterobacteriaceae***	negative/10g	AOAC
*Cronobacter spp***	negative/10g	AOAC
*Staphylococcus aureus***	negative/10g	AOAC
Bacillus cereus spores**	negative/10g	AOAC
*Listeria monocytogenes***	negative/25g	AOAC

*Analysis regularly performed from selected lots in compliance with Balchem's documented quality control program.
**Microbiological testing is done quarterly on representative samples.

LO-ODOR ™ TECHNOLOGY

52 Sunrise Park Road • New Hampton, New York 10958 • Tel. 845.326.5675 • Fax 845.326.5717 • www.balchem.com

Product Specification Sheet

Retest date	3 years from date of manufacture
Physical Properties	See MSDS sheet
Applications	Nutritional additive
Packaging	Net weight = 25 Kg (55.115 lbs), in a 12-gallon fiber drum, with two polyethylene liners. Drum dimensions: 22.75"H x 12.5" D = 1.6 cft. Gross weight = 26.3 kg (57 lbs) Heat treated wooden pallets are ISPM 15 compliant measuring 40" x 48" x 4" Full pallet qty is 24 drums, 600 kg. Pallets are wrapped with 80 gauge stretch film.
Health and safety	See MSDS sheet
Regulatory info United States	Balchem manufactures according to Good Manufacturing Practices, GMPs as defined in 21 CFR, part 110. Choline Bitartrate is Generally Regarded As Safe (GRAS) when used according to 21 CFR 182.8250
Europe	Choline Bitartrate is currently acceptable for use in foods for particular nutritional uses, as described in: Directive 2009/39/EC Commission Regulation No. 953/2009
Contacts	Balchem Corporation 52 Sunrise Park Road, New Hampton, NY 10958 Phone +1 845 326 5675 Fax 845-326-5717 Email:nutrients@balchem.com
Note	These conditions can be subject to amendments
Certifications	Halal certified by IFANCA, the Islamic Food and Nutrition Council of America Kosher certified by Orthodox Union, the Union of Orthodox Jewish Congregations of America
Version	Jan 2011 Revision 03

VitaCholine™

LO-ODOR ™ TECHNOLOGY

Product Specification Sheet

Choline Bitartrate Regular

USP FCC

Product code USA product code: F6492120

Formula $C_9H_{19}NO_7$

Synonyms
(2-Hydroxyethyl) trimethylammonium bitartrate
Choline hydrogen tartrate
(L+)-choline bitartrate

CAS N°: **87-67-2** (*choline bitartrate from natural L(+)-tartaric acid*)

Appearance White, crystalline solid, hygroscopic powder, free from foreign materials

Quality

Determination	Specification	Reference
Appearance	passes test	
Assay	99.0 % w/w minimum	USP
Identification test*	passes test B	USP
Infrared spectrum*	passes test	USP
Specific rotation*	between +17.5° and +18.5°	USP
pH (10% solution)	3-4	USP
Water	0.5 % w/w maximum	USP
Residue on ignition	0.1% w/w maximum	USP
Arsenic*	2 mg/kg maximum	USP
Lead*	0.3 mg/kg maximum	USP
Heavy metals as Lead*	10 mg/kg maximum	USP
Chromatographic purity*	passes test	USP
Residual solvents*	passes test	USP
1,4-Dioxane*	10 mg/kg maximum	USP
Total amines as TMA	10 mg/kg maximum	USP
Total plate count**	100 cfu/g maximum	AOAC
Yeast and molds**	30 cfu/g maximum	AOAC
*Escherichia coli***	negative/10g	AOAC
*Salmonella***	negative/25g	AOAC
Total coliform**	negative/10g	AOAC
*Enterobacteriaceae***	negative/10g	AOAC
*Cronobacter spp***	negative/10g	AOAC
*Staphylococcus aureus***	negative/10g	AOAC
Bacillus cereus spores**	negative/10g	AOAC
*Listeria monocytogenes***	negative/25g	AOAC

*Analysis regularly performed from selected lots in compliance with Balchem's documented quality control program.
**Microbiological testing is done quarterly on representative samples.

LO-ODOR ™ TECHNOLOGY

52 Sunrise Park Road • New Hampton, New York 10958 • Tel. 845.326.5675 • Fax 845.326.5717 • www.balchem.com

Product Specification Sheet

Retest date	3 years from date of manufacture
Physical Properties	See MSDS sheet
Applications	Nutritional additive
Packaging	Net weight = 25 Kg (55.115 lbs), in a 12-gallon fiber drum, with two polyethylene liners. Drum dimensions: 22.75"H x 12.5" D = 1.6 cft. Gross weight = 26.3 kg (57 lbs) Heat treated wooden pallets are ISPM 15 compliant measuring 40" x 48" x 4" Full pallet qty is 24 drums, 600 kg. Pallets are wrapped with 80 gauge stretch film.
Health and safety	See MSDS sheet
Regulatory info United States	Balchem manufactures according to Good Manufacturing Practices, GMPs as defined in 21 CFR, part 110. Choline Bitartrate is Generally Regarded As Safe (GRAS) when used according to 21 CFR 182.8250
Europe	Choline Bitartrate is currently acceptable for use in foods for particular nutritional uses, as described in: Directive 2009/39/EC Commission Regulation No. 953/2009
Contacts	Balchem Corporation 52 Sunrise Park Road, New Hampton, NY 10958 Phone +1 845 326 5675 Fax 845-326-5717 Email:nutrients@balchem.com
Note	These conditions can be subject to amendments
Certifications	Halal certified by IFANCA, the Islamic Food and Nutrition Council of America Kosher certified by Orthodox Union, the Union of Orthodox Jewish Congregations of America
Version	Jan 2011 Revision 02

VitaCholine™

LO-ODOR ™ TECHNOLOGY

BALCHEM
ANIMAL NUTRITION & HEALTH

Product Specification Sheet
CHOLINE CHLORIDE 70% AQUEOUS

IFN 7-01-228

Product Code: F3060030

A 70% solution of choline chloride in water
An officially recognized vitamin ingredient for animal feed use as per 21 CFR 582.5252
Liquid Choline chloride conforming to AAFCO definition #90.25
Nutritional Additives – Vitamins and Provitamins according to 1831/2003/EC

Product Specification:

Appearance - Clear to light amber liquid with a slight amine odor.
Substrate Composition – 70 to 72% Choline Chloride
Substrate Content - 70.0% Choline Chloride (318,000 mg/lb or 700,000 mg/kg) *Minimum*
Equivalent to 60.8% Choline Hydroxide (276,000 mg/lb or 608,000 mg/kg) *Minimum*
Equivalent to 52.2% Choline cation (237,000 mg/lb or 522,000 mg/kg) *Minimum*
pH – 6.5 to 9.0

Typical Properties:

Dioxin TEQ	≤ 1.0 ng/kg	Arsenic (As)	≤ 4 ppm
Dioxin + PCBs TEQ	≤ 1.5 ng/kg	Cadmium (Cd)	≤ 0.5 ppm
Fluorine	≤ 500 ppm	Lead (Pb)	≤ 10 ppm
Mercury (Hg)	≤ 0.2 ppm		

This product meets all E.U. feed hygiene requirements including low dioxin levels and low heavy metal content. EU undesirable substances are verified, at a minimum, annually.
No animal products or animal byproducts are used in the manufacturing process.
This material is free of risk for BSE/TSE.

Application: A liquid choline chloride feed additive for all species of livestock. Do not use as final feed.

Ingredients: Choline Chloride, Water

Dosage: There is no restriction for the maximum level of choline chloride in feed. Use in accordance with in-house requirements or with current NRC guidelines.

Precautions: Generally regarded as safe (GRAS). Avoid contact with eyes and skin. Wash thoroughly after handling.

Storage: Keep from extreme heat or cold. Recommended storage temperature 50° - 90°F (10° - 32°C). Close container when not in use.

Packaging: 500 lbs in a 55 gallon polyethylene drum
2500 lbs in a 275 gallon IBC
Bulk shipments

Shelf life: Best if used within 2 years from manufacturing date

Made in the USA

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BALCHEM
ANIMAL NUTRITION & HEALTH

Product Specification Sheet
CHOLINE CHLORIDE 75% AQUEOUS

IFN 7-01-228

Product Code: F3090030

A 75% solution of choline chloride and water
An officially recognized vitamin ingredient for animal feed use as per 21 CFR 582.5252
Liquid Choline chloride conforming to AAFCO definition #90.25
Nutritional Additives – Vitamins and Provitamins according to 1831/2003/EC

Product Specification:

Appearance - Clear to light amber liquid with a slight amine odor.
Substrate Composition – 75 to 76% Choline Chloride
Substrate Content - 75.0% Choline Chloride (340,000 mg/lb or 750,000 mg/kg) *Minimum*
Equivalent to 65.1% Choline Hydroxide (295,000 mg/lb or 651,000 mg/kg) *Minimum*
Equivalent to 56.0% Choline ion (254,000 mg/lb or 560,000 mg/kg) *Minimum*
pH – 6.5 to 9.0

Typical Properties:

Dioxin TEQ	≤1.0 ng/kg	Arsenic (As)	≤ 4 ppm
Dioxin + PCBs TEQ	≤1.5 ng/kg	Cadmium (Cd)	≤ 0.5 ppm
Fluorine	≤ 500 ppm	Lead (Pb)	≤ 10 ppm
Mercury (Hg)	≤ 0.2 ppm		

This product meets all E.U. feed hygiene requirements including low dioxin levels and low heavy metal content. EU undesirable substances are verified, at a minimum, annually.
No animal products or animal byproducts are used in the manufacturing process.
This material is free of risk for BSE/TSE.

Application: A liquid choline chloride feed additive for all species of livestock. Do not use as final feed.

Ingredients: Choline Chloride, Water

Dosage: There is no restriction for the maximum level of choline chloride in feed. Use in accordance with in-house requirements or with current NRC guidelines.

Precautions: Generally regarded as safe (GRAS). Avoid contact with eyes and skin. Wash thoroughly after handling.

Storage: Keep from extreme heat or cold. Recommended storage temperature 50° - 90°F (10° - 32°C). Close container when not in use.

Packaging: 500 lbs in a 55 gallon polyethylene drum
2500 lbs in a 275 gallon IBC
Bulk shipments

Shelf life: Best if used within 2 years from manufacturing date

Made in the USA

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Product Specification Sheet

CC 60
Choline chloride 60% on vegetable carrier

Grade	**Feed Grade**				
					Method of analysis
Specification	Choline chloride	% w/w		60±1	SAM 269.22
Product characteristics					Method of analysis
	Trimethylamine (TMA)	% w/w	max	0.04	SMA 839.04
	Water	% w/w	max.	2.5	SAM 280.17
	Apparent bulk density	kg/m^3		550-700	SAM 243.06
	Packed bulk density	kg/m^3		600-800	SAM 720.06
	Residue on 2.0 mm	%	max.	2	SAM 721.06
	Residue on 0.850 mm	%	max.	35	SAM 721.06
	Sampling procedure				SAM 918.02

For a cross-check of the choline chloride content, a description of the *Ion Chromatography* method (SMA 839.05) is available on request.

Registration

The product is registered in the Community register of Feed Additives pursuant to Regulation 1831/2003/EC.
According to the Directive 95/69/EC and all amendments and to the Regulation 183/2005/EC the production site has the registration number: **α ITM 00001 NO**

Expiry date

2 years when stored in original packing and storage temperature is max 40°C.
Expiry date relates only to assay, corrected for humidity pick up during storage

Formula

$[HOCH_2CH_2N(CH_3)_3]Cl$

Synonyms

(2-hydroxyethyl) trimethylammoniumchloride

Appearance

Free-flowing tan colored powder with a faint characteristic odor.

Physical properties

See our Safety Data Sheet.

Applications

see our website

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Product Specification Sheet

Packing and transport

Plastic bag of 25 kilos net.
Also possible on pallets (size: 1000 x 1200 mm, also called "CP 6") with shrink film.
Standard pallet dimensions:

Net weight:	- 1,250 kg
Gross weight:	- 1,275 kg
Pallet size (l x w x h):	- 1300 x 1080 x 1450 mm

Polypropylene woven FIBC with 1000 kg net weight (weight accuracy ± 20 kgs) placed on a pallet (size 1140 x 1140 mm, also called "CP 9").
Standard dimensions:

Net weight:	- 1000 kg ± 20 kg
Gross weight:	- 1023 kg ± 20 kg
Unit size (l x w x h):	- 1220 x 1220 x 1330 mm
Pallet size (l x w x h)	- 1220 x 1220 x 1480 mm

Bulk in tankcar trucks.

Health and safety

See our Safety Data Sheet.

Technical service

Our technical service department will be pleased to advise you.
Do not hesitate to contact us.

Marketing

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ISO 9001
ISO 14001
Certified by BVQI
FAMI-QS

Note

These conditions can be subject to amendments.

Version

May 2007 Revision 00

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Product Specification Sheet

CC 70
Choline chloride 70% on vegetable carrier

Grade

Feed Grade

Specification

			Method of analysis
Choline chloride	% w/w	70±2	SAM 269.22

Product characteristics

				Method of analysis
Trimethylamine (TMA)	% w/w	max	0.04	SMA 839.04
Water	% w/w	max.	2.5	SAM 280.17
Apparent bulk density	kg/m^3		600-750	SAM 243.06
Packed bulk density	kg/m^3		650-850	SAM 720.06
Residue on 2.0 mm	% max.		2	SAM 721.06
Residue on 0.850 mm	% max.		35	SAM 721.06
Sampling procedure				SAM 918.02

For a cross-check of the choline chloride content, a description of the "Ion Chromatography" (SMA 839.05), method is available on request.

Registration

The product is registered in the Community register of Feed Additives pursuant to Regulation 1831/2003/EC.
According to the Directive 95/69/EC and all amendments and to the Regulation 183/2005/EC the production site has the registration number: **α ITM 00001 NO**

Expiry date

2 years when stored in original packing and storage temperature is max 40°C.
Expiry date relates only to assay, corrected for humidity pick up during storage

Formula

$[HOCH_2CH_2N(CH_3)_3]Cl$

Synonyms

(2-hydroxyethyl) trimethylammoniumchloride

Appearance

Free-flowing tan colored powder with a faint characteristic odor.

Physical properties

See our Safety Data Sheet.

Applications

see ourwebsite

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Product Specification Sheet

Packing and transport	**Plastic bag** of 25 kilos net. Also possible on pallets (size: 1000 x 1200 mm, also called "CP 6") with shrink film. Standard pallet dimensions: Net weight: - 1,250 kg Gross weight: - 1,275 kg Pallet size (l x w x h): - 1300 x 1100 x 1400 mm **Polypropylene woven FIBC** with 1000 kg net weight (weight accuracy ± 20 kgs) placed on a pallet (size 1140 x 1140 mm, also called "CP 9"). Standard dimensions: Net weight: - 1000 kg ± 20 kg Gross weight: - 1023 kg ± 20 kg Unit size (l x w x h): - 1250 x 1250 x 1200 mm Pallet size (l x w x h) - 1250 x 1250 x 1350 mm **Bulk** in tankcar trucks
Health and safety	See our Safety Data Sheet.
Technical service	Our technical service department will be pleased to advise you. Do not hesitate to contact us.

Marketing

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Certifications

Site: Marano Ticino
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Fax : +39 0321 979246

ISO 9001
ISO 14001

Note	These conditions can be subject to amendments.
Version	May 2007 Revision 00

BALCHEM
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Product Specification Sheet

Choline chloride 50% on silica carrier

Grade	**FEED GRADE**			
				Method of analysis
Specification	Choline chloride	% w/w	50±1	SAM 269.21
Product characteristics				Method of analysis
	Trimethylamine (TMA)	% w/w	max 0.03	SMA 839.04
	Apparent bulk density	kg/m^3	450-600	SAM 243.06
	Packed bulk density	kg/m^3	600-750	SAM 720.06
	Residue on 0.5 mm	%	max. 10	SAM 721.06

For a cross-check of the choline chloride content, a description of "Ion Chromatography" (SMA 839.05), method is available on request.

Registration

The product is registered in the Community register of Feed Additives pursuant to Regulation 1831/2003/EC.
According to the Directive 95/69/EC and all amendments and to the Regulation 183/2005/EC the production site has the registration number: **α ITM 00001 NO**

Expiry date

2 years when stored in original packing and storage temperature is max 40^{o} C.
Expiry date relates only to assay, corrected for humidity pick up during storage.

Formula

$[HOCH_2CH_2N(CH_3)_3]Cl$

Synonyms

(2-hydroxyethyl) trimethylammoniumchloride

Appearance

Free-flowing white powder. None or slight amine odour.

Physical properties

See our Safety Data Sheet.

Applications

See our website

BALCHEM
World-Class Quality Worldwide Service

Product Specification Sheet

Packing and transport

Polyethylene (PE) bag of 25 kilos net.
Also possible on pallets (size: 1000 x 1200 mm, also called "CP 6") with shrink film.
Standard pallet dimensions:

Net weight:	- 1,250 kg
Gross weight:	- 1,276 kg
Pallet size (l x w x h):	- 1300 x 1050 x 1700 mm

Polypropylene woven FIBC with 1000 kg net weight (weight acccuracy 20 kgs) placed on a pallet (size 1140 x 1140 mm, also called "CP 9").
Standard dimensions:

Net weight:	- 1000 ± 20 kg
Gross weight:	- 1022 ± 20 kg
Unit size (l x w x h):	- 1140 x 1140 x 1700 mm
Pallet size (l x w x h):	- 1140 x 1140 x 1850 mm

Health and safety

See our Safety Data Sheet.

Technical service

Our technical service department will be pleased to advise you.
Do not hesitate to contact us.

Marketing

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Certifications

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ISO 9001
ISO 14001
Certified by BVQI
FAMIQS

Note

These conditions can be subject to amendments.

Version May 2007 Revision 00

BALCHEM
ANIMAL NUTRITION & HEALTH

Product Specification Sheet
ReaShure® Choline

IFN 7-01-228
Product Code: F3428016

Rumen protected encapsulated choline chloride
Nutritional Additives – Vitamins and Provitamins according to 1831/2003/EC
US patents # 6,797,291 #6,013,286 #5,190,775

Product Specification:

Appearance - Tan to Brown, Free-Flowing Granules
Substrate Composition - Choline Chloride
Substrate Content - 28.8% Choline Chloride (288,000 mg/kg) *Minimum*
Equivalent to 25.0% Choline Hydroxide (250,000 mg/kg) *Minimum*
Equivalent to 21.5% Choline cation (215,000 mg/kg) *Minimum*

Typical Properties:

Loss on Drying	≤ 1.0%	Arsenic (As)	≤ 4 ppm
Ash	≤ 1.0%	Cadmium (Cd)	≤ 0.5 ppm
Dioxin TEQ	≤ 1.0 ng/kg	Lead (Pb)	≤ 10 ppm
Dioxin + PCBs TEQ	≤ 1.5 ng/kg	Mercury (Hg)	≤ 0.2 ppm
Fluorine	≤ 500 ppm		

This product meets all E.U. feed hygiene requirements including low dioxin levels and low heavy metal content. EU undesirable substances are verified, at a minimum, annually.
No animal products or animal byproducts are used in the manufacturing process.
This material is free of risk for BSE/TSE.

Application: A rumen protected, encapsulated choline chloride feed additive in a chemically stable form for ruminant livestock. Do not use as final feed.

Ingredients: Hydrogenated Vegetable Oil, Choline Chloride, Corn Cob (carrier)
This product may contain ingredients sourced from GM varieties.

Dosage: There is no restriction for the maximum level of choline chloride in feed. Recommended inclusion rate is 60 grams per head per day.

Precautions: Generally regarded as safe (GRAS). Avoid contact with eyes and skin. Avoid breathing dust. Wash thoroughly after handling.

Storage: Keep dry in sealed bags. Store below 50°C. Recommended storage temperature 10° - 32°C.

Packaging: 25-kg poly-lined bags

Shelf life: Best if used within 2 years from manufacturing date, if kept dry in unopened bags.

Made in the USA

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Appendix Section 4.

Organic Materials Research Institute listing of choline salts for feed applications

LIVESTOCK Vitamins & Minerals

Appendix B

Listings for Livestock Nutrients by Source

This appendix represents OMRI's policy for listing sources of livestock vitamins and minerals. OMRI's policy is based on the NOP rule § 205.237(a), which allows the use of nonsynthetic feed additives and supplements as well as those that are permitted by the National List. NOP Rule §205.603(d)(1-2) permits "trace minerals / vitamins used for enrichment or fortification when FDA approved." Forms of vitamins and minerals listed here include those regulated by FDA as listed in 21 CFR 582 (Subpart F, Nutrients and/or Dietary Supplements) and 21 CFR 573, as well as those included in §57, Mineral Products, and §90, Vitamins of the Association of American Feed Control Officials (AAFCO) 2009 *Official Publication.*

OMRI considers use of all livestock vitamins and minerals to be Allowed with Restrictions by § 205.237(b)(2) of the NOP Rule, which states that "the producer of an organic operation must not provide feed supplements or additives in amounts above those needed for adequate nutrition and health maintenance for the species at its specific stage of life." Some sources of vitamins may be unacceptable either by interpretation of the NOP or under different standards. OMRI has identified forms that may be obtained from animal slaughter by-products, which are prohibited for feeding ruminants and poultry under NOP Rule § 205.237(b)(5). Some vitamin and mineral products can also contain products obtained from genetically modified organisms prohibited as 'excluded methods' by the NOP Rule at § 205.105(e). Because of the development and commercialization of new products and/or changes in regulatory status, the table below may not be complete and is subject to change.

Calcium

Bone ash — **Prohibited**
AAFCO: 57.1 — FDA: n/a
Animal slaughter byproducts.

Bone charcoal — **Prohibited**
AAFCO: 57.2 — FDA: n/a
Animal slaughter byproducts.

Bone charcoal, spent — **Prohibited**
AAFCO: 57.17 — FDA: n/a
Animal slaughter byproducts.

Bone meal, cooked — **Prohibited**
AAFCO: 57.141 — FDA: n/a
Animal slaughter byproducts.

Bone meal, steamed — **Prohibited**
AAFCO: 57.18 — FDA: n/a
Animal slaughter byproducts.

Bone phosphate — **Prohibited**
AAFCO: 57.14 — FDA: n/a
Animal slaughter byproducts.

Calcite — **Allowed with Restrictions**
AAFCO: 57.3 — FDA: n/a

Calcium amino acid chelate — **Allowed with Restrictions**
AAFCO: 57.142 — FDA: n/a

Calcium amino acid complex — **Allowed with Restrictions**
AAFCO: 57.150 — FDA: n/a

Calcium carbonate — **Allowed with Restrictions**
AAFCO: 57.10 — FDA: 582.1191, 582.5191

Calcium carbonate, precipitated — **Allowed with Restrictions**
AAFCO: 57.7 — FDA: n/a

Calcium chloride — **Allowed with Restrictions**
AAFCO: 57.51 — FDA: 582.1193, 582.6193

Calcium citrate — **Allowed with Restrictions**
AAFCO: n/a — FDA: 582.1195, 582.5195

Calcium formate — **Prohibited**
AAFCO: T57.152 — FDA: n/a
Withdrawn from AAFCO. Calcium formate is currently considered an unapproved food additive and an food additive petition must be approved prior to its use in feeds.

Calcium gluconate — **Allowed with Restrictions**
AAFCO: 57.52 — FDA: 582.1199

Calcium glycerophosphate — **Allowed with Restrictions**
AAFCO: n/a — FDA: 582.5201

Calcium hydroxide — **Allowed with Restrictions**
AAFCO: 57.53 — FDA: 582.1205

Calcium iodate — **Allowed with Restrictions**
AAFCO: 57.54 — FDA: 582.80

Calcium iodobehenate — **Allowed with Restrictions**
AAFCO: 57.55 — FDA: n/a

Calcium lactate — **Allowed with Restrictions**
AAFCO: n/a — FDA: 582.1207

Calcium oxide — **Allowed with Restrictions**
AAFCO: 57.56 — FDA: 582.1210, 582.5210

Vitamin B complex

Inositol — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5370

Vitamin B1 (Thiamine)

Thiamine — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5875

Thiamine hydrochloride — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5875

Thiamine mononitrate — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5878

Vitamin B12 (Cyanocobalamin)

Cyanocobalamin — **Allowed with Restrictions**
AAFCO: n/a FDA: 582.5945
May not be produced by excluded methods (GMOs).

Vitamin B12 supplement — **Allowed with Restrictions**
AAFCO: 90.11 FDA: n/a
May not be produced by excluded methods (GMOs).

Vitamin B2 (Riboflavin)

Riboflavin — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5695
AAFCO refers to 'crystalline riboflavin commercial feed grade.'

Riboflavin supplement — **Allowed with Restrictions**
AAFCO: 90.13 FDA: n/a

Riboflavin-5-phosphate — **Allowed with Restrictions**
AAFCO: 90.26 FDA: 582.5697

Vitamin B3 (Niacin)

Niacin supplement — **Allowed with Restrictions**
AAFCO: 90.16 FDA: n/a
May not come from slaughter sources.

Niacin, Nicotinic acid — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5530

Niacinamide, nicotinamide — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5535

Vitamin B5 (Pantothenic acid)

Calcium pantothenate — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5212

Sodium pantothenate — **Allowed with Restrictions**
AAFCO: n/a FDA: 582.5772

Vitamin B6 (Pyridoxine)

Pyridoxine hydrochloride — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5676

Vitamin B7 (Biotin)

Biotin — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5159

Vitamin B9 (Folic acid)

Folic acid, crystalline folic acid feed grade — **Allowed with Restrictions**
AAFCO: 90.25 FDA: n/a

Vitamin C

Ascorbic acid — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5013

Ascorbyl palmitate — **Prohibited**
AAFCO: 18.1 FDA: 582.3149
Chemical preservative, not a nutrient.

Calcium ascorbate — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.3189

Calcium-L ascorbyl-2-monophosphate,

Vitamin Choline

Betaine — **Allowed with Restrictions**
AAFCO: 90.17 FDA: n/a
Hydrochloride or anhydrous. May not come from slaughter sources (stearyl betaine).

Choline bitartrate — **Allowed with Restrictions**
AAFCO: 90.26 FDA: 582.5250

Choline chloride — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 582.5252

Choline pantothenate — **Allowed with Restrictions**
AAFCO: 90.25 FDA: n/a

Choline xanthate — **Allowed with Restrictions**
AAFCO: 90.25 FDA: 573. 300

Vitamin Choline *Continued from previous page*

Ferric choline citrate — **Allowed with Restrictions**
AAFCO: 90.26 — FDA: 582.5250

Vitamin D

Cholcalciferol (D-activated animal sterol) — **Allowed with Restrictions**
AAFCO: 90.7 — FDA: n/a
May not be from slaughter byproducts.

Cod liver oil with added vitamin A and D — **Allowed with Restrictions**
AAFCO: 90.2 — FDA: n/a

Ergocalciferol (D-activated plant sterol) — **Allowed with Restrictions**
AAFCO: 90.8 — FDA: n/a

Vitamin D oil — **Allowed with Restrictions**
AAFCO: 90.5 — FDA: n/a

Vitamin D2 — **Allowed with Restrictions**
AAFCO: n/a — FDA: 582.5950
May not be from slaughter byproducts.

Vitamin D2 supplement — **Allowed with Restrictions**
AAFCO: 90.4 — FDA: n/a
May not be from slaughter byproducts.

Vitamin D3 (cholcalciferol) — **Allowed with Restrictions**
AAFCO: 90.7 — FDA: 582.5953
May not be from slaughter byproducts.

Vitamin D3 supplement — **Allowed with Restrictions**
AAFCO: 90.15 — FDA: n/a
May not be from slaughter byproducts.

Vitamin E

α-Tocopherol acetate — **Allowed with Restrictions**
AAFCO: 90.25 — FDA: 582.5892

Tocopherols — **Allowed with Restrictions**
AAFCO: 90.25 — FDA: 582.5890

Vitamin E supplement — **Allowed with Restrictions**
AAFCO: 90.12 — FDA: n/a

Vitamin K

Menadione dimethylpyrimidinol bisulfite — **Allowed with Restrictions**
AAFCO: 90.25 — FDA: 573.620
FDA and AAFCO limits rates: Chickens and turkeys, 2g/ton of feed; Swine: 10g/ton of feed. NRC does not recommend for ruminants. May not come from slaughter byproducts.

Menadione nicotinamide bisulfite — **Allowed with Restrictions**
AAFCO: 90.25 — FDA: 573.625
FDA and AAFCO limits rates: Chickens and turkeys, 2g/ton of feed; Swine: 10g/ton of feed. May not come from slaughter byproducts.

Menadione sodium bisulfite complex — **Allowed with Restrictions**
AAFCO: 90.25 — FDA: n/a
AAFCO & FDA limit rate: Chickens and turkeys, 2g/ton of feed.

Zinc

Zinc acetate — **Allowed with Restrictions**
AAFCO: 57.114 — FDA: 582.80

Zinc amino acid chelate — **Allowed with Restrictions**
AAFCO: 57.142 — FDA: n/a

Zinc amino acid complex — **Allowed with Restrictions**
AAFCO: 57.150 — FDA: n/a

Zinc carbonate — **Allowed with Restrictions**
AAFCO: 57.115 — FDA: 582.80

Zinc chloride — **Allowed with Restrictions**
AAFCO: 57.116 — FDA: 582.80, 582.5985

Zinc chlorine diammine complex — **Allowed with Restrictions**
AAFCO: 57.143 — FDA: n/a

Zinc gluconate — **Allowed with Restrictions**
AAFCO: n/a — FDA: 582.5988

Zinc lysine complex — **Allowed with Restrictions**
AAFCO: 57.151 — FDA: n/a

Zinc methionine complex — **Allowed with Restrictions**
AAFCO: 57.151 — FDA: n/a

Zinc oxide — **Allowed with Restrictions**
AAFCO: 57.117 — FDA: 582.80, 582.5991

Zinc polysaccharide complex — **Allowed with Restrictions**
AAFCO: 57.29 — FDA: n/a

Zinc proteinate — **Allowed with Restrictions**
AAFCO: 57.23 — FDA: n/a
Nonorganic protein must not be derived from excluded methods (GMOs) or slaughter byproducts.

Zinc stearate — **Allowed with Restrictions**
AAFCO: n/a — FDA: 582.5994
May not come from slaughter sources.

Zinc sulfate — **Allowed with Restrictions**
AAFCO: 57.118 — FDA: 582.80, 582.5997

AAFCO: Refers to the Association of American Feed Control Officials (AAFCO) *Official Publication*

FDA: Food and Drug Administration rules at 21 CFR 582 and 573

Appendix Section 5.

Letter from Pennsylvania Certified Organic, re: applications of Reashure® rumen-protected choline chloride

PENNSYLVANIA
CERTIFIED ORGANIC

406 S. Pennsylvania Avenue • Centre Hall, PA 16828
(814) 364-1344 • fax (814) 364-4431
patty@paorganic.org

March 30, 2006

Balchem Corporation

Pennsylvania Certified Organic has completed a review of the Product Reassure Choline to National Organic Program requirements. We have determined this product to be allowed by our clients for organic production as a feed additive/supplement.

PCO reviews materials at the request of our certified organic producers, as part of their applications or annual reviews. If you'd like your products to be reviewed by the Organic Materials Review Institute (OMRI), please contact them directly at www.omri.org or (541) 343-7600.

Manufacturers and distributors of products listed as allowed are not permitted to use this information to advertise or sell their products. Use of the Pennsylvania Certified Organic (PCO) name or logo on product packaging or marketing materials is expressly prohibited.

Please contact me if you have any questions.

Sincerely,

Patty Neiner
Materials Review

Appendix Section 6

Nutrient Content Claims for choline

6. Choline Nutrient Content Claims*

Claim	Conditions of use	Choline Content (mg Choline/RACC)
Good Source of Choline **Contains/Provides Choline** **Plus Choline** **Fortified/Enriched with Choline** **More Choline** **Added Choline** **Extra Choline**	Product must contain 10-19% of the Daily Consumption Value of choline per Reference Amount Customarily Consumed (RACC)	≥55 mg
Excellent Source of Choline **High/Rich in Choline**	Product must contain ≥20% of the Daily Consumption Value of choline per RACC	≥110 mg

*According to the Food and Drug Administration Modernization Act of 1997 (FDAMA), nutrient content claims are allowed in food and supplement labeling when they are based on current, published, authoritative statements from certain federal scientific bodies, including the National Academy of Sciences. All are based on an adult Daily Consumption Value, and may not be used in products intended for consumers under 4 years of age.

http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/ucm056975.htm
http://www.fda.gov/Food/LabelingNutrition/LabelClaims/FDAModernizationActFDAMAClaims/ucm073599.htm

Appendix Section 7.

Environmental Protection Agency evaluation of choline chloride to determine requirement for a tolerance

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA–HQ–OPP–2008–0671; FRL–8802–4]

Choline chloride; Exemption from the Requirement of a Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes an exemption from the requirement of a tolerance for residues of choline chloride (CAS Reg. No. 67–48–1) applied pre-harvest on all raw agricultural commodities when applied/used as a solvent. Loveland Products, Inc., submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting an exemption from the requirement of a tolerance. This regulation eliminates the need to establish a maximum permissible level for residues of choline chloride.

DATES: This regulation is effective January 6, 2010. Objections and requests for hearings must be received on or before March 8, 2010, and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: EPA has established a docket for this action under docket identification (ID) number EPA–HQ–OPP–2008–0671. All documents in the docket are listed in the docket index available at *http://www.regulations.gov*. Although listed in the index, some information is not publicly available, e.g., Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available in the electronic docket at *http://www.regulations.gov*, or, if only available in hard copy, at the OPP Regulatory Public Docket in Rm. S–4400, One Potomac Yard (South Bldg.), 2777 S. Crystal Dr., Arlington, VA. The Docket Facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The Docket Facility telephone number is (703) 305–5805.

FOR FURTHER INFORMATION CONTACT: Deirdre Sunderland, Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (703) 603–0851; e-mail address: *sunderland.deirdre@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. Potentially affected entities may include, but are not limited to:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed in this unit could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. If you have any questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

B. How Can I Access Electronic Copies of this Document?

In addition to accessing electronically available documents at *http://www.regulations.gov*, you may access this **Federal Register** document electronically through the EPA Internet under the ''**Federal Register**'' listings at *http://www.epa.gov/fedrgstr*. You may also access a frequently updated electronic version of 40 CFR part 180 through the Government Printing Office's e-CFR cite at *http://www.gpoaccess.gov/ecfr*.

C. Can I File an Objection or Hearing Request?

Under section 408(g) of FFDCA, 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. The EPA procedural regulations which govern the submission of objections and requests for hearings appear in 40 CFR part 178. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA–HQ–OPP–2008–0671 in the subject line on the first page of your submission. All requests must be in writing, and must be mailed or delivered to the Hearing Clerk on or before March 8, 2010.

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing that does not contain any CBI for inclusion in the public docket that is described in **ADDRESSES**. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit your copies, identified by docket ID number EPA–HQ–OPP–2008–0671, by one of the following methods:

- *Federal eRulemaking Portal*: *http://www.regulations.gov*. Follow the on-line instructions for submitting comments.
- *Mail*: Office of Pesticide Programs (OPP) Regulatory Public Docket (7502P), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001.
- *Delivery*: OPP Regulatory Public Docket (7502P), Environmental Protection Agency, Rm. S–4400, One Potomac Yard (South Bldg.), 2777 S. Crystal Dr., Arlington, VA. Deliveries are only accepted during the Docket Facility's normal hours of operation (8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays). Special arrangements should be made for deliveries of boxed information. The Docket Facility telephone number is (703) 305–5805.

II. Background and Statutory Findings

In the **Federal Register** of December 3, 2008 (73 FR 73648) (FRL–8391–3), EPA issued a notice pursuant to section 408 of FFDCA, 21 U.S.C. 346a, as amended by FQPA (Public Law 104–170), announcing the filing of a pesticide petition (PP 8E7387) by Loveland Products, Inc., P.O. Box 1286, Greeley, CO 80632–1286. The petition requested that 40 CFR 180.920 be amended by establishing an exemption from the requirement of a tolerance for residues of choline chloride when used as an inert ingredient in pesticide formulations applied pre-harvest. That notice included a summary of the petition prepared by the petitioner. There were no comments received in response to the notice of filing.

Section 408(b)(2)(A)(i) of FFDCA allows EPA to establish an exemption from the requirement for a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the tolerance is ''safe.'' Section 408(b)(2)(A)(ii) of FFDCA defines ''safe'' to mean that ''there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including

all anticipated dietary exposures and all other exposures for which there is reliable information.'' This includes exposure through drinking water and in residential settings, but does not include occupational exposure. Section 408(b)(2)(C) of FFDCA requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to ''ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue....''

EPA performs a number of analyses to determine the risks from aggregate exposure to pesticide residues. First, EPA determines the toxicity of pesticides. Second, EPA examines exposure to the pesticide through food, drinking water, and through other exposures that occur as a result of pesticide use in residential settings.

III. Inert Ingredient Definition

Inert ingredients are all ingredients that are not active ingredients as defined in 40 CFR 153.125 and include, but are not limited to, the following types of ingredients (except when they have a pesticidal efficacy of their own): Solvents such as alcohols and hydrocarbons; surfactants such as polyoxyethylene ploymers and fatty acids; carriers such as clay and diatomaceous earth; thickeners such as carrageenan and modified cellulose; wetting, spreading, and dispersing agents; propellants in aerosol dispensers; microencapsulating agents; and emulsifiers. The term ''inert'' is not intended to imply nontoxicity; the ingredient may or may not be chemically active. Generally, EPA has exempted inert ingredients from the requirement of a tolerance based on the low toxicity of the individual inert ingredients.

IV. Toxicological Profile

Consistent with section 408(b)(2)(D) of FFDCA, EPA has reviewed the available scientific data and other relevant information in support of this action and considered its validity, completeness and reliability and the relationship of this information to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children. The nature of the toxic effects caused by choline chloride are discussed in this unit. The following provides a brief summary of the risk assessment and conclusions from the Agency's review of choline chloride. The Agency's full decision document for this action is available in the Agency's electronic docket (regulations.gov) under the docket number EPA–HQ–OPP–2008–0671.

Choline chloride is a quaternary ammonium salt which dissociates in water resulting in a positively charged quaternary hydroxyl alkylammonium ion and a negatively charged chloride ion. Choline is an essential component of the human diet and acts as a precursor to acetylcholine, phospholipids, and the methyl donor betaine. It is important for the structural integrity of cell membranes, cholinergic neurotransmission, transmembrane signaling, methyl metabolism, and lipid and cholesterol transport and metabolism.

Choline was officially made an ''essential nutrient'' in 1998 and adequate intake (AI) levels were established (women-425 milligram/day (mg/day), pregnant women-450 mg/day, men and lactating women-550 mg/day). The Daily Upper Intake Level for choline is 3.5 grams for adults. Research indicates that many individuals are not getting enough choline, with daily intake levels far below the AI.

Chloride is a binary compound of chlorine; a salt of hydrochloric acid. Chloride is the major extracellular anion and contributes to many body functions including the maintenance of osmotic pressure, acid-base balance, muscular activity, and the movement of water between fluid compartments. The World Health Organization has performed two assessments which determined that from a toxicological point of view, there were no concerns for the chloride ion. It was considered to be naturally-occurring and a normal participant of animal and human metabolism.

Choline chloride has demonstrated a low acute oral toxicity with LD_{50} values for rats ranging from 3,150 to ≥ 6,000 milligram/kilogram (mg/kg) and LD_{50} for mice in the range of 3,900 to 6,000 mg/kg. Although appropriate animal studies are lacking for acute dermal toxicity, an *in vitro* percutaneous absorption study performed under occluded and unoccluded conditions showed that choline chloride is expected to have a low potential for percutaneous absorption. Acceptable acute inhalation studies are not available. Studies conducted in the early 1960's showed only slight transient irritation of the skin and eye.

Repeat dose animal studies on choline chloride are limited. One study in mice evaluated the impact of 200 mg/kg/day choline chloride given orally or intranasally for 28 days. No adverse effects were observed with regards to body weight, food and water consumption, hematology, clinical biochemistry, or histopathology of various organs (lung, heart, liver, spleen, and kidney). Results from intranasal exposure to choline chloride were comparable with their respective controls and to other treatment groups. The no adverse effects are observed (NOAEL) for oral and intranasally administered choline chloride is ≥ 200 mg/kg/day.

A 72–week feeding study in rats administered 500 mg/kg/day of choline chloride and observed the animals for 30 weeks post exposure. There were no significant difference between the control and treated group in relation to body weights, relative liver weight, survival rates, and the number of neoplastic liver nodules, hepatocellular carcinomas, lung tumors, leukemia, or other tumors. This study resulted in a NOAEL of 500 mg/kg/day (the highest dose tested).

Choline is a precursor to the vital neurotransmitter acetylcholine. Studies show that choline has beneficial effects on the nervous system and memory. Choline is necessary to promote proper development in the fetus and infant and prevent cognitive problems. Choline chloride is not expected to cause neurotoxicity and it is not a known endocrine disruptor nor are its metabolites related to any class of known endocrine disruptors. Based on the results of the *in vitro* and *in vivo* studies the Agency concluded that choline chloride is not expected to be carcinogenic or mutagenic.

Since the 1930's choline chloride has been used as a widespread nutrient in animal feed without adverse effects reported on fertility or teratogenicity. The Food and Drug Administration (FDA) requires choline be added to non-milk based infant formulas at a minimum concentration of 7 mg for every 100 kilocalories (21 CFR 107.100). Although one study did show developmental effects, they were only seen at very high doses (≥4,160 mg/kg/day) and only in the presence of maternal toxicity. There were no observed adverse effects for both mothers and pups exposed to 1,250 mg/kg/day. Based on this information the Agency concluded that choline chloride, when used as an inert ingredient, will not cause reproductive or developmental toxicity and therefore, does not anticipate an increased risk to infants and children.

V. Aggregate Exposures

In examining aggregate exposure, section 408 of FFDCA directs EPA to consider available information

concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

EPA establishes exemptions from the requirement of a tolerance only in those cases where it can be clearly demonstrated that the risks from aggregate exposure to pesticide chemical residues under reasonably foreseeable circumstances will pose no appreciable risks to human health. In order to determine the risks from aggregate exposure to pesticide inert ingredients, the Agency considers the toxicity of the inert in conjunction with possible exposure to residues of the inert ingredient through food, drinking water, and through other exposures that occur as a result of pesticide use in residential settings. If EPA is able to determine that a finite tolerance is not necessary to ensure that there is a reasonable certainty that no harm will result from aggregate exposure to the inert ingredient, an exemption from the requirement of a tolerance may be established.

Exposure from the use of choline chloride is expected through the oral route via food and drinking water. Exposure via the dermal route may occur for those individuals applying the product both occupationally and residentially. Due to the rapid degradation of the chemical and the natural presence of choline and chloride in the environment, exposure from the use of choline chloride as an inert ingredient in pesticide products is not expected to increase the aggregate exposure to all subpopulation including infants and children and therefore a quantitative exposure assessment has not been performed.

VI. Cumulative Effects

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider ''available information'' concerning the cumulative effects of a particular pesticide's residues and ''other substances that have a common mechanism of toxicity.''

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to choline chloride and any other substances, and these chemicals do not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that these chemicals have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at *http://www.epa.gov/pesticides/cumulative/*.

VII. Additional Safety Factor for the Protection of Infants and Children.

Section 408 of FFDCA provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure unless EPA determines that a different margin of safety will be safe for infants and children. EPA concluded that the FQPA safety factor for choline chloride should be reduced to 1X.

The database for choline chloride is adequate to make a determination of safety for infants and children. Choline is a natural component of a variety of commonly consumed foods. It has been added as a supplement to infant formula in the United States for decades. In addition to dietary consumption of choline and chloride, choline is made endogenously in the human body. Choline is a precursor to the vital neurotransmitter acetylcholine. Studies show that choline has beneficial effects on the nervous system and memory. Choline is necessary to promote proper development in the fetus and infant and prevent cognitive problems. Choline chloride is not expected to cause neurotoxicity.

Chloride is also important for many biological functions. It helps to maintain the fluid balance of cells, proper blood volume, blood pressure, and the pH of body fluids. The World Health Organization has performed two assessments which determined that from a toxicological point of view, there were no concerns for the chloride ion. It was considered to be naturally-occurring and a normal participant of animal and human metabolism.

Choline chloride has been used as a widespread nutrient in animal feed since the 1930's without adverse effects reported on fertility or teratogenicity. Although one study in mice did show developmental effects, they were only seen at very high doses (≥4,160 mg/kg/day) and only in the presence of maternal toxicity. There were no observed adverse effects for both mothers and pups exposed to 1,250 mg/kg/day.

Exposure to choline chloride is not expected to significantly increase the pre-existing levels found in commonly eaten foods. Due to the negligible anticipated crop residues and subsequent exposure, the low toxicity of the chemical and its metabolites, the bodies need for choline from a dietary source, and the beneficial role choline plays in fetal development and memory; the safety factor has been reduced to 1 X.

VIII. Determination of Safety for U.S. Population

In addition to its low toxicity, exposure to choline chloride will be limited. The expected exposure pathway is via the oral and the dermal routes. Humans are currently exposed to choline and chloride on a daily basis through commonly eaten foods (both naturally occurring and when added as a nutrient) and through the bodies natural ability to synthesize the nutrient. It is unlikely that the exposure from choline chloride, when used as an inert ingredient applied pre-harvest to food commodities, will significantly increase the natural concentration of choline and chloride in foods. Choline and chloride are also found naturally in the environment. Choline chloride is readily biodegradable and because of its high water solubility it is expected that most of the inert will be washed from the plant prior to consumption. Once in water, its preferred media, it will be broken into a quaternary hydroxyl alkylammonium ion and a chloride ion.

Taking into consideration all available information on choline chloride, it has been determined that there is a reasonable certainty that no harm to any population subgroup, including infants and children, will result from aggregate exposure to this chemical. Therefore, the exemption from the requirement of a tolerance for residues of choline chloride (CAS Reg. No. 67–48–1), when used as an inert ingredient in pre-harvest applications, under 40 CFR 180.920 can be considered safe under section 408(q) of the FFDCA.

IX. Other Considerations

A. Analytical Method(s)

An analytical method is not required for enforcement purposes since the Agency is establishing an exemption from the requirement of a tolerance without any numerical limitation.

B. International Tolerances

The Agency is not aware of any country requiring a tolerance for choline chloride nor have any CODEX Maximum Residue Levels (MRLs) been established for any food crops at this time.

X. Conclusions

Therefore, a tolerance exemption is established for choline chloride (CAS Reg. No. 67–48–1) when used as inert ingredient in pesticide formulations applied to growing crops only.

XI. Statutory and Executive Order Reviews

This final rule establishes a tolerance under section 408(d) of FFDCA in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled *Regulatory Planning and Review* (58 FR 51735, October 4, 1993). Because this final rule has been exempted from review under Executive Order 12866, this final rule is not subject to Executive Order 13211, entitled *Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use* (66 FR 28355, May 22, 2001) or Executive Order 13045, entitled *Protection of Children from Environmental Health Risks and Safety Risks* (62 FR 19885, April 23, 1997). This final rule does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq.*, nor does it require any special considerations under Executive Order 12898, entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations* (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under section 408(d) of FFDCA, such as the exemption in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*) do not apply.

This final rule directly regulates growers, food processors, food handlers, and food retailers, not States or tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of section 408(n)(4) of FFDCA. As such, the Agency has determined that this action will not have a substantial direct effect on States or tribal governments, on the relationship between the national government and the States or tribal governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian tribes. Thus, the Agency has determined that Executive Order 13132, entitled *Federalism* (64 FR 43255, August 10, 1999) and Executive Order 13175, entitled *Consultation and Coordination with Indian Tribal Governments* (65 FR 67249, November 9, 2000) do not apply to this final rule. In addition, this final rule does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (Public Law 104–4).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA), Public Law 104–113, section 12(d) (15 U.S.C. 272 note).

XII. Congressional Review Act

The Congressional Review Act, 5 U.S.C. 801 *et seq.*, generally provides that before a rule may take effect, the agency promulgating the rule must submit a rule report to each House of the Congress and to the Comptroller General of the United States. EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of this final rule in the **Federal Register**. This final rule is not a ''major rule'' as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: December 24, 2009.

Lois Rossi,

Director, Registration Division, Office of Pesticide Programs.

■ Therefore, 40 CFR chapter I is amended as follows:

PART 180—[AMENDED]

■ 1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

■ 2. In §180.920, the table is amended by adding alphabetically the following inert ingredients:

§ 180.920 Inert ingredients used pre-harvest; exemptions from the requirement of a tolerance.

Inert ingredients	Limits	Uses
* * *	*	*
Choline chloride (CAS Reg. No. 67–48–1)	---------- ------	As a solvent
* * *	*	*

[FR Doc. E9–31280 Filed 1–5–10; 8:45 am]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA–HQ–OPP–2009–0610; FRL–8802–5]

Dibenzylidene Sorbitol; Exemption from the Requirement of a Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes an exemption from the requirement of a tolerance for residues of dibenzylidene sorbitol (CAS Reg. No. 32647–67–9) under 40 CFR 180.920 when used as the inert ingredient in pesticdes formulations applied in or on growing crops. Dow Agrosciences LLC submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting an exemption from the requirement of a tolerance. This regulation eliminates the need to establish a maximum permissible level for residues of dibenzylidene sorbitol.

DATES: This regulation is effective January 6, 2010. Objections and requests for hearings must be received on or before March 8, 2010, and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: EPA has established a docket for this action under docket identification (ID) number EPA–HQ–OPP–2009–0610. All documents in the docket are listed in the docket index available at *http://www.regulations.gov*. Although listed in the index, some information is not publicly available, e.g., Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available in the electronic docket at *http://www.regulations.gov*, or, if only

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDE, AND TOXIC SUBSTANCES

October 16, 2009

MEMORANDUM

SUBJECT: Decision Document for Petition Number 8E7387;
Choline Chloride, CAS Reg. No 67-48-1

FROM: Deirdre Sunderland, Industrial Hygienist
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505P)

TO: PV Shah, Chief
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505P)

EXCUTIVE SUMMARY

Choline chloride is a quaternary ammonium salt which dissociates in water resulting in a positively charged quaternary hydroxyl alkylammonium ion and a negatively charged chloride ion. Choline is an essential component of the human diet and acts as a precursor to acetylcholine, phospholipids, and the methyl donor betaine. It is important for the structural integrity of cell membranes, cholinergic neurotransmission, transmembrane signaling, methyl metabolism, and lipid and cholesterol transport and metabolism.

Choline is found naturally in foods in both esterified forms and as free choline. Historically, it has been used as a food additive for animal husbandry, in plant growth regulator formulations, and as food supplements for humans. Choline was officially made an “essential nutrient” in 1998 and adequate intake (AI) level were established (women-425 mg/day, pregnant women- 450 mg/day, men and lactating women- 550 mg/day). The Daily Upper Intake Level for choline is 3.5 grams for adults. Research indicates that many individuals are not getting enough choline, with daily intake levels far below the AI.

Chloride is a binary compound of chlorine; a salt of hydrochloric acid. Chloride is the major extracellular anion and contributes to many body functions

including the maintenance of osmotic pressure, acid-base balance, muscular activity, and the movement of water between fluid compartments. The World Health Organization has performed two assessments which determined that from a toxicological point of view, there were no concerns for the chloride ion. It was considered to be naturally-occurring and a normal participant of animal and human metabolism.

Choline chloride has demonstrated a low acute oral toxicity with LD_{50} values for rats ranging from 3150 to ≥ 6000 mg/kg and LD_{50} for mice in the range of 3900 to 6000 mg/kg. Although appropriate animals studies are lacking for acute dermal toxicity, an in vitro percutaneous absorption study performed under occluded and unoccluded conditions showed that choline chloride is expected to have a low potential for percutaneous absorption. Acceptable acute inhalation studies are not available.

Studies were conducted in the early 1960's which resulted in only slight transient irritation of the skin and eye; however, these studies were not performed under OECD guidelines and therefore the degree of irritation is not classifiable under the Globally Harmonized System of Classification and Labeling of Chemicals (GHS). Choline chloride is not expected to cause skin sensitization.

Repeat dose animal studies on choline chloride are limited. One study in mice, evaluated the impact of 200 mg/kg/day choline chloride given orally or intranasally for 28 days. No adverse effects were observed with regards to body weight, food and water consumption, hematology, clinical biochemistry (Urea, BUN, HDL, TC, ALT, AST, and creatinine), or histopathology of various organs (lung, heart, liver, spleen, and kidney). Results from intranasal exposure to choline chloride were comparable with their respective controls and to other treatment groups. The NOAEL for oral and intranasally administered choline chloride is ≥ 200 mg/kg/day.

A 72-week feeding study in rats administered 500 mg/kg/day of choline chloride and observed the animals for 30 weeks post exposure. There were no significant difference between the control and treated group in relation to body weights, relative liver weight, survival rates, and the number of neoplastic liver nodules, hepatocellular carcinomas, lung tumors, leukemia, or other tumors. This study resulted in a NOAEL of 500 mg/kg.

Choline is a precursor to the vital neurotransmitter acetylcholine. Studies show that choline has beneficial effects on the nervous system and memory. Choline is necessary to promote proper development in the fetus and infant and prevent cognitive problems. Choline chloride not expected to cause neurotoxicity.

Choline chloride is not a known endocrine disruptors nor is it or its metabolites related to any class of known endocrine disruptors. Based on the

results of the in vitro and in vivo studies the Agency concluded that choline cloride is not expected to be carcinogenic or mutagenic.

Since the 1930's choline chloride has been used as a widespread nutrient in animal feed without adverse effects reported on fertility or teratogenicity. The Food and Drug Administration (FDA) requires choline be added to non-milk based infant formulas at a minimum concentration of 7 mg for every 100 kilocalories (21 CFR 107.100). Although one study did show developmental effects, they were only seen at very high doses (≥4,160 mg/kg/day) and only in the presence of maternal toxicity. There were no observed adverse effects for both mothers and pups exposed to 1250 mg/kg/day. Based on this information the Agency concluded that choline chloride, when used as an inert ingredient, will not cause reproductive or developmental toxicity and therefore, does not anticipate an increased risk to infants and children.

In addition to its low toxicity, exposure to choline chloride will be limited. Humans are currently exposed to choline on a daily basis through commonly consumed foods (both naturally occurring and when added as a nutrient) and through the bodies natural ability to synthesize the nutrient. It is unlikely that the exposure from choline chloride, when used as an inert ingredient applied pre-harvest to food commodities, will significantly increase the current concentration of choline in foods. Choline chloride is readily biodegradable and because of its high water solubility it is expected that most of the inert will be washed from the plant prior to consumption. Once in water, its preferred media, it will be broken into in a quaternary hydroxyl alkylammonium ion and a chloride ion.

Similar to humans, choline is a dietary requirement for many animals including avian and aquatic species. Based on this information, the biodegradability of the chemical, and the available toxicity data, the Agency concluded that choline chloride is unlikely to be harmful to mammalian, aquatic, and avian organisms.

In light of the prevalence of choline in the diet, the body's natural ability to synthesis it, the natural occurrence of both choline and chloride, and their low toxicity the Agency concluded that there is no increased risk to humans from the use of choline chloride as an inert ingredient in pesticide products. Therefore, choline chloride has been approved as an inert ingredient in pesticide products used on all food commodities under 40 CFR 180.920.

I. BACKGROUND AND USES

In October 2008 Loveland Products, Inc. submitted a petition to amend 40 CFR 180.920 by establishing an exemption from the requirement of tolerance for the use of choline chloride (Ethanaminium, 2-hydroxy-N, N, N-trimethyl-, chloride; CAS Reg. No. 67-48-1) as an inert ingredient in pesticide products when used as a solvent on all pre-harvest food commodities.

Choline chloride is a quaternary ammonium salt which dissociates in water resulting in a positively charged quaternary hydroxyl alkylammonium ion and a negatively charged chloride ion. (OECD, 2004) Choline is an essential component of the human diet and acts as a precursor to acetylcholine, phospholipids, and the methyl donor betaine. It is important for the structural integrity of cell membranes, cholinergic neurotransmission, transmembrane signaling, methyl metabolism, and lipid and cholesterol transport and metabolism.

Choline is found naturally in foods (e.g. eggs, liver meats, fungi, soybeans, fish, nuts, beans, and wheat germ) in both esterified forms (e.g. phosphocholine, glycerophosphocholine, shingomyeline, and phosphatidylchoine) and as free choline. Historically, it has been used as a food additive for animal husbandry, in plant growth regulator formulations, and as food supplements for humans. Choline was officially made an “essential nutrient” in 1998.

An adequate intake (AI) level for choline has been established by the Food and Nutrition Board (FNB) of the National Academy of Science’s Institute of Medicine at 550 mg/day for adult men and lactating women. The AI for women is 425 mg/day and 450 mg/day for pregnant women. This AI was set based on the amount necessary to prevent liver abnormalities as indicated by serum levels of the liver enzyme alanine aminotransferase (ALT). Daily Upper Intake Levels (UL, the highest level of intake that is not likely to cause harm) for choline are: 1 gram daily for children 1-8 years, 2 grams for children 9-13 years, 3 grams for children 14-18 years, and 3.5 grams for adults over 18 years of age”.(National Academy of Sciences (NAS), 1998)

Chloride is a binary compound of chlorine; a salt of hydrochloric acid. Chloride is the major extracellular anion and contributes to many body functions including the maintenance of osmotic pressure, acid-base balance, muscular activity, and the movement of water between fluid compartments.

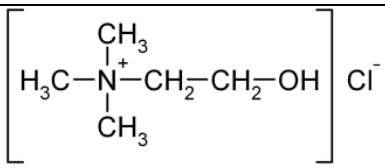
II. PHYSICAL AND CHEMICAL PROPERTIES

Choline chloride is a quaternary ammonium salt which dissociates in water resulting in a positively charged quaternary hydroxyl alkylammonium ion and a negatively charged chloride ion. Based on its chemical structure choline chloride is not expected to undergo hydrolysis. The Mackay Level I V2.11 model indicates that for pure choline chloride water is the preferred medium with almost 100% distribution. Other compartments such as air, soil, sediment, fish, and aerosol are expected to only receive a negligible amount of choline chloride (<0.00000005%).

The Mackay model results are consistent with the PCKOCWIN model which resulted in a $\log K_{oc}$ of 0.37 indicating that choline chloride will not adsorb to soil and sediment or suspended solids. According to OECD-criteria, choline chloride is readily biodegradable (MITI I-Test: 93% biodegradation within 14 days). A BOD_5 test performed on choline chloride obtained a $BOD_5/ThOD_5$ ratio of 75% which confirms the biodegradability of choline chloride. (OECD, 2004 citing MITI, 1992 and BASF AG 1984) Although estimated bioconcentration factors (BCF) for choline chloride vary between models, all study results indicate that the potential for bioaccumulation is low.

Using the HENRYWIN model to calculate Henry's Law Constant resulted in 2.06 $X10^{-11}$ $Pa*m^3$/mole indicating that choline chloride will not rapidly evaporate into the atmosphere (OECD, 2004 citing BASF AG 2003c). In the event that choline chloride does enter the atmosphere it is expected to be rapidly degraded based on the AOP v1.90 model calculation for OH-radicals ($t_{1/2}$ of approximately 6.9 hours based on a 12 hour day). (OECD, 2004 citing BASF AG 2004a)

Table 1: Summary of physico-chemical properties[1]

Property	Value	Remarks and Secondary Reference Citations
Physical state	white crystalline solid Liquid, colorless, amine-like odor	Pure choline chloride Solution 75% w/w in water; BASF AG (2002)
Physical structure		SCCNFP, 2003
Molecular formula	$C_5H_{14}NO.Cl$	
Synonyms	Ethanaminium, 2-hydroxy-N, N, N-trimethyl-, chloride; Biocoline; Cholinium chloride; Hepachloride; Lipotril; Luridin chloride; Paresan; Trimethyl (2-hydroxyethyl) ammonium chloride	Confirmed with CAS Online
Melting point	247 °C	The information corresponds to the pure substance; ICSC 0853 (2004)
Boiling point	Not applicable due to decomposition on heating	
Relative density	1.1 g/cm^3 at 20°C	70 ± 1% choline chloride. 30% water, less than 0.05% impurities measured; BASF AG (1974). Data refer to a technical data overview, no details of method used and year the study was performed is given. Further, as the value refers to a solution the density of the pure substance may differ.
Viscosity	21 mPa*s at 20°C	70 ± 1% choline chloride. 30% water, less than 0.05% impurities measured; BASF AG (1974). Data refer to a technical data overview, no details of method used and year the study was performed is given.
Vapor pressure	6.57 x 10^{-8} Pa at 25°C	Calculated using MPBPWIN v1.40, refers to the pure substance; BASF AG (2003a)
Water solubility	Ca. 650 g/l	50% choline chloride powder; pH=6-7; measured; BASF AG (1974); Study reliability was not assignable. A calculated value for the pure substance of 1000g/l was estimated using WSKOW v1.40; BASF AG (2003b)
Partition coefficient n-octanol/water ($\log K_{ow}$)	-3.77 at 25°C	Solution 75% w/w in water; measured; BASF AG (1988a)
Henry's law constant	2.06* 10E-11 Pa*m^3/mole at 25°C	Calculated using HENRYWIN v3.10 (bond method), refers to the pure substance; BASF AG (2003d)
$\log K_{oc}$	0.37	Calculated using the PCKOCWIN v1.66 calculation program (K_{oc} = 2.3), refers to the pure substance; BASF AG (2003e)

[1] Source of all information (except *)- OECD SIDS Initial Assessment Report (2004) for-Choline Chloride

III. METABOLISM / PHARMACOKINETICS

Choline is a necessary component of the human diet and acts as a precursor to the neurotransmitter acetylcholine, phospholipids, and the methyl donor betaine. The body requires choline which it obtains through direct ingestion of foods/supplements containing choline or through a de novo biosynthesis process. According to the OECD SIDS document on choline chloride (2004),

> There is an endogenous pathway for the de novo biosynthesis of the choline moiety via the sequential methylation of phosphatidylethanolamine using S-adenosylmethionine as the methyl donor. Thus, the demand for dietary choline is modified by metabolic methyl-exchange relationships between choline and three nutrients: methionine, folate, and vitamin B12.

This de novo process allows the body to produce choline; however, the body's natural synthesis of choline is not sufficient to meet its needs and therefore, dietary choline is required. In light of this evidence, choline was recognized as an essential nutrient in 1998. Effects have been observed with regards to the liver, kidney and brain of choline deficient animals/humans in studies where choline has been withheld. (Politizer Shronts, 1997; Zeisel et al., 1991)

Once ingested, choline is absorbed from the lumen of the small intestine. Prior to adsorption from the gastrointestinal tract some choline is metabolized by internal bacteria to form betaine and methylamines. Pancreatic enzymes can also breakdown dietary phosphatidylcholine (a.k.a. lecithin) to form free choline. Choline is important for the structural integrity of cell membranes, cholinergic neurotransmission, transmembrane signaling, methyl metabolism and lipid and cholesterol transport and metabolism.

Chloride is a binary compound of chlorine; a salt of hydrochloric acid. Chloride is the major extracellular anion and contributes to many body functions including the maintenance of osmotic pressure, acid-base balance, muscular activity, and the movement of water between fluid compartments. The World Health Organization (WHO) has performed two assessments which determined that from a toxicological point of view, there were no concerns for the chloride ion. It was considered to be naturally-occurring and a normal participant of animal and human metabolism.

IV. TOXICOLOGY

A. Acute Toxicity

Oral

LD_{50} levels reported in rats for choline chloride show a range from 3150 and ≥ 6000 mg/kg. Restlessness, hypoactivity, increased frequency of

respiration, convulsions, ruffled coat, staggered gait, and dyspnea were reported. Some animals experienced diarrhea and in one study 3 out of 10 rats in the high dose group had inflamed lungs at necropsy. (OECD, 2004) Similarly, the LD_{50} reported for mice was in the range of 3900 to 6000 mg/kg.

Dermal

No acute dermal animal studies are available. An *in vitro* percutaneous absorption study was conducted in compliance with GLP under OECD draft guideline 428, using human epidermal skin. Liquid scintillation counting was used to determine skin absorption of radiolabelled (50 mCi of $1,2^{-14}$ C) choline chloride. Skin samples were mounted on Franz-type diffusion cells, and [^{14}C]-choline chloride was applied to the surface of the skin for 24 hours. Each sample area was dosed with a single dose of approximately 10 µl/cm² of a 5% choline in water solution. Samples were evaluated at 1, 2, 6, 12, and 24 hours under occluded and non-occluded conditions.

This study showed that 7.42 µg/cm² and 13.86 µg/cm² (1.9 % and 3.43 %) of the applied dose was absorbed under occluded and non-occluded conditions respectively, with most remaining in the epidermis (5.90µg/cm² and 10.7 µg/ cm²) and dermis (1.06 µg/cm² and 2.40 µg/cm²). Only 0.457 µg/cm² (0.127 %) and 0.383 µg/cm² (0.110 %), of the applied dose penetrated into the receptor fluid for occluded and unoccluded cells, respectively. Under the conditions of this study, choline chloride is expected to have a low potential for percutaneous absorption (SCCNFP, 2003 and SCCP, 2008).

Inhalation- No valid data available.

Skin Irritation

Minor skin irritation (questionable reddening after 24 hour only) was noted on the back of 1 of 2 rabbits treated with an aqueous formulation of the test substance (70% choline chloride and 30% water). Observations were made at 24hrs, 2, 3 or 8 days after exposure. This study, however, was an old non-GLP (Good Laboratory Practices), non-guideline study whose degree of irritation would not be classifiable under the globally harmonized system (GHS). Compared to OECD TG 404, this test was harsher due to the longer exposure time (20 vs. 4 hrs) and the use of an occlusive rather than a semi-occlusive dressing. These factors may lead to an overestimation of the skin irritation capabilities of the test substance; therefore, the results are more conservative then current studies would indicate. (OECD, 2004 citing BASF AG, 1963)

Eye Irritation

An eye irritation study performed on choline chloride was conducted broadly to OECD test guideline 405, although, it did not comply with GLP due to

the age of the study. One eye of a male and female rabbit were exposed to a 70% chlorine chloride aqueous solution. The other eye was used as the control. After 10 minutes reddening and tear secretions were observed. Slight reddening persisted up to three hours after application. Observations were made at 1 and 3 hours post application and 1 and 8 days. At 1 day post application no effects were noted. (OECD, 2004 citing BASF AG, 1963c)

Skin Sensitization

No data are available on the sensitization of choline chloride in animals. According to the OECD SIDS report (2004) on choline chloride, “the skin sensitization potential of chlorine chloride for humans is regarded as negligible”. Furthermore, the Scientific Committee on Cosmetic Products and Non-food Products Intended for Consumers (SCCNFP) is of the opinion that dermal exposure to choline chloride, in rinse off products at 5%, is not anticipated to pose any serious risk. (2003)

B. Repeat Dose Studies

Although studies have been conducted to evaluate the possible medicinal benefits of choline chloride in humans, acceptable repeat dose animal studies are limited. Available animal studies have been presented below.

Male and female Balb/c mice were treated with 200mg/kg/day orally or intranasally for 28 days. For orally exposed animals, 200 mg/kg/day was administered by oral gavage once daily until day 28. Intranasally exposed animals were given 200mg/kg/day in a 50 µl vehicle every other day for 28 days. Choline chloride administration by both the oral and intranasal routes of exposure did not cause adverse effects with regards to body weight, food and water consumption, hematology, clinical biochemistry (Urea, BUN, HDL, TC, ALT, AST, and creatinine), or histopathology of various organs (lung, heart, liver, spleen, and kidney). Results from intranasal exposure to choline chloride were comparable with their respective controls and to other treatment groups (intraperitoneal exposure was also assessed). (Mehta, 2009) The NOAEL for oral and intranasally administered choline chloride is ≥ 200 mg/kg/day.

In a limited 72 week feeding study, Fischer 344 rats were given approximately 500 mg/kg/day of choline chloride. Animals were observed for 30 weeks post exposure during which time the test animals and the controls received the same untreated diet. Histopathology performed at week 103 was restricted to the liver and organs that developed gross abnormalities. There were no significant difference between the control and treated group in relation to body weights, relative liver weight, or survival rates. The number of neoplastic liver nodules, hepatocellular carcinomas, lung tumors, leukemia, or other tumors was not increased in treated animals. This study resulted in a NOAEL of 500 mg/kg/day. (OECD, 2004 citing Shivapurkar, 1986)

C. Neurotoxicity

Choline is a known precursor to a vital neurotransmitter, acetylcholine. The peripheral nervous system uses acetylcholine in skeletal muscle movement, as well as in the regulation of smooth muscle and cardiac muscle. In the central nervous system acetylcholine is believed to be involved in learning, memory, and mood. Choline chloride has been evaluated for its medicinal use in treating neurological conditions such as tardive dyskinesia, Alzheimers, Huntington's disease, ataxia, and memory loss in the elderly. (Mohs et al., 1979; Snell et al., 1980)

Two studies which evaluated the effects of choline chloride on memory in rats showed a positive correlation between choline and memory functions and a third study showed no effect. The first study supplemented rats prenatally by adding choline to the drinking water of their dams. Another treatment group was made deficient of choline during early development by withhold it from the dam's diet. A third group was used as controls.

After being maintained on a choline-sufficient diet for 120 days postnatally, the rats began 12-arm radial maze training. The results of the study (Meck and Williams, 1999) indicated:

> Both choline-supplemented and choline-deficient rats performed more accurately than control littermates when trials were spaced. These differences in spatial ability did not appear to be a function of differential response or cue-use strategies. Choline-supplemented rats showed little proactive interference when trials were massed; whereas control rats demonstrated moderate levels and choline-deficient rats exhibited high levels of proactive interference as a function of massed trials. These data suggest that the behavioral consequences of early dietary availability of choline may involve the modification of the discriminative abilities used to attend to stimuli that demarcate the end of one trial and the start of another as well as the capacity for remembering the locations that have been visited during a trial.

A second study utilized a T-maze design to investigate the effect of choline supplementation on memory consolidation in young female Sprague-Dawley rats. One group of rats received choline chloride daily for two weeks and a second group was used as a control. In the dark area (DA) of the maze, which is naturally preferred by the rat, an electric foot-shock (0.1 mA at 60V) was delivered when the rats entered the area. Both the treated and control groups showed a preference for the DA and15 minutes after passive avoidance both groups avoided entry into the DA. This suggests that both groups had acquired short-term memory of the negative stimuli; however, when the test was repeated 24 hours after training the control group did not avoid entry to the DA, whereas the group who received the choline supplements either avoided entry or entered after a significantly longer latency period. According to the author, "These results suggest that supplementation with choline facilitated the consolidation of short-

term memory of the avoidance learning into intermediate long-term memory in young rats." (Gossell-Williams et al., 2006)

In the third study, male Long-Evans rats were fed diets containing either (i) choline chloride 1250 mg/L, (ii) choline chloride 250 mg/L and GD3 24 mg/L, or (iii) choline chloride 250 mg/L on postnatal days 5-18. A fourth group was reared normally. The study found "all rats were equally proficient at using spatial short-term memory, regardless of the choline or ganglioside content of the preweaning diet". (Mohs et al., 1979)

D. Carcinogenicity/Mutagencity

In vitro studies designed to investigate the ability of choline chloride to induce gene mutation in bacteria were negative. Three Ames test were conducted with Salmonella typhimurium strains TA 98, 100, 1535, 1537, and/or 1538, up to 10,000 µg/plate and E. coli WP2 uvrA up to 5,000 µg/plate with and without metabolic activation. Although all of the studies were tested up to at least the limit dose of 5 mg/plate, two of the tests did not show bacterial toxicity. The third study showed a 50% survival at the highest dose tested. (OECD, 2004 citing Haworth et al., 1984; JETOC, 1997; Litton Bionetics, 1977; and NTP, 1983).

NTP reported on three experiments designed to look at choline chlorides potential to cause chromosomal aberrations. In one study a small but statistically significant increase in simple aberrations was seen at 50 and 500 µg/ml (the highest dose tested) in the absence of S9 only. Two reliable Chinese Hamster Ovary Cell studies, however, showed that cytotoxicity (50% survival) only occurred at choline chloride concentration of 5000 µg/ml. One hundred cells were examined per dose and treatment group and S9 from Aroclor induced rat livers were used for metabolic activation (OECD, 2004 citing Bloom et al., 1982; Galloway et al., 1985; and NTP, 1984).

Two parallel sister chromatid exchange assays at two different laboratories were conducted on Chinese Hamster Ovary cells at concentrations up to 500 and 5000 µg/ml, respectively and gave ambiguous results. According to OECD SIDS (2004),

> Cytotoxicity (50% survival) was observed at 5000 µg/ml Metabolic activation was with S9 from Aroclor induced rate livers. Approximately 1000 chromosomes were examined per dose and treatment group. The increase (sporadic and not dose related) in SCEs that was observed with metabolic activation in laboratory two was not reproduced in laboratory one. Laboratory one showed a weak positive at the top dose without metabolic activation, but a comparison with laboratory two was not possible due to insufficient numbers of cells analyzed.

A third study using Chinese hamster ovary cells showed no increase in the number of sister chromatid exchanges at concentrations up to 5000 µg/ml with and without metabolic activation. (OECD, 2004 citing NTP 1984) Negative results

were also obtained from a gene conversion assay using *Saccharomyces cerevisiae* strain D4 with choline chloride concentration between 12.5 and 50 mg/ml with and without metabolic activation. (OECD, 2004 citing Litton Bionetics, 1977).

The SIDS document concluded that;

> Choline chloride does not have any structural alerts for genotoxicity. It did not produce gene mutations, clastogenicity, or DNA damage when tested in vitro. It can be concluded from these studies that choline chloride does not have any mutagenic potential.

An epidemiologic study released in 2007 evaluated the relationship between choline and betaine intake and the risk of colorectal adenoma in US women enrolled in the Nurses' Health Study. The study evaluated responses from female registered nurses aged 30-55 years who responded to a baseline questionnaire on lifestyle and major illnesses in 1976. Every 2 years, a follow-up questionnaire was sent to the women to update information regarding diet and lifestyle and to ascertain new diagnoses of major illnesses. The study found that higher choline intake was associated with an elevated risk of colorectal adenoma; however, the investigators stated that: (Cho et al., 2007)

> Our findings do not support an inverse association between choline intake and risk of colorectal adenoma. The positive association between choline intake and colorectal adenoma that we observed could represent effects of other components in the foods from which choline was derived and should be investigated further.

On the contrary, multiple studies have indicated that choline many have an inverse relationship to breast cancer risk. (Xu et al., 2008; Shannon et al., 2005; Frazier et al., 2003)

E. Reproductive/Developmental

Choline has been shown to have positive effects on development. Research suggests that adequate amounts of choline during pregnancy and breastfeeding can help ensure healthy fetal brain development. Studies have shown that pregnant women consuming a choline deficient diet have a significantly higher rate of neural tube and oral cleft defects in their offspring. (Xu et al., 2008) Adequate prenatal choline levels may also have long-lasting positive effects on cognitive function, including memory. However, sufficient research has not been done on the effects of choline on pregnant women and their unborn babies.

A developmental toxicity study exposed NMRI mice to 1250, 4160, 10800, or 20000 mg/kg/day every other day from gestation day 1 to 18. In all but the lowest group, maternal body weight gain was reduced. Those exposed to ≥4,160 mg/kg/day showed almost no net weight gain and those exposed to the highest tested dose (20,000 mg/kg/day) showed weight loss. Embryonic/fetal lethality

was recorded at 35% and 69% for those tested with 4,160 and 10,800 mg/kg/day, respectively. No resorptions occurred in the lowest dose group; conversely, all fetuses in the highest dose group were resorbed. There was no statistically significant, dose related increases in malformations between the treated and control groups. (OECD, 2004 citing BASF AG, 1966)

In all but the lowest dosed group, developmental toxicity was observed; however, it was not observed in the absence of maternal toxicity. It is important to bare in mind that all of the levels tested in this study are much greater than the usual limit dose used for a non-toxic compound (i.e. 1000 mg/kg/day). There were no observed effects for those both mothers and pups tested with 1250 mg/kg/day; therefore, the NOAEL for maternal toxicity and developmental toxicity is 1250 mg/kg/day. Due to a lack of sufficient pups, a NOEAL for teratogenicity was not determined. (OECD, 2004 citing BASF AG 1966)

Currently, there is a study sponsored by the National Institute of Mental Health that will “evaluate the safety and effectiveness of taking choline supplements during pregnancy and whether taking choline during pregnancy will have an effect on infant development”. The study is expected to be completed in March 2010. (NIMH, 2006-2010 proposed)

F. Endocrine

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) “may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate". Choline chloride is not a known endocrine disruptors nor is it or its metabolites related to any class of known endocrine disruptors.

G. Special Consideration for Infants and Children (FQPA Safety Factor)

FFDCA section 408 provides that EPA shall apply an additional tenfold margin of exposure (safety) for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the data base unless EPA determines that a different margin of exposure (safety) will be safe for infants and children.

Choline is a natural component of a variety of commonly consumed foods (e.g. (per100g food)- eggs (251mg), wheat germ (152 mg), bacon (125 mg), dried soybeans (116 mg), pork (103 mg), cod (83 mg), beef (80 mg), chicken (70 mg), and salmon (65 mg))(USDA, 2004). It has been added as a supplement to infant formula in the US for decades (Politizer Shronts, 1997). In addition to dietary consumption, choline is made endogenously in the human body.

Choline chloride has been used as a widespread nutrient in animal feed since the 1930's without adverse effects reported on fertility or teratogenicity. Although one study in mice did show developmental effects, they were only seen at very high doses (≥4,160 mg/kg/day) and only in the presence of maternal toxicity. There were no observed adverse effects for both mothers and pups exposed to 1250 mg/kg/day. Evidence has shown that choline has beneficial properties in regards to proper growth and development and neurological function.

Exposure to choline chloride not expected to significantly increase the pre-existing levels found in commonly eaten foods. Choline chloride residues on food is expected to be minimal. Because of its high water solubility most of the inert will be washed from the plant prior to consumption. Once in water, it will be broken into in a quaternary hydroxyl alkylammonium ion and a chloride ion.

Due to the low toxicity of the chemical, the bodies need for choline from a dietary source, and the beneficial role choline plays in fetal development; the safety factor has been reduced to 1 X.

V. ENVIRONMENTAL FATE AND DRINKING WATER

Physical chemical properties coupled with modeling indicate that water is expected to be the preferred media for choline chloride. The Mackay model showed a 100% water distribution and the PCKOCWIN model resulted in a log K_{oc} of 0.37, indicating that choline chloride will not adsorb to soil and sediment or suspended solids. Once in water choline chloride, a quaternary ammonium salt, dissociates resulting in a positively charged quaternary hydroxyl alkylammonium ion and a negatively charged chloride ion. (OECD, 2004) Choline chloride is not expected to undergo hydrolysis.

According to the OECD-criteria, choline chloride is readily biodegradable (MITI I-Test: 93% biodegradation within 14 days). A BOD_5 test performed on choline chloride obtained a $BOD_5/ThOD_5$ ratio of 75% which also indicates that choline chloride is readily biodegradable. (OECD, 2004 citing MITI, 1992 and BASF AG, 1984) Although estimated bioconcentration factors (BCF) for choline chloride vary between models, all results indicated that the potential for bioaccumulation is low.

Using the HENRYWIN model to calculate Henry's Law Constant resulted in 2.06 $X10^{-11}$ $Pa*m^3$/mole indicating that choline chloride will not rapidly evaporate into the atmosphere. (OECD, 2004 citing BASF AG, 2003c) In the atmosphere choline chloride is expected to be rapidly degraded based on the AOP v1.90 model calculation for OH-radicals ($t_{1/2}$ of approximately 6.9 hours based on a 12 hour day) (OECD, 2004 citing BASF AG, 2004a).

Choline, an essential dietary nutrient, is present in a variety of foods and is synthesized by the body. Because of its natural presence in the environment and its readily biodegradable nature, choline chloride when used as an inert ingredient in pesticide formulations, is not expected to significantly increase the levels of naturally occurring choline drinking water or the environment.

VI. EXPOSURE ASSESSMENT

A. Exposure Profile

Humans are currently exposed to choline on a daily basis through commonly eaten foods (both naturally occurring and when added as a nutrient) and through the bodies natural ability to synthesize the nutrient. It is unlikely that the exposure from choline chloride, when used as an inert ingredient applied pre-harvest to food commodities, will significantly increase the natural concentration of choline present in foods. Because of its high water solubility it is expected that most of the inert will be washed from the plant prior to consumption. Once in water, it will be broken into in a quaternary hydroxyl alkylammonium ion and a chloride ion. Choline is an essential nutrient and a requirement in many of the bodies functions.

B. Aggregate Exposure

Section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA) directs the Agency to evaluate aggregate exposure from “pesticide chemical residue and to other related substances, including dietary exposure under the tolerance and all other tolerances in effect for the pesticide chemical residue, and exposure from other non-occupational sources”. The expected exposure pathway for choline chloride is through the oral and the dermal routes of exposure.

Although a method is not require to determine the residues on food when an exemption from tolerance is granted it is expected that because of the low oral and dermal toxicity, the rapid degradation of the chemical, and the natural presence of choline and chloride in the environment, aggregate exposure will result in minimal risk to all subpopulation including infants and children. Based on the physical and chemical properties, the inhalation route is not a likely exposure pathway; therefore, the anticipated risk from inhalation exposure is considered minimal. (Cho et al., 2007)

C. Cumulative Exposure

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." Unlike other pesticides for which EPA has followed a cumulative risk

approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to choline chloride and any other substances, and these chemicals do not appear to produce toxic metabolites produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that choline chloride has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/

VII. RISK CHARACTERIZATION

Choline chloride is a quaternary ammonium salt which dissociates in water resulting in a positively charged quaternary hydroxyl alkylammonium ion and a negatively charged chloride ion. (OECD, 2004) Choline is an essential component of the human diet and acts as a precursor to acetylcholine, phospholipids, and the methyl donor betaine. It is important for the structural integrity of cell membranes, cholinergic neurotransmission, transmembrane signaling, methyl metabolism, and lipid and cholesterol transport and metabolism.

Choline is found naturally in foods (e.g. eggs, liver meats, fungi, soybeans, fish, nuts, beans, and wheat germ) in both esterified forms (e.g. phosphocholine, glycerophosphocholine, shingomyeline, and phosphatidylchoine) and as free choline. Historically, it has been used as a food additive for animal husbandry, in plant growth regulator formulations, and as food supplements for humans. Choline was officially made an “essential nutrient” in 1998. The adequate intake (AI) level for choline in women is 425 mg/day and 450 mg/day for pregnant women. Men and lactating women have a slightly higher AI at 550 mg/day. Daily Upper Intake Level for choline is 3.5 grams for adults. (NAS, 1998) Research on choline in the diets of the US population using the NHANES, 2003–2004 data indicates that many individuals are not getting enough choline, with daily intake levels far below the AI. (Jensen et al., 2007)

Chloride is a binary compound of chlorine; a salt of hydrochloric acid. Chloride is the major extracellular anion and contributes to many body functions including the maintenance of osmotic pressure, acid-base balance, muscular activity, and the movement of water between fluid compartments. The World Health Organization has performed two assessments which determined that from a toxicological point of view, there were no concerns for the chloride ion. It was considered to be naturally-occurring and a normal participant of animal and human metabolism.

Choline chloride has demonstrated a low acute oral toxicity with LD_{50} values for rats ranging from 3150 to ≥ 6000 mg/kg and LD_{50} for mice in the range of 3900 to 6000 mg/kg. Although appropriate animals studies are lacking for acute dermal toxicity, an in vitro percutaneous absorption study performed under occluded and unoccluded conditions showed that choline chloride is expected to have a low potential for percutaneous absorption. Acceptable acute inhalation studies are not available.

Studies were conducted in the early 1960's to evaluate the eye and skin irritation potential of choline chloride. Because their age, the studies were not performed under OECD guidelines and therefore the degree of irritation is not classifiable under the Globally Harmonized System of Classification and Labeling of Chemicals (GHS). Although these results would not be classifiable under GHS, it is important to note that only slight transient irritation was observed in the skin and eye irritation studies. Choline chloride is not expected to cause skin sensitization.

Repeat dose animal studies on choline chloride are limited. One study using male and female Balb/c mice, evaluated the impact of 200 mg/kg/day choline chloride given orally or intranasally for 28 days. No adverse effects were observed with regards to body weight, food and water consumption, hematology, clinical biochemistry (Urea, BUN, HDL, TC, ALT, AST, and creatinine), or histopathology of various organs (lung, heart, liver, spleen, and kidney). Results from intranasal exposure to choline chloride were comparable with their respective controls and to other treatment groups (intraperitoneal exposure was also assessed). The NOAEL for oral and intranasally administered choline chloride is ≥ 200 mg/kg/day.

A 72 week feeding study administered 500 mg/kg/day of choline chloride to Fischer 344 rats and observed the animals for 30 weeks post exposure during which time the test animals and the controls received the same untreated diet. There were no significant difference between the control and treated group in relation to body weights, relative liver weight, survival rates, and the number of neoplastic liver nodules, hepatocellular carcinomas, lung tumors, leukemia, or other tumors. This study resulted in a NOAEL of 500 mg/kg.

Choline is a precursor to the vital neurotransmitter acetylcholine. Studies show that choline has beneficial effects on the nervous system and memory. Choline is necessary to promote proper development in the fetus and infant and prevent cognitive problems. Choline chloride not expected to cause neurotoxicity.

Choline chloride is not a known endocrine disruptors nor is it or its metabolites related to any class of known endocrine disruptors. Based on the results of the in vitro studies the Agency feels that choline chloride is not expected to be carcinogenic or mutagenic.

Since the 1930's choline chloride has been used as a widespread nutrient in animal feed without adverse effects reported on fertility or teratogenicity. The Food and Drug Administration (FDA) requires choline be added to non-milk based infant formulas at a minimum concentration of 7 mg for every 100 kilocalories (21 CFR 107.100). Although one study did show developmental effects, they were only seen at very high doses (≥4,160 mg/kg/day) and only in the presence of maternal toxicity. There were no observed adverse effects for both mothers and pups exposed to 1250 mg/kg/day. Based on this information the Agency does not feel that choline chloride, when used as an inert ingredient, will cause reproductive or developmental toxicity and therefore, does not anticipate an increased risk to infants and children.

Choline has demonstrated a beneficial effect on ischemic cardiac arrhythmias and preventing liver and renal dysfunction. (Liu, 2008, Canadian journal; Zeisel, 2000). Recent studies suggested that cholines anti-inflammatory properties may be an effective treatment for asthma, a chronic inflammatory disease. (Mehta et al., 2007) Other documented benefits include a reduction in DNA hypomethylation and tumor development in the liver.

In addition to its low toxicity, exposure to choline chloride will be limited. The expected exposure pathway is via the oral and the dermal routes. Humans are currently exposed to choline on a daily basis through commonly eaten foods (both naturally occurring and when added as a nutrient) and through the bodies natural ability to synthesize the nutrient. It is unlikely that the exposure from choline chloride, when used as an inert ingredient applied pre-harvest to food commodities, will significantly increase the natural concentration of choline in foods. Choline chloride is readily biodegradable and because of its high water solubility it is expected that most of the inert will be washed from the plant prior to consumption. Once in water, its preferred media, it will be broken into in a quaternary hydroxyl alkylammonium ion and a chloride ion.

Similar to humans, choline is a dietary requirement for many animals including avian and aquatic species. Based on this information, the biodegradability of the chemical, and the available toxicity data, the Agency feels that choline chloride is unlikely to be harmful to mammalian, aquatic, and avian organisms.

In light of the prevalence of choline in the diet, the body's natural ability to synthesis it, and its low toxicity the Agency does not feel that there is an increased risk to humans from the use of choline chloride as an inert ingredient in pesticide products. Therefore, choline chloride has been approved as an inert ingredient in pesticide products used on all food commodities under 40 CFR 180.920.

ECOTOXOCITY

Similar to humans, choline is a dietary requirement for many animals including avian and aquatic species. Based on this information, the biodegradability of the chemical, and the available toxicity data (Table 2), the Agency feels that choline chloride is unlikely to be harmful to mammalian, aquatic, and avian organisms.

Acute toxicity testing in fish resulted in a LC50 (96h) for *oryzias latipes* and *limanda limanda* at >100mg/L and >1000mg/L, respectively. For the invertebrate *Daphnia magna* the EC50 (48h) is 349 mg/L and the NOEC (21d) is 30.2 mg/L.

Table 2: Acute toxicity of choline chloride to aquatic organisms[2]

Species	Method	Effect Concentration (mg/L)	Remark/Reference
Acute Toxicity to Fish			
***Oryzias latipes* (freshwater species)**	**OECD 203 (flowthrough system)**	**LC_{50} (96h) > 100 (nominal and measured)**	**purity of test substance: 100.2 %, reliability: 1; MOE Japan (1999a), KEY STUDY**
Leuciscus idus (freshwater species)	DIN 38412, part 15, static	LC_{50} (96h) > 10,000 (nominal)	no symptoms detectable; two tests with a) 78 % choline chloride watery solution (BASF AG, 1988b) and b) 50 % choline chloride as powder (BASF AG, 1988c) are available, non GLP, no analytics (reliability 2)
Limanda limanda (marine species)	according to OECD 203, semistatic	LC_{50} (96h) > 1,000 (nominal)	75 % choline chloride watery solution; limit test (only 1,000 mg/L tested); ICI (1983) (reliability 2)
Acute and chronic toxicity to aquatic invertebrates			
***Daphnia magna* (freshwater species)**	**OECD 202 (static)**	**EC_{50} (48h) = 349 mg/l (nominal and measured)**	**purity of test substance: 100.2 %, reliability: 1; MOE Japan (1999b), KEY STUDY**
Daphnia magna (freshwater species)	Directive 79/831 EEC, C2, static	LC_{50} (48h) > 500 (nominal) NOEC (48hr) = 125	78 % choline chloride watery solution; non GLP, no analytics (reliability 2); BASF AG, 2003g
***Daphnia magna* (freshwater species)**	**according OECD 211 (renewal system)**	**NOEC (21d) = 30.2 mg/L (nominal and measured)**	**purity of test substance: 100.2 %, reliability: 1; MOE Japan (1999c), KEY STUDY**
Acute toxicity to aquatic plants e.g. algae			
***Pseudokirchneriella subcapitata* (freshwater species)**	**OECD 201**	**ErC_{50} (72h) > 1,000 (nominal and measured), 72h NOEC (growth rate) = 32**	**purity of test substance: 100.2 %, reliability: 1; MOE Japan (1999d), KEY STUDY**
Scenedesmus subspicatus (fresh water)	DIN 38412, part 9, static	Er(b)C_{50} (72h) > 500(nominal), 72h NOEC (growth rate and biomass) >500	78 % choline chloride watery solution; non GLP, no analytics (reliability 2); BASF AG, 2003h

[2] Table adopted from OECD-SIDS on Choline Chloride (2004)

Bibliography

Cho E, Willett WC, Colditz GA, Fuchs CS, Wu K, Chan AT, Zeisel SH, & Giovannucci EL (2007) Dietary choline and betaine and the risk of distal colorectal adenoma in women. *Journal of the National Cancer Institute*, 99 (16): 1224-31

Dietary Reference Intakes, Institute of Medicine of the National Academies, National Academies Press, Washington, DC, 2006

Environmental Working Group, Skin Deep Cosmetic Safety Database. Choline chloride. Retrieved on 5/19/09 from http://www.cosmeticsdatabase.com/ingredient.php?ingred06=701343&nothanks=1

Frazier AL, Ryan CT, Rockett H, Willett WC, & Colditz GA (2003) Adolescent diet and risk of breast cancer. *Breast Cancer Research,* 5: R59-R64

Gossell-Williams M, Simon O, Young L, & West M (2006) Choline supplementation facilitates short-term memory consolidation into Q intermediate long-term memory of young Sprague-Dawley rats. *West Indian Medical Journal*, 55(1):4-8

Jensen HH, Batres-Marquez SP, Carriquiry A, & Schalinske KL (2007) Choline in the diets of the US population: NHANES, 2003-2004, (presented at Experimental Biology 2007, Washington DC). *The FASEB Journal*, 21:lb219

Meck WH & Williams CL (1999) Choline supplementation during prenatal development reduces proactive interference in spatial memory. *Developmental Brain Research,* 118:51–59

Mehta AK, Arora N, Gaur SN, Singh BP (2009) Acute toxicity assessment of choline by inhalation, intraperitoneal and oral routes in Balb/c mice. *Regulatory Toxicology and Pharmacology,* 54: 282–286

Mehta AK, Gaur SN, Arora N, & Singh BP (2007) Effect of choline chloride in allergen-induced mouse model of airway inflammation. *European Respiratory Journal*, 30: 662–671

Mohs RC, Davis KL, Tinklenberg JR, Hollister LE, Yesavage JA, & Kopell BS (1979) Choline chloride treatment of memory deficits in the elderly. *American Journal of Psychiatry*, 136:1275-1277

National Academy of Sciences (NAS). Institute of Medicine. Food and Nutrition Board. (1998) Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. National Academy Press, Washington DC, 20418

National Institute of Mental Health (NIMH) (2006-2010 proposed) Safety and effectiveness of taking choline supplements during pregnancy for improving infant brain development. ClinicalTrials.gov Identifier: NCT00332124. Retrieved on 5/20/09 from http://clinicaltrials.gov/ct2/show/NCT00332124

Opinion of the Scientific Committee on Cosmetic Products and Non-food Products (SCCNFP) Intended for Consumers Concerning: Choline Chloride (2003) SCCNFP/0672/03, SCCNFP is a subdivision of the European Commission

Organization for Economic and Cooperative Development (OECD) (2004) Screening Information Data Set (SIDS) Initial Assessment Report (SIAR) for Choline Chloride (CAS No. 67-48-1) and IUCLID Data Set; UNEP Publications

Politizer Shronts E (1997) Essential nature of choline with implications for total parenteral nutrition. *Journal of the American Dietetic Association*, 97(6):639-46, 649

Shannon J, Ray R, Wu C, Nelson Z, Gao DL, Li W, Hu W, Lampe J, Horner N, Satia J, Patterson R, Fitzgibbons D, Porter P, & Thomas D (2005) Food and botanical groupings and risk of breast cancer: A case-control study in Shanghai, China. *Cancer Epidemiology, Biomarkers & Prevention*, 14 (1): 81-90.

Scientific Committee on Consumer Products (SCCP) (2008) Opinion on choline chloride. As reported to the European Commission on April, 15 2008

Snell APJ, Cleary M, & Sambrook M (1980)Treatment of tardive dyskinesia with choline and tetrabenazine. *Postgraduate Medical Journal*, 56, 663-664

U.S. Department of Agriculture. (2004) USDA database for the choline content of common foods. U.S. Department of Agriculture, Beltsville, Maryland

Xu X, Gammon MD, Zeisel SH, Lee YL, Wetmur JG, Teitelbaum SL, Bradshaw PT, Neugut AI, Santella RM, & Chen J (2008) Choline metabolism and risk of breast cancer in a population-based study. *The FASEB Journal*, 28: 2045-2052

Zeisel SH (2000) Choline: Needed for normal development of memory. *Journal of the American College of Nutrition*, 19, (90005), 528S-531S Published by the American College of Nutrition

Zeisel SH, Da Costa K, Franklin PD, Alexander EA, Lamont JT, Sheard NF, and Beiser A (1991) Choline, an essential nutrient for humans. *The FASEB Journal*, 5, 2093-2098.

Appendix Section 8.

United States Department of Agriculture evaluation of choline chloride as an ingredient for salt replacement (sodium reduction) in processed meat and poultry products

USDA United States Department of Agriculture
Food Safety and Inspection Service

Office of Policy and Program Development

Risk & Innovations Management Division
George Washington Carver Center
5601 Sunnyside Ave: STOP 5271
Beltsville, MD 20705-5271

March 15, 2011

Kristine V. Lukasik, Ph.D.
Manager, Scientific and Technical Product Support
Food, Pharma and Human Nutrition
Balchem Corporation
52 Sunrise Park Road
New Hampton, NY 10958-0600

Dear Dr. Lukasik:

This letter is in response to your February 14, 2011, e-mail notification requesting a revision to the Food Safety and Inspection Service (FSIS) no objection letter, dated January 25, 2011. Specifically, you are requesting permission to use choline chloride and a conditioned choline chloride product, C-Salt™ (with 2% added magnesium stearate), as a direct replacement for sodium chloride according to Good Manufacturing Practices (GMPs) in meat, poultry, and egg products (Log No. 10-ING-0658-N-A).

In your submission, you describe the function of choline chloride alone as a direct replacement for sodium chloride and to improve the palatability of reduced sodium food products including processed, ready-to-eat (RTE), fresh and frozen meat, poultry, and egg products with or without stated standards of identity or composition. You also describe the function of a conditioned choline chloride product, C-Salt™ (with 2% added magnesium stearate) as similar to choline chloride. The 2% magnesium stearate is added for better flow characteristics and reduced hygroscopicity.

You stated that up to 50% of the weight of sodium chloride in a product could be replaced by choline chloride or C-Salt™ with little or no loss of salty flavor. However, a more typical usage level will be replacement of 30% of the weight of sodium chloride with choline chloride or C-Salt™.

During its evaluation, FSIS consulted with the Food and Drug Administration (FDA) for a safety determination regarding the use of choline chloride and choline chloride plus magnesium stearate (C-Salt™) in meat, poultry, and egg products.

Regarding safety, FDA determined that, in accordance with 21 CFR 182.8252, choline chloride is Generally Recognized as Safe (GRAS) when used in accordance with good manufacturing practice (GMP) as a nutrient. Balchem Corporation (Balchem) stated that the intended use for choline chloride is as an enhancer of salty flavor in meat,

poultry, and egg products. Therefore, FDA determined that Balchem's stated intended use would not be covered under 21 CFR 182.8252.

However, as highlighted in Balchem's notification, the Flavor and Extract Manufacturers Association (FEMA) of the United States has evaluated and found choline chloride to be GRAS when used at low levels as a flavoring agent in several food categories, including meat and poultry products. The average maximum use level (parts per million) specified in meat and poultry products is 1200 for each product category. Egg products, as a category, were not assigned a use level. Over the years, FDA has generally not challenged FEMA's determination with regard to their flavor GRAS decisions. Therefore, since Balchem states that the intended use of the choline chloride is as an enhancer of salty flavor, FDA had no safety concerns with this use of choline chloride in meat and poultry products, provided the use does not exceed 1200 ppm. Conversely, since 21 CFR 182.8252 does not authorize the use of choline chloride as a flavor ingredient and because FEMA does not list a use level for egg products, FDA can not comment on the safety of choline chloride in egg products as an enhancer of salty flavor.

In accordance with 21 CFR 184.1440, magnesium stearate, meeting specifications set forth in the Food Chemicals Codex, is considered GRAS by FDA for use as a lubricant and release agent as defined in 21 CFR 170.3(o)(18), a nutrient supplement as defined in 21 CFR 170.3(o)(20), and as a processing aid as defined in 21 CFR 170.3(o)(24). Furthermore, FDA determined that magnesium stearate could be used in food with no other limitation than current GMP and at levels not to exceed GMP. In section IV, entitled "Conditions of Use," of Balchem's notification that was submitted to FSIS, Balchem stated that the magnesium stearate in C-Salt™ functions as a processing aid. The subsequent clarification by Balchem provided to FDA in the email of November 18, 2010, stated that magnesium stearate is added to choline chloride to improve its flow characteristics.

Previously, in accordance with 21 CFR 101.100(a)(3), FDA had determined that magnesium stearate would not function as a processing aid and would not be covered under 21 CFR 184.1440. With this in mind, FDA could not comment on the safety of magnesium stearate in this notification. However, FSIS received an e-mail from FDA, dated February 14, 2011, that FDA had reevaluated their previous stance of magnesium stearate's function as a processing aid. FDA stated that because of the amount of magnesium stearate in the final meat, poultry, or egg product would be very small, as well as the fact that the only reason for magnesium stearate's use is to maintain choline chloride's free-flowing status, FDA felt that it would act as a processing aid and thus had no safety concerns with its use in meat, poultry or egg products.

In closing, FDA had no safety concerns with the use of choline chloride as an enhancer of salty flavor in meat and poultry products provided the use level does not exceed 1200 ppm. Furthermore, because 21 CFR 182.8252 does not authorize the use choline chloride as a flavoring ingredient and because FEMA does not list a use

level for egg products, FDA could not comment on the safety of choline chloride as an enhancer of salty flavor in egg products. FDA had no safety concerns with the use of the conditioned choline chloride product, C-Salt™ (with 2% added magnesium stearate) in meat, poultry, or egg products.

The Food Safety and Inspection Service (FSIS) has also completed its review of your submitted information and in conjunction with the FDA opinion stated above, has no objection to the use of choline chloride alone or the conditioned choline chloride product, C-Salt™ (with 2% added magnesium stearate) as a direct replacement for sodium chloride in meat and poultry products including processed, ready-to-eat (RTE), fresh and frozen meat and poultry products with or without stated standards of identity or composition provided the use level of choline chloride does not exceed 1200 ppm. Choline chloride must be listed as "choline chloride" on the ingredient statement in the proper order of predominance.

However, because FDA cannot give a safety determination on the use of choline chloride or the conditioned choline chloride C-Salt™ (with 2% added magnesium stearate) in egg products, FSIS cannot permit the use of choline chloride or the conditioned choline chloride C-Salt™ (with 2% added magnesium stearate) in egg products at this time.

This letter should not be considered as validation that your chemical or process would be effective in any particular official establishment.

The use of this ingredient, as described in your notification, will need to be factored into a hazard analysis and if appropriate, incorporated into a Hazard Analysis and Critical Control Point (HACCP) plan, Sanitation Standard Operating Procedures (Sanitation SOPs) or other prerequisite program validated for its application, and verified on an "on-going" basis for its effectiveness. If the establishment does not address the effects of using this ingredient in its hazard analysis, FSIS would be unable to determine that product processed using this ingredient is not adulterated, and therefore the product would not be eligible to bear the mark of inspection.

Any future changes or revisions to your February 14, 2011, notification are to be submitted to the Risk, Innovations, and Management Division (RIMD) as a revised notification prior to implementation. Balchem Corporation should provide a copy of this letter to each establishment and make it available for the FSIS inspector's review prior to its use.

If you have any further questions, please contact Dr. David Zeitz at (321) 327-2576 or David.Zeitz@fsis.usda.gov.

Sincerely,

William K. Shaw, Jr., Ph.D.
Director
Risk, Innovations, and Management Division
Office of Policy and Program Development

Appendix Section 9.

All product labels for choline products manufactured by Balchem Corporation for the food and feed industries

Choline Bitartrate USP/FCC

BALCHEM™ ENCAPSULATES

LO-ODOR™ TECHNOLOGY

Product Code F6492120

CHEMICAL NAME: (2-HYDROXYETHYL) TRIMETHYLAMMONIUM BITARTRATE

LOT NO. B XXXXXXX

NET WT. XXXXX

CONTENTS	APPROXIMATE PERCENTAGE	CAS NUMBER
CHOLINE BITARTRATE	100	87-67-2

MANUFACTURE DATE: XXXXXXXXX1

RETEST DATE IN TWO YEARS

Manufactured By:
BCP Ingredients
299 Extension St.
Verona, MO 65769
417-498-2241

BCP C10 - 35660 03/02

Choline Chloride USP/FCC

BALCHEM™ ENCAPSULATES

Product Code F6522120

"DESICCANT BAG INSIDE"

CHEMICAL NAME: CHOLINE CHLORIDE

LOT NO. cc XXXXXXX

NET WT. XXXXXX

CONTENTS	APPROXIMATE PERCENTAGE	CAS NUMBER
CHOLINE CHLORIDE	100	67-48-1

MANUFACTURE DATE: XXXXXXXXX1

RETEST DATE IN ONE YEAR.

Manufactured By:
BCP Ingredients
299 Extension St.
Verona, MO 65769
417-498-2241

BCP C14 - 18034 109 03/02

C-SALT

BALCHEM™ ENCAPSULATES

Product Code F6526120

CAUTION: SEE MSDS SHEET PRIOR TO USE

CHEMICAL NAME: CHOLINE CHLORIDE

CONTENTS	APPROXIMATE PERCENTAGE	CAS NUMBER
CHOLINE CHLORIDE	98	67-48-1
MAGNESIUM STEARATE	2	557-04-0

LOT NO. CCM XXXXXXX

NET WT. XXXXXX

MANUFACTURE DATE: XXXXXXXXX1

RETEST DATE IN ONE YEAR.

Manufactured By:
BCP Ingredients Inc.
299 Extension St.
Verona, MO 65769
417-498-2241

BCP C14 - 33306 03/02

Choline Bitartrate USP/FCC 20 Mesh, Conditioned

111

BALCHEM™ ENCAPSULATES

LO-ODOR™ TECHNOLOGY

Product Code F6502120

CAUTION: SEE MSDS SHEET PRIOR TO USE

CHEMICAL NAME: (2-HYDROXYETHYL) TRIMETHYLAMMONIUM BITARTRATE

LOT NO CBS XXXXXXX

NET WT. XXXXXXX

CONTENTS	APPROXIMATE PERCENTAGE	CAS NUMBER
CHOLINE BITARTRATE	99	87-67-2
SILICON DIOXIDE	1	112945-52-5

(Conditioned with 1.0% Silicon Dioxide)

MANUFACTURE DATE: XXXXXXXXX1

RETEST DATE IN 3 YEARS.

Manufactured By:
BCP Ingredients Inc.
299 Extension St.
Verona, MO 65769
417-498-2241

BCP C11 - 17520

03/02

Choline Bitartrate USP/FCC Conditioned, 40 Mesh

BALCHEM™ ENCAPSULATES

LO-ODOR™ TECHNOLOGY

Product Code F6472120

CAUTION: SEE MSDS SHEET PRIOR TO USE

CHEMICAL NAME: (2-HYDROXYETHYL) TRIMETHYLAMMONIUM BITARTRATE

LOT NO: CBS 468

NET WT. 25KG

CONTENTS	APPROXIMATE PERCENTAGE	CAS NUMBER
CHOLINE BITARTRATE	98.5	87-67-2
SILICON DIOXIDE	1.5	112945-52-5

(Conditioned with 1.5% Silicon Dioxide)

MANUFACTURE DATE: 5/6/2011

RETEST DATE IN 3 YEARS.

Manufactured By:
BCP Ingredients Inc.
299 Extension St.
Verona, MO 65769
417-498-2241

21851 03/02

BALCHEM™

Balchem Corporation
52 Sunrise Park Road
New Hampton, NY 10958
USA
Website: www.balchem.com

LO-ODOR™ TECHNOLOGY

Petition to Include Choline Salts on the National List

Balchem Corporation

CHOLINE BITARTRATE Conditioned

USP FCC (before conditioning)

CHEMICAL NAME: (2-HYDROXYETHYL) TRIMETHYLAMMONIUM BITARTRATE

EURO-K
KOSHER PARVE LAMEHADRIN
RABBI G.M. GARELIK - RABBI A. HAZAN
BETH DIN TZEDEK OF MILAN, ITALY

ISLAMIC FOOD COUNCIL OF EUROPE
حلال
HALAL

GB	CHOLINE BITARTRATE	NL	CHOLINEBITARTRAAT
D	CHOLINBITARTRAT	DK	CHOLINBITARTRAT
F	BITARTRATE DE CHOLINE	N	KOLINBITARTRAT
I	BITARTRATO DI COLINA	S	KOLINBITARTRAT
E	BITARTRATO DE COLINA	SF	KOLIINIBITARTRAATI
P	BITARTRATO DE COLINA	GR	ΥΔΡΟΓΟΝΟΤΡΥΓΙΚΗ ΧΟΛΙΝΗ

INTENDED USE
To be used as ingredients in food; in particular for infant formulae, processed cereal-based foods, baby foods and foodstuffs for particular nutritional uses.
This product does not contain GMO.

RECOMMENDED STORAGE
Keep bags tightly cloosed; product is hygroscopic.
Store at room temperature.

RETEST DATE
3 years

CAUTION
See MSDS sheet prior to use.

INGREDIENTS	APPROXIMATE %	CAS N°
CHOLINE BITARTRATE	99	87-67-2
SILICON DIOXIDE	1	112945-52-5

BALCHEM PRODUCT CODE

EU: 5400543

USA: F6672118

EMERGENCY: Tel (+39) 0321 9791 **Fax** (+39) 0321 979246

Manufactured by: BALCHEM ITALIA
Via del Porto, SNC
28040 Marano Ticino (NO)
ITALY

NET WEIGHT

25 KG

Choline Bitartrate USP/FCC Conditioned Regular

LO-ODOR ™TECHNOLOGY

Product Code F6512120

BALCHEM™ ENCAPSULATES

CAUTION: SEE MSDS SHEET PRIOR TO USE

CBC XXXXXXXX

CHEMICAL NAME: (2-HYDROXYETHYL) TRIMETHYLAMMONIUM BITARTRATE LOT NO.

NET WT. XXXXXX

CONTENTS	APPROXIMATE PERCENTAGE	CAS NUMBER
CHOLINE BITARTRATE	99	87-67-2
SILICON DIOXIDE	1	112945-52-5

(Conditioned with 1.0% Silicon Dioxide)

MANUFACTURE DATE: XXXXXXXXX1

RETEST DATE IN 3 YEARS

Manufactured By:
BCP Ingredients Inc.
299 Extension St.
Verona, MO 65769
417-498-2241

BCP C33 31909 03/02

BALCHEM
ANIMAL NUTRITION & HEALTH
World-Class Quality Worldwide Service

Choline Chloride 70% aq.

For use only by feed manufacturers

Ingredients: Choline chloride, water.

Storage: Store away from excessive heat or cold.
Container should be closed when not in use.

Guaranteed analysis: Choline chloride 700,000 mg/kg
Equivalent to Choline 607,600 mg/kg

Registered by: Balchem Corporation
P.O. Box 600, New Hampton, NY 10958 USA

Product code F3060030 Lot no. 123456 Net wt. 2500 lb

Canadian feed registration no. XXXXXX Made in USA

Manufacture Date: Mar 2008 Retest Date: Mar 2010 Rev 04/04/08

BALCHEM
ANIMAL NUTRITION & HEALTH
World-Class Quality Worldwide Service

Choline Chloride 75% aq.

For use only by feed manufacturers

Ingredients: Choline chloride, water.

Storage: Store away from excessive heat or cold.
Container should be closed when not in use.

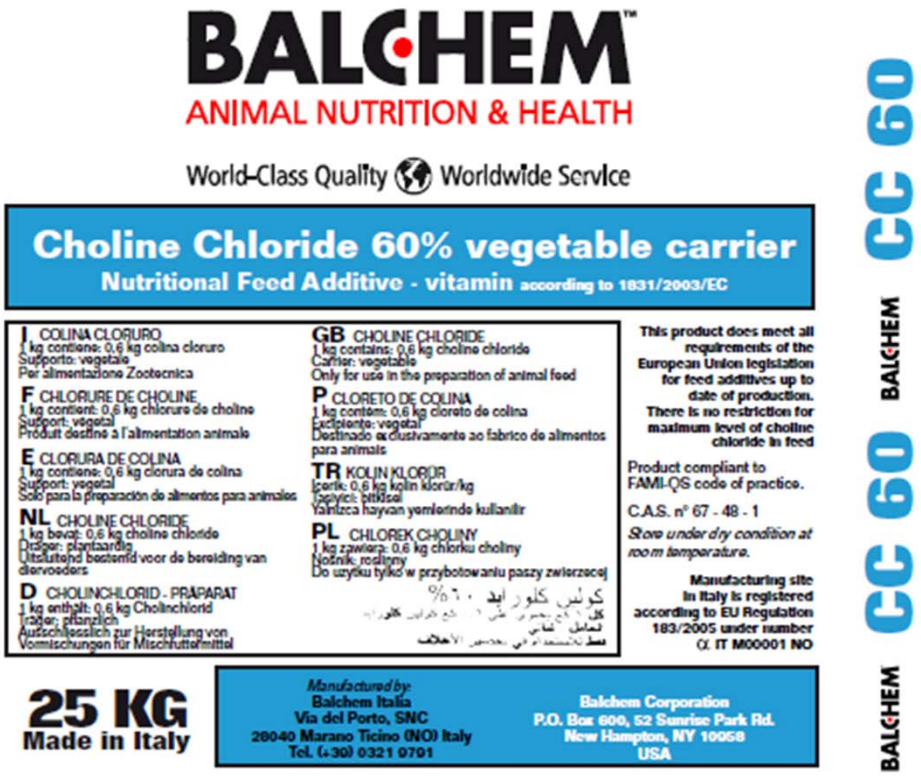
Guaranteed analysis: Choline chloride minimum 750,000 mg/kg
Equivalent to Choline minimum 651,000 mg/kg

Registered by: Balchem Corporation
P.O. Box 600, New Hampton, NY 10958 USA

Product code F3090030-E-500 Lot no. 123456 Net wt. 500 lbs (227 kg)

Canadian Feed Registration No. 990898 Made in USA

Manufacture Date: Mar 2008 Retest Date: Mar 2010 Rev 04/29/08



BALCHEM™
ANIMAL NUTRITION & HEALTH

World-Class Quality Worldwide Service

Choline Chloride Minimum 60%

IFN 7-01-228

Net weight 25 Kg

Ingredients: Choline chloride - Vegetable carrier - Moisture (max 2%)

Storage: Hygroscopic material - Keep dry in sealed bags

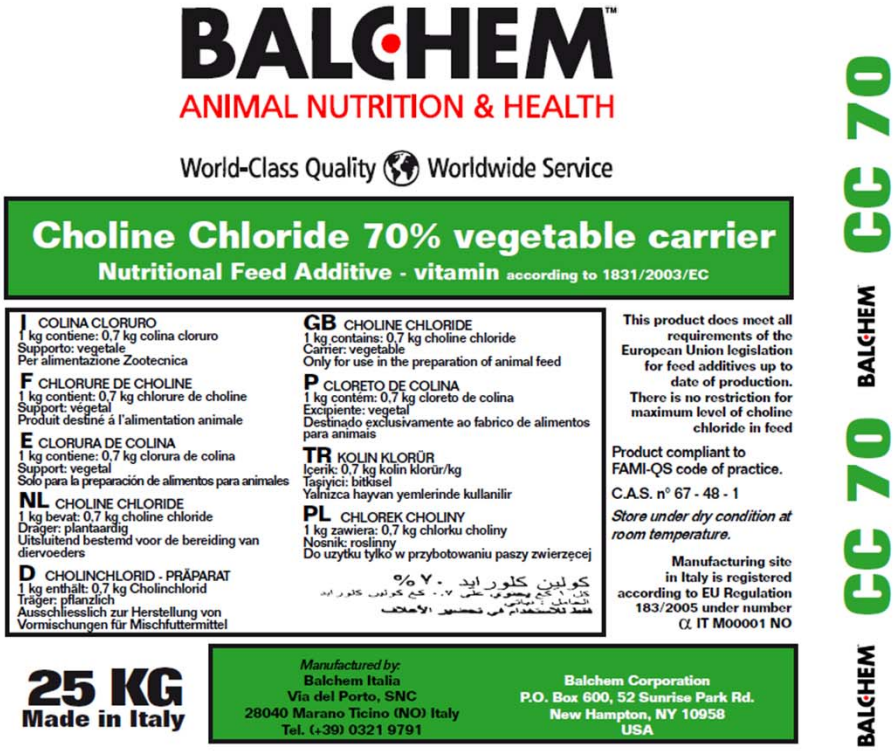
Guaranteed analysis	choline chloride 600,000 ppm (minimum)
Equivalent to	*choline hydroxide 520,740 ppm (minimum)*
Equivalent to	*choline ion 447,600 ppm (minimum)*

Directions for use:
Use in accordance with local feed regulations

Balchem Corporation
P.O. Box 600
52 Sunrise Park Rd.
New Hampton, NY 10958
USA

Manufactured by:
Balchem Italia
Via del Porto, SNC
28040 Marano Ticino (NO)
ITALY
α IT M00001 NO

Made in Italy
Product code F3070030



BALCHEM™

ANIMAL NUTRITION & HEALTH

World-Class Quality Worldwide Service

Choline Chloride Minimum 70%

IFN 7-01-228

Net weight 25 Kg

Ingredients: Choline chloride - Vegetable carrier - Moisture (max 2%)

Storage: Hygroscopic material - Keep dry in sealed bags

Guaranteed analysis	choline chloride 700,000 ppm (minimum)
Equivalent to	*choline hydroxide 607,530 ppm (minimum)*
Equivalent to	*choline ion 522,200 ppm (minimum)*

Directions for use:
Use in accordance with local feed regulations

Balchem Corporation
P.O. Box 600
52 Sunrise Park Rd.
New Hampton, NY 10958
USA

Manufactured by:
Balchem Italia
Via del Porto, SNC
28040 Marano Ticino (NO)
ITALY
α IT M00001 NO

Made in Italy
Product code F3080030

BALCHEM™
ANIMAL NUTRITION & HEALTH
World-Class Quality Worldwide Service

Choline Chloride 50% on silica

Nutritional Feed Additive - vitamin according to 1831/2003/EC

I COLINA CLORURO
1kg contiene: 0,5 kg colina cloruro
Supporto: minerale
Per alimentazione zootecnica.

F CHLORURE DE CHOLINE
1kg contient: 0,5 kg chlorure de choline
Support: mineral
Produit destiné à l'alimentation animale.

E CLORURO DE COLINA
1kg contiene: 0,5 kg clorura de colina
Excipiente: mineral
Sólo para la preparación de alimentos para animales.

P CLORETO DE COLINA
1kg contém: 0,5 kg de cloreto de colina
Excipiente: mineral
Destinado exclusivamente ao fabrico de alimentos para animais.

PL CHLOREK CHOLINY
1kg zawiera: 0,5 kg chlorku choliny
Nosnik: mineralny
Do uzytko tylko w przygotowaniu paszy zwierzęcej.

TR KOLIN KLORÜR
İçerik: 0,5 kg kolin clorür/kg
Taşiyici: mineral
Yalnizca hayvan yemlerinde kullanir.

NL CHOLINE CHLORIDE
1kg bevat: 0,5 kg choline chloride
Drager: mineraal
Uitsluitend bestemd voor de bereiding van diervoeders.

D CHOLINCHLORID
1kg enthält: 0,5 kg Cholinchlorid
Träger: mineral
Ausschliesslich für die Herstellung von Futtermitteln.

GB CHOLINE CHLORIDE
1kg contains: 0,5 kg choline chloride
Carrier: mineral
Only for use in the preparation of animal feed.

كولين كلورايد ٥٠%
كل ١ كغ يحتوي على ٠,٥ كغ كولين كلورايد
الحامل : سيليكات
فقط للاستخدام في تحضير الأعلاف

Manufacturing site in Italy is registered according to EU Regulation 183/2005 under number
α IT M 00001 NO

Store under dry condition at room temperature.

UN: not classified

Made in Italy

25 KG net weight

This product does meet all requirements of the European Union legislation for feed additives up to date of production.
There is no restriction for maximum level of choline chloride in feed

Shelf life: 2 years (retest recommended)

Product compliant to FAMI-QS code of practice.

C.A.S. n° 67 - 48 - 1

Balchem Corporation
P.O. Box 600, 52 Sunrise Park Rd.
New Hampton, NY 10958
USA

Manufactured by:
Balchem Italia
Via del Porto, SNC
28040 Marano Ticino (NO) Italy
Tel. (+39) 0321 9791

ReaShure®

RUMEN PROTECTED CHOLINE CHLORIDE

GUARANTEED ANALYSIS:

Choline Chloride (minimum) 28.0%

Equivalent to choline chloride (minimum) ..... 288,000 mg/kg
Equivalent to choline hydroxide (minimum).....250,000 mg/kg
Equivalent to choline ion (minimum).....215,000 mg/kg

INGREDIENTS:
Hydrogenated Vegetable Oil, Choline Chloride, Corn Cob (carrier)

FEEDING DIRECTIONS:
Recommended inclusion rate is 60 g per head per day

RECOMMENDED STORAGE:
Keep dry in sealed bags. Store below 50° C
Recommended storage temperature 10°–32°C

US Patent # 6,797,291

Lot Number: Lot No.

Date of Manufacture: Month Year

Best if used within 2 years of manufacture

Net Weight
25 kg

Product Code
F3428016

Rev. Feb. 2011

Manufactured by:
Balchem Corporation
52 Sunrise Park Road
New Hampton, NY 10958 USA

Appendix Section 10.

Balchem Corporation statements on microbial stability and safety of choline salt preparations

BALCHEM CORPORATION

Microbial Statement

Choline Chloride USP, FCC

Balchem Corporation uses potable water for the production of Choline Chloride, USP,FCC. This water is tested by the local regulatory agencies and as a matter of good public health, we test the drinking water every two weeks for total plate count and coliform.

Since we use ethylene oxide as a primary raw material, it is extremely unlikely that any bacterial would survive. Ethylene oxide is used extensively as a sterilant for foodstuffs and medical supplies.

Choline Chloride is a salt, a medium in which bacteria will not readily grow, we have determined by historical data that testing random selected batches every six months is acceptable. Historical data has shown absolutely zero bacteria counts of any bacteria species.

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John Keller
QC Manager

Version May 2010

BALCHEM
ENCAPSULATES

Balchem Corporation
P.O. Box 600
New Hampton, New York 10958
Tel 877-222-8811
Fax 845.326.5717

www.balchem.com

Balchem has implemented a Skip-Lot Testing program for our Choline Bitartrate and Choline Cloride products sold into human nutrition applications. Skip-Lot testing is an accepted industry standard.

Skip-lot sampling is defined as a reduced level of sampling or testing for a particular specified parameter(s) based upon one or more of the following:

- Statistical analysis of an adequate quantity of historical data. Balchem has several years of historical data supporting the results defined on the COA's for Choline Salts produced in our facilities as pass/fail.

- Statistical confidence in the capability of the manufacturing process as determined by suitable verification; or

- Ongoing monitoring of the process using recognized statistical process control (SPC) techniques

Based upon adequate process verification, in-process controls and statistical confidence, a skip-lot sampling plan is recognized by the U.S. Pharmacopeia as a acceptable (suitable) alternative to testing every batch. Balchem's certificate of analysis does list several lot attributes exemplified by "pass/fail" results or "less than or greater than" a specified value that establishes compliance with a specification parameter. By issuance of a C of A, Balchem certifies that if tested, the lot will meet each and every specification parameter printed on the C of A regardless of whether the lot was tested for the specific parameter or whether it was "skipped".

Dried choline salts have been observed not to support microbial growth. For verification that the dried choline salts continues to meet its microbial specification, one or two lots are examined every quarter. Typical results for the Total Plate Count as well as Yeast, Mold, and Total Coliform continue to register as "non detect" (i.e near 0). Results for the pathogenic organisms (E. coli, Salmonella et al) continue to be a non-detect.

John Keller
Quality Manager
Verona Mo. Facility

Appendix Section 11.

All Material Safety Data Sheets (MSDS) for choline products manufactured by Balchem Corporation for the food and feed industries

Choline Bitartrate FCC, USP Regular FPN MSDS - English

Revised: 20 December 2010
Supersedes: 9 September 2010

MATERIAL SAFETY DATA SHEET

According to OSHA Regulation 29 CFR 1910.1200 and Regulation (EC) No. 1907/2006 [as amended by (EU) No. 453/2010]

SECTION 1: IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1 Product identifier

Chemical name:	Choline Bitartrate
Product label name:	Choline Bitartrate FCC, USP Regular
Other names or synonyms of identification:	2-hydroxyethyl(trimethyl)azanium
Number of Registration:	Not applicable
C.A.S. Registry number:	87-67-2 (choline bitartrate)
EINECS number:	201-763-4
EINECS name:	Choline Bitartrate
Molecular weight:	253.3 (choline bitartrate)
Molecular formula:	$C_9NH_{19}O_7$ (choline bitartrate)

1.2 Relevant identified uses of the substance or mixture and uses advised against

Ingredient in foods and dietary supplements

1.3 Details of the supplier of the safety data sheet

Supplier:	Balchem Italia Srl,	Balchem Corporation
Address:	Via del Porto, snc 28040 Marano Ticino (NO) – Italy Italy	52 Sunrise Park Road New Hampton, NY 10958 USA
Telephone number:	0039 (0)321 9791	+1 (845) 326-5600
Fax:		+1 (845) 326-5615
Web:	www.balchem.com	www.balchem.com
E-mail:	sds@balchem.com	sds@balchem.com

1.4 Emergency telephone number

An emergency number is not required for this product.

Emergency telephone 24h/24:	001-703-527-3887 – CHEMTREC International 800-424-9300 – CHEMTREC USA
Emergency telephone only during office hours:	0039-(0)321-9791 BALCHEM ITALIA S.r.l.

SECTION 2: HAZARDS IDENTIFICATION

2.1 Classification of the substance or mixture

Classification of the substance according to Directive 67/548/EEC

None: material is not hazardous.

Classification of the substance according to (EC) No 1272/2008

None: material is not hazardous.

2.2 Label elements

None: material is not hazardous

Hazard statement:

None: material is not hazardous

2.3 Other hazards

None

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

Choline Bitartrate: 96 – 100% (up to 0.5% moisture) CAS: 86-67-2

3.2 Mixtures

See Section 3.1

SECTION 4: FIRST AID MEASURES

4.1 Description of first aid measures

Inhalation: For significant exposure to any nuisance particles (dust or mist), remove to fresh air and, if there is difficulty breathing, get medical attention. Breathing dust from any source may cause respiratory irritation. Breathing large amounts of dust from any source may cause injury.

Skin: No first aid is required. As a precaution, wash with soap and water. Wash contaminated clothing before reuse.

Eye: To prevent mechanical irritation, flush with clean, low-pressure water.

Ingestion: No first aid required for ingesting small amounts.

4.2 Most important symptoms and effects, both acute and delayed

Symptoms: Acute – None
Chronic – None

4.3 Indication of any immediate medical attention and special treatment needed

There are no adverse effects from exposure to this product.

SECTION 5: FIREFIGHTING MEASURES

5.1 Extinguishing media

Water, Foam, CO_2, Dry Chemical

5.2 Special hazards arising from the substance or mixture

Hazardous Combustion Products: No specific hazards. Combustion will produce compounds of carbon, hydrogen, nitrogen, and oxygen.

Other Fire and Explosion Hazards: Possible dust explosion. The particle size as produced and the hygroscopic nature of the product are expected to limit potential for dust explosion.

5.3 Advice for firefighters

Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source, is a potential dust explosion hazard. This material may present an explosion and deflagration hazard risk when dispersed and ignited in air. Secondary explosions may also pose a risk once an initial explosion occurs with the presence of a combustible dust or powder in the area.

SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

6.1.1 For non-emergency personnel

Dust should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Avoid dispersal of dust in the air (e.g., avoid clearing dust surfaces with compressed air).

6.1.2 For emergency responders

No specific protective equipment is required.

6.2 Environmental precautions

Water runoff can cause environmental damage due to high BOD.

6.3 Methods and material for containment and cleaning up

Vacuum or sweep material and place in a disposal container.

6.4 Reference to other sections

See Section 8: Exposure Controls/ Personal Protection and Section 13: Disposal Considerations

SECTION 7: HANDLING AND STORAGE

7.1 Precautions for safe handling

Avoid contact with eyes, skin and clothing. Wash thoroughly after handling. Avoid breathing dust.

7.2. Conditions for safe storage, including any incompatibilities

Choline bitartrate is hygroscopic (will absorb moisture from air). Ensure containers are properly secured before moving. Minimize dust generation and accumulation. Routine housekeeping should be instituted to ensure that dusts do not accumulate on surfaces. Dry powders can build static electricity charges when subjected to the friction of transfer and mixing operations. Provide adequate precaution, such as electrical grounding and bonding, or inert atmospheres.

7.3. Specific end use(s)

No additional recommendations.

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters

Choline Bitartrate: OSHA Nuisance Dust PELs (29 CFR 1910.1000): Respirable fraction = 5 mg/m^3; Total = 15 mg/m^3

8.2. Exposure controls

Provide ventilation and particulate control to maintain airborne levels below the exposure guidelines. It is recommended that all dust control equipment such as local exhaust ventilation and material transport systems involved in handling of this product contain explosion relief vents or an explosion suppression system or an oxygen-deficient environment. Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work are (i.e., there is no leakage from the equipment). Use only appropriately classified electrical equipment and powered industrial trucks.

Eye/Face Protection: If there is a potential for exposure to particles (mist or dust) which would cause mechanical injury to the eye, wear chemical goggles.

Skin Protection: No additional precautions.

Respiratory Protection: In dusty atmospheres, use an approved dust respirator. In confined or poorly ventilated areas or emergency and other conditions where the exposure guidelines may be greatly exceeded, use an approved positive pressure self-contained breathing apparatus.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Product:	Choline Bitartrate
Appearance:	White crystal
Physical state:	Solid
Odor:	Slight amine (fish-like) odor; threshold not determined
Specific Gravity:	Not determined
pH:	Choline bitartrate: 3 - 4 for a 25% wt/vol solution
Melting Point:	Choline bitartrate: 150 °C (270 °F)
Boiling Point:	Not available
Flash Point:	None
Evaporation Rate:	Not available (assumed to be essentially zero)
Flammability:	Not flammable
Flammability Limits:	Not flammable
Vapor Pressure:	Not available (assumed to be essentially zero)
Vapor Density (air=1):	Not available (assumed to be essentially zero)
Bulk Density:	Choline bitartrate: 0.84 grams/cubic centimeter
Solubility:	Choline bitartrate: 4.3 g/100 mL methanol @ 50ºF 8.0 g/100 mL methanol @ 100ºF 123 g/100 mL water @ 50°F 268 g/100 mL water @ 100°F
Octanol/Water Partition Coefficient	Not available
Autoignition Temperature:	752°F (400°C) as dust
Viscosity:	Not available
Explosive Properties:	Choline bitartrate for particles < 75 micron diameter and 0.1 wt% moisture is classified as ST1 dust explosion and has a rate of pressure rise 484 bar/s, overpressure of 7.7 bar, Kst of 131 bar-m/s, and a minimum ignition energy averaging 24 mJ. A second test yielded a minimum explosive concentration of 50 mg/L and an autoignition temperature of 400 °C.
Oxidizing Properties:	Not an oxidizer
Volatile Organic Chemical Content:	Not available (assumed to be essentially zero)

9.2. Other information

No additional information.

SECTION 10: STABILITY AND REACTIVITY

10.1. Reactivity

Not considered reactive.

10.2. Chemical stability

Stable

10.3. Possibility of hazardous reactions

No hazardous reactions expected.

10.4. Conditions to avoid

Do not heat to boiling or decomposition in sealed container.

10.5. Incompatible materials

Avoid contact with strong acids and bases as well as iron, mild steel and galvanized steel.

10.6. Hazardous decomposition products

Compounds of carbon, hydrogen, nitrogen, oxygen, chlorine.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information on toxicological effects

100% Choline Bitartrate: No data available.

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity

100% Choline Bitartrate: No data available.

12.2. Persistence and degradability

Expected to be readily biodegradable.

12.3. Bioaccumulative potential

Not bioaccumulative.

12.4. Mobility in soil

Not determined.

12.5. Results of PBT and vPvB assessment

Not determined.

12.6. Other adverse effects

Not determined.

SECTION 13: DISPOSAL CONSIDERATIONS

13.1. Waste treatment methods

Product: Not considered a hazardous waste under US Federal Hazardous Waste Regulations (40 CFR 261) or EU Directive 91/689/EEC. Consult local regulations regarding proper disposal as they may be more restrictive or otherwise different from Federal/International regulations.

Packaging: Dispose of packaging contaminated by product in accordance with regulations.

SECTION 14: TRANSPORT INFORMATION

14.1. UN number

Not hazardous.

14.2. UN proper shipping name

Not hazardous.

14.3. Transport hazard class(es)

Not hazardous.

14.4. Packing group

Not hazardous.

14.5. Environmental hazards

Not hazardous.

14.6. Special precautions for user

Not hazardous.

14.7. Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

Not hazardous.

SECTION 15: REGULATORY INFORMATION

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

U.S. Federal Regulations

OSHA: This product is not hazardous under the criteria of the Federal OSHA Hazard Communication Standard 29 CFR 1910.1200.
PSM: This product is not subject to Process Safety Management (29 CFR 1910.119).
FIFRA: Not applicable
TSCA: On TSCA inventory
CERCLA: Reportable Quantity – None (40 CFR 302.4)

SARA TITLE III: Section 302 Extremely Hazardous Substances – None (40 CFR 355)
Section 311/312 Hazard Categories – None (40 CFR 370.2)
Section 313 Toxic Chemicals – None (40 CFR 372.65)

RMP: Not listed under the Risk Management Plan (40 CFR 68).
RCRA: If discarded in purchased form, this product is not a listed or characteristic hazardous waste. However, under RCRA, it is the responsibility of the product user to determine at the time of disposal whether a material containing the product or derived from the product should be classified as a hazardous waste (40 CFR 261.20-24).
CWA: Release into a waterway may require reporting to the National Response Center @ 800-424-8802 (40 CFR 116.4).
FDA/USDA: Follow Good Manufacturing Practice (GMP). GRAS per 21 CFR 182.8250.

International Regulations

Canadian Dangerous Substance List (DSL): Listed (published 5 April 1994)
European Inventory of Existing Commercial Chemical Substances (EINECS): No. 201-763-4
Australian Inventory of Chemical Substances (AICS): Listed.
Korean Existing Chemicals List (ECL): No. KE-2091
EU Regulations:
Food law: Regulation (EC) 178/2002
Food hygiene law: Regulation (EC) 852/2004
Food contaminates: Regulation (EC) 1881/2006
Microbiological in Food: Regulation (EC) EC 2073/2005
Food additive purity: Regulation (EC) 2008/84 – tartaric acid E344
REACH: Regulation (EC) No 1907/2006 Registration, Evaluation, Authorisation and Restriction of Chemicals does not apply to food.
Safety Data Sheets: Regulation (EU) No 453/2010 does not apply to non-hazardous materials.
CLP: Regulation (EC) No 1272/2008 Classification, Labeling and Packaging does not apply to non-hazardous materials.
Hazardous Waste: Directive (EU) 91/689/EEC - If discarded in purchased form, this product is not a hazardous waste.

USA State Regulations
This product is not subject to California Proposition 65. There are no known additional requirements necessary for compliance with state right-to-know regulations.

15.2. Chemical safety assessment

Not completed.

SECTION 16: OTHER INFORMATION

Reason for Issue: Updated to format of EU 453/2010.

Risk Phrases Used: None used

Hazard Ratings – The following NFPA hazard ratings are recommended for this product:
Fire - 1; Health – 0; Reactivity – 0; Specific Hazard - None

For safe handling, refer to NFPA 654, *Standard for the prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids***.**

The following abbreviations may be used in this document:

% - percent
μg/kg - micrograms per kilogram
g/kg – grams per kilogram
lb/ft^3 – pounds per cubic foot
mg/kg – milligrams per kilogram
mg/m^3 – milligrams per cubic meter
mmHg – millimeters of mercury
ppm – parts per million
w/w – Weight per weight
ACGIH – American Council of Governmental Industrial Hygienists
AICS – Australian Inventory of Chemical Substances
CAS – Chemical Abstract Service
CERCLA – Comprehensive Emergency Response, Compensation and Liability Act
CFR – Code of Federal Regulations
CWA – Clean Water Act
D.O.T. – Department of Transportation
DSL – Domestic Substance List (Canada)
ECL – Existing Chemicals List (Korea)
EINECS – European Inventory of Existing Commercial Substances
FDA – Food and Drug Administration
FIFRA – Federal Insecticide, Fungicide and Rodenticide Act
IDLH – Immediately Dangerous to Life and Health
LD_{50} – Lethal dose for 50% mortality of subject species
LD_{LO} – Lethal dose low; the lowest dose of a substance introduced by any route other than inhalation reported to have caused death in humans or animals.
LFL – Lower Flammable Limit
MSHA – Mine Safety Health Administration
NFPA – National Fire Protection Association
NIOSH – National Institute of Occupational Safety and Health
OSHA – Occupational Safety and Health Administration
PEL – Permissible Exposure Limit (default 8-hour day, 40-hour week TWA)
PSM – Process Safety Management
RCRA – Resource Conservation and Recovery Act
REL – Recommended Exposure Limit (default 10-hour day, 40-hour week TWA)
RMP – Risk Management Plan
SARA – Superfund Amendment and Reauthorization Act
STEL – Short Term Exposure Limit (default 15-minute TWA)
TD_{LO} – Lowest dose to which humans or animals have been exposed and reported to produce a toxic effect other than cancer
TSCA – Toxic Substance Control Act
TWA – Time Weighted Average
UFL – Upper Flammable Limit
USDA – United States Department of Agriculture

Choline Bitartrate Conditioned FPN MSDS - English

Revised: 4 February 2011
Supersedes: 20 December 2010

MATERIAL SAFETY DATA SHEET

According to OSHA Regulation 29 CFR 1910.1200 and Regulation (EC) No. 1907/2006 [as amended by (EU) No. 453/2010]

SECTION 1: IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1 Product identifier

Chemical name:	Choline Bitartrate
Product label name:	Choline Bitartrate Conditioned Choline Bitartrate 20 Mesh Conditioned Choline Bitartrate 40 Mesh Conditioned
Other names or synonyms of identification:	2-hydroxyethyl(trimethyl)azanium
Number of Registration:	Not applicable
C.A.S. Registry number:	87-67-2 (choline bitartrate)
EINECS number:	201-763-4
EINECS name:	Choline Bitartrate
Molecular weight:	253.3 (choline bitartrate)
Molecular formula:	$C_9NH_{19}O_7$ (choline bitartrate)

1.2 Relevant identified uses of the substance or mixture and uses advised against

Ingredient in foods and dietary supplements

1.3 Details of the supplier of the safety data sheet

Supplier:	Balchem Italia Srl,	Balchem Corporation
Address:	Via del Porto, snc 28040 Marano Ticino (NO) – Italy Italy	52 Sunrise Park Road New Hampton, NY 10958 USA
Telephone number:	0039 (0)321 9791	+1 (845) 326-5600
Fax:		+1 (845) 326-5615
Web:	www.balchem.com	www.balchem.com
E-mail:	sds@balchem.com	sds@balchem.com

1.4 Emergency telephone number

An emergency number is not required for this product.

Emergency telephone 24h/24:	001-703-527-3887 – CHEMTREC International 800-424-9300 – CHEMTREC USA
Emergency telephone only during office hours:	0039-(0)321-9791 BALCHEM ITALIA S.r.l.

SECTION 2: HAZARDS IDENTIFICATION

2.1 Classification of the substance or mixture

Classification of the substance according to Directive 67/548/EEC

None: material is not hazardous.

Classification of the substance according to (EC) No 1272/2008

None: material is not hazardous.

2.2 Label elements

None: material is not hazardous

Hazard statement:

None: material is not hazardous

2.3 Other hazards

None

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

See Section 3.2

3.2 Mixtures

Choline Bitartrate	96 – 100%	CAS# 87-67-2
Amorphous Silica	0 – 4%	CAS# 63231-67-4
Water	< 0.5%	CAS# 7732-18-5

SECTION 4: FIRST AID MEASURES

4.1 Description of first aid measures

Inhalation: For significant exposure to any nuisance particles (dust or mist), remove to fresh air and, if there is difficulty breathing, get medical attention. Breathing dust from any source may cause respiratory irritation. Breathing large amounts of dust from any source may cause injury.

Skin: No first aid is required. As a precaution, wash with soap and water. Wash contaminated clothing before reuse.

Eye: To prevent mechanical irritation, flush with clean, low-pressure water.

Ingestion: No first aid required for ingesting small amounts.

4.2 Most important symptoms and effects, both acute and delayed

Symptoms: Acute – None
Chronic – None

4.3 Indication of any immediate medical attention and special treatment needed

There are no adverse effects from exposure to this product.

SECTION 5: FIREFIGHTING MEASURES

5.1 Extinguishing media

Water, Foam, CO_2, Dry Chemical

5.2 Special hazards arising from the substance or mixture

Hazardous Combustion Products: No specific hazards. Combustion will produce compounds of carbon, hydrogen, nitrogen, and oxygen.

Other Fire and Explosion Hazards: Possible dust explosion. The particle size as produced and the hygroscopic nature of the product are expected to limit potential for dust explosion.

5.3 Advice for firefighters

Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source, is a potential dust explosion hazard. This material may present an explosion and deflagration hazard risk when dispersed and ignited in air. Secondary explosions may also pose a risk once an initial explosion occurs with the presence of a combustible dust or powder in the area.

SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

6.1.1 For non-emergency personnel

Dust should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Avoid dispersal of dust in the air (e.g., avoid clearing dust surfaces with compressed air).

6.1.2 For emergency responders

No specific protective equipment is required.

6.2 Environmental precautions

Water runoff can cause environmental damage due to high BOD.

6.3 Methods and material for containment and cleaning up

Vacuum or sweep material and place in a disposal container.

6.4 Reference to other sections

See Section 8: Exposure Controls/ Personal Protection and Section 13: Disposal Considerations

SECTION 7: HANDLING AND STORAGE

7.1 Precautions for safe handling

Avoid contact with eyes, skin and clothing. Wash thoroughly after handling. Avoid breathing dust.

7.2. Conditions for safe storage, including any incompatibilities

Choline bitartrate is hygroscopic (will absorb moisture from air). Ensure containers are properly secured before moving. Minimize dust generation and accumulation. Routine housekeeping should be instituted to ensure that dusts do not accumulate on surfaces. Dry powders can build static electricity charges when subjected to the friction of transfer and mixing operations. Provide adequate precaution, such as electrical grounding and bonding, or inert atmospheres.

7.3. Specific end use(s)

No additional recommendations.

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters

Choline Bitartrate: OSHA Nuisance Dust PELs (29 CFR 1910.1000): Respirable fraction = 5 mg/m^3; Total = 15 mg/m^3

8.2. Exposure controls

Provide ventilation and particulate control to maintain airborne levels below the exposure guidelines. It is recommended that all dust control equipment such as local exhaust ventilation and material transport systems involved in handling of this product contain explosion relief vents or an explosion suppression system or an oxygen-deficient environment. Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work are (i.e., there is no leakage from the equipment). Use only appropriately classified electrical equipment and powered industrial trucks.

Eye/Face Protection: If there is a potential for exposure to particles (mist or dust) which would cause mechanical injury to the eye, wear chemical goggles.

Skin Protection: No additional precautions.

Respiratory Protection: In dusty atmospheres, use an approved dust respirator. In confined or poorly ventilated areas or emergency and other conditions where the exposure guidelines may be greatly exceeded, use an approved positive pressure self-contained breathing apparatus.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Product:	Choline Bitartrate
Appearance:	White crystal
Physical state:	Solid
Odor:	Slight amine (fish-like) odor; threshold not determined
Specific Gravity:	Not determined
pH:	Choline bitartrate: 3 - 4 for a 25% wt/vol solution
Melting Point:	Choline bitartrate: 150 °C (270 °F)
Boiling Point:	Not available
Flash Point:	None
Evaporation Rate:	Not available (assumed to be essentially zero)
Flammability:	Not flammable
Flammability Limits:	Not flammable
Vapor Pressure:	Not available (assumed to be essentially zero)
Vapor Density (air=1):	Not available (assumed to be essentially zero)
Bulk Density:	Choline bitartrate: 0.84 grams/cubic centimeter
Solubility:	Choline bitartrate: 4.3 g/100 mL methanol @ 50ºF 8.0 g/100 mL methanol @ 100ºF 123 g/100 mL water @ 50°F 268 g/100 mL water @ 100°F
Octanol/Water Partition Coefficient	Not available
Autoignition Temperature:	752°F (400°C) as dust
Viscosity:	Not available
Explosive Properties:	Choline bitartrate for particles < 75 micron diameter and 0.1 wt% moisture is classified as ST1 dust explosion and has a rate of pressure rise 484 bar/s, overpressure of 7.7 bar, Kst of 131 bar-m/s, and a minimum ignition energy averaging 24 mJ. A second test yielded a minimum explosive concentration of 50 mg/L and an autoignition temperature of 400 °C.
Oxidizing Properties:	Not an oxidizer
Volatile Organic Chemical Content:	Not available (assumed to be essentially zero)

9.2. Other information

No additional information.

SECTION 10: STABILITY AND REACTIVITY

10.1. Reactivity

Not considered reactive.

10.2. Chemical stability

Stable

10.3. Possibility of hazardous reactions

No hazardous reactions expected.

10.4. Conditions to avoid

Do not heat to boiling or decomposition in sealed container.

10.5. Incompatible materials

Avoid contact with strong acids and bases as well as iron, mild steel and galvanized steel.

10.6. Hazardous decomposition products

Compounds of carbon, hydrogen, nitrogen, oxygen, chlorine.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information on toxicological effects

100% Choline Bitartrate: No data available.

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity

100% Choline Bitartrate: No data available.

12.2. Persistence and degradability

Expected to be readily biodegradable.

12.3. Bioaccumulative potential

Not bioaccumulative.

12.4. Mobility in soil

Not determined.

12.5. Results of PBT and vPvB assessment

Not determined.

12.6. Other adverse effects

Not determined.

SECTION 13: DISPOSAL CONSIDERATIONS

13.1. Waste treatment methods

Product: Not considered a hazardous waste under US Federal Hazardous Waste Regulations (40 CFR 261) or EU Directive 91/689/EEC. Consult local regulations regarding proper disposal as they may be more restrictive or otherwise different from Federal/International regulations.

Packaging: Dispose of packaging contaminated by product in accordance with regulations.

SECTION 14: TRANSPORT INFORMATION

14.1. UN number

Not hazardous.

14.2. UN proper shipping name

Not hazardous.

14.3. Transport hazard class(es)

Not hazardous.

14.4. Packing group

Not hazardous.

14.5. Environmental hazards

Not hazardous.

14.6. Special precautions for user

Not hazardous.

14.7. Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

Not hazardous.

SECTION 15: REGULATORY INFORMATION

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

U.S. Federal Regulations

OSHA: This product is not hazardous under the criteria of the Federal OSHA Hazard Communication Standard 29 CFR 1910.1200.
PSM: This product is not subject to Process Safety Management (29 CFR 1910.119).
FIFRA: Not applicable
TSCA: On TSCA inventory
CERCLA: Reportable Quantity – None (40 CFR 302.4)

SARA TITLE III: Section 302 Extremely Hazardous Substances – None (40 CFR 355)
Section 311/312 Hazard Categories – None (40 CFR 370.2)
Section 313 Toxic Chemicals – None (40 CFR 372.65)

RMP: Not listed under the Risk Management Plan (40 CFR 68).
RCRA: If discarded in purchased form, this product is not a listed or characteristic hazardous waste. However, under RCRA, it is the responsibility of the product user to determine at the time of disposal whether a material containing the product or derived from the product should be classified as a hazardous waste (40 CFR 261.20-24).
CWA: Release into a waterway may require reporting to the National Response Center @ 800-424-8802 (40 CFR 116.4).
FDA/USDA: Follow Good Manufacturing Practice (GMP). GRAS per 21 CFR 182.8250.

International Regulations

Canadian Dangerous Substance List (DSL): Listed (published 5 April 1994)
European Inventory of Existing Commercial Chemical Substances (EINECS): No. 201-763-4
Australian Inventory of Chemical Substances (AICS): Listed.
Korean Existing Chemicals List (ECL): No. KE-20913
EU Regulations:
Food law: Regulation (EC) 178/2002
Food hygiene law: Regulation (EC) 852/2004
Food contaminates: Regulation (EC) 1881/2006
Microbiological in Food: Regulation (EC) EC 2073/2005
Food additive purity: Regulation (EC) 2008/84 – tartaric acid E344, silicon dioxide E551
REACH: Regulation (EC) No 1907/2006 Registration, Evaluation, Authorisation and Restriction of Chemicals does not apply to food.
Safety Data Sheets: Regulation (EU) No 453/2010 does not apply to non-hazardous materials.
CLP: Regulation (EC) No 1272/2008 Classification, Labeling and Packaging does not apply to non-hazardous materials.
Hazardous Waste: Directive (EU) 91/689/EEC - If discarded in purchased form, this product is not a hazardous waste

USA State Regulations
This product is not subject to California Proposition 65. There are no known additional requirements necessary for compliance with state right-to-know regulations.

15.2. Chemical safety assessment

Not required.

SECTION 16: OTHER INFORMATION

Reason for Issue: Added product name.

Risk Phrases Used: None used

Hazard Ratings – The following NFPA hazard ratings are recommended for this product:
Fire - 1; Health – 0; Reactivity – 0; Specific Hazard - None

For safe handling, refer to NFPA 654, *Standard for the prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids*.

The following abbreviations may be used in this document:

% - percent
μg/kg - micrograms per kilogram
g/kg – grams per kilogram
lb/ft^3 – pounds per cubic foot
mg/kg – milligrams per kilogram
mg/m^3 – milligrams per cubic meter
mmHg – millimeters of mercury
ppm – parts per million
w/w – Weight per weight
ACGIH – American Council of Governmental Industrial Hygienists
AICS – Australian Inventory of Chemical Substances
CAS – Chemical Abstract Service
CERCLA – Comprehensive Emergency Response, Compensation and Liability Act
CFR – Code of Federal Regulations
CWA – Clean Water Act
D.O.T. – Department of Transportation
DSL – Domestic Substance List (Canada)
ECL – Existing Chemicals List (Korea)
EINECS – European Inventory of Existing Commercial Substances
FDA – Food and Drug Administration
FIFRA – Federal Insecticide, Fungicide and Rodenticide Act
IDLH – Immediately Dangerous to Life and Health
LD_{50} – Lethal dose for 50% mortality of subject species
LD_{LO} – Lethal dose low; the lowest dose of a substance introduced by any route other than inhalation reported to have caused death in humans or animals.
LFL – Lower Flammable Limit
MSHA – Mine Safety Health Administration
NFPA – National Fire Protection Association
NIOSH – National Institute of Occupational Safety and Health
OSHA – Occupational Safety and Health Administration
PEL – Permissible Exposure Limit (default 8-hour day, 40-hour week TWA)
PSM – Process Safety Management
RCRA – Resource Conservation and Recovery Act
REL – Recommended Exposure Limit (default 10-hour day, 40-hour week TWA)
RMP – Risk Management Plan
SARA – Superfund Amendment and Reauthorization Act
STEL – Short Term Exposure Limit (default 15-minute TWA)
TD_{LO} – Lowest dose to which humans or animals have been exposed and reported to produce a toxic effect other than cancer
TSCA – Toxic Substance Control Act
TWA – Time Weighted Average
UFL – Upper Flammable Limit
USDA – United States Department of Agriculture

SAFETY DATA SHEET
According to Regulation (EC) No. 1907/2006

CHOLINE BITARTRATE

1. IDENTIFICATION OF THE SUBSTANCE OR PREPARATION AND THE COMPANY/UNDERTAKING

Product label name Choline bitartrate
Supplier Balchem Italia Srl, Via del Porto, snc 28040 Marano Ticino (NO) Italy Tel. 0039 (0)321 9791
E-mail address of person responsible for safety data sheet SDS@balchem.com

Emergency telephone 24H/24 + 1-703-527-3887 CHEMTREC	Emergency telephone only during office hours +39-(0)321-9791 BALCHEM ITALIA S.r.l.

Intended use pharmaceutical ingredient
Date of last issue / Revision # 2007/07/11 / 0.04

2. HAZARDS IDENTIFICATION

Not classified as hazardous according to the EEC Dangerous Substance Directive and Dangerous Preparation Directive.

3. COMPOSITION/INFORMATION ON INGREDIENTS

This product is to be considered as a substance in conformance to EC directives.
Information on hazardous ingredients
Chemical description Choline bitartrate
Composition / information on ingredients

Number	% w/w	CAS-number	Chemical name
1	99	000087-67-2	(R,[R*,R*])-2,3-Dihydroxybutanedioic acid, monocholine salt

	Annex-1 number	EC-number	Symbol(s)	Risk-phrase(s)
1		201-763-2		

4. FIRST AID MEASURES

Symptoms and effects No typical symptoms and effects known
First aid
Inhalation not relevant
Skin Wash off with water.
Eye Rinse thoroughly with plenty of water.
Ingestion not relevant.

SAFETY DATA SHEET
According to Regulation (EC) No. 1907/2006

CHOLINE BITARTRATE

Advice to physician
No additional information available.

5. FIRE-FIGHTING MEASURES

Extinguishing media
usual means

Unsuitable extinguishing media
none

Hazardous decomposition/ combustion products
none known

Protective equipment
none known

Fire and explosion hazard
none known

6. ACCIDENTAL RELEASE MEASURES

Personal precautions
For personal protection see Section 8.

Environmental precautions
Collect as much as possible in a clean container for (preferable) reuse or disposal.

Methods for cleaning up
Collect as much as possible in a clean container for (preferable) reuse or disposal. Rinse remnant with plenty of water.

7. HANDLING AND STORAGE

Handling
The usual precautions for handling chemicals should be observed.

Fire and explosion prevention
not applicable.

Storage requirements
Keep bags tightly closed. Product is hygroscopic.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering controls
No specific recommendations

Personal protection

Respiratory
not relevant

Hand
gloves

Eye
not relevant

Skin and body
not relevant

In this country no exposure limit has been established

9. PHYSICAL AND CHEMICAL PROPERTIES

SAFETY DATA SHEET
According to Regulation (EC) No. 1907/2006

CHOLINE BITARTRATE

Appearance crystal
Colour white
Odour none
Boiling point/range not applicable
Melting point/range 147-151 ℃
Flash point not applicable
Flammability not applicable
Explosive properties none
Oxidising properties none
Vapour pressure not applicable
Density not relevant
Bulk density 700 kg/m³
Solubility in water 2000 g/l (20 ℃)
Solubility in other solvents not available
pH value 3.4 - 3.7 (at 10 g/l water, 20 ℃)
Partition coefficient n-octanol/water not available
Relative vapour density (air=1) not relevant
Viscosity not relevant
Autoignition temperature not applicable
Explosion limits not applicable

10. STABILITY AND REACTIVITY

Conditions to avoid	
	none known
Stability Stable under recommended storage and handling conditions (see section 7).	
Incompatibles none known	

SAFETY DATA SHEET
According to Regulation (EC) No. 1907/2006

CHOLINE BITARTRATE

Decomposition
none known

11. TOXICOLOGICAL INFORMATION

No experimental toxicological data of the product as such available yet.

12. ECOLOGICAL INFORMATION

Choline bitartrate

Fate

Degradation Abiotic
Biodegradable

13. DISPOSAL CONSIDERATIONS

Product
Can be incinerated together with domestic garbage, provided the necessary technical provisions are satisfied, following consultation with the waste disposal firm and the appropriate authorities.

Contaminated packaging
Waste disposal in accordance with regulations.

14. TRANSPORT INFORMATION

Land transport

Class
not restricted

Classification Code
not relevant / not relevant

RID class
not restricted

Hazard Identification No.
not relevant

Substance Identification No.
not relevant

TREM-Card or ERG number
not relevant

UN number
none

Proper Shipping Name
not relevant

Sea transport (IMDG-code/ IMO)

Class
not restricted

Packing group
not relevant

UN number
none

EMS
not relevant

SAFETY DATA SHEET
According to Regulation (EC) No. 1907/2006

CHOLINE BITARTRATE

Marine pollutant no
Proper Shipping Name not relevant

Air transport (ICAO-TI/ IATA-DGR)
UN number none
Class not restricted
Packing group not relevant
Proper Shipping Name not relevant

15. REGULATORY INFORMATION

Product label name Choline bitartrate
Labelling according to EC directives
EC-number not applicable

R(isk) phrase(s)	
Code	**Description**
none	none

S(afety) phrase(s)	
Code	**Description**
none	none
German Water Hazard Class (WGK) 0 (Internal assessment)	

16. OTHER INFORMATION

R-phrase information		
Chemical name	R(isk) phrase(s)	
(R,[R*,R*])-2,3-Dihydroxybutanedioic acid, monocholine salt		

History
Date of printing/ pdf file generated 2007/07/11

SAFETY DATA SHEET
According to Regulation (EC) No. 1907/2006

CHOLINE BITARTRATE

Revision 0.04
Composed by Dr. P. Thomas S. Robustellini
Changes were made in section 1, 16
This information only concerns the above mentioned product and does not need to be valid if used with other product(s) or in any process. The information is to our best present knowledge correct and complete and is given in good faith but without warranty. It remains the user's own responsibility to make sure that the information is appropriate and complete for his special use of this product.

Choline Chloride FCC, USP FPN MSDS - English

Revised: 20 December 2010
Supersedes: 9 September 2010

MATERIAL SAFETY DATA SHEET

According to OSHA Regulation 29 CFR 1910.1200 and Regulation (EC) No. 1907/2006
[as amended by (EU) No. 453/2010]

SECTION 1: IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1 Product identifier

Chemical name:	Choline Chloride
Product label name:	Choline Chloride FCC, USP
Other names or synonyms of identification:	2-Hydroxy-N,N,N-trimethylethanaminium chloride
Number of Registration:	Not applicable
C.A.S. Registry number:	67-48-1 (choline chloride)
EINECS number:	200-655-4
EINECS name:	Choline Chloride
Molecular weight:	139.6 (choline chloride)
Molecular formula:	$C_5H_{14}ClNO$ (choline chloride)

1.2 Relevant identified uses of the substance or mixture and uses advised against

Ingredient in foods and dietary supplements

1.3 Details of the supplier of the safety data sheet

Supplier:	Balchem Italia Srl,	Balchem Corporation
Address:	Via del Porto, snc 28040 Marano Ticino (NO) – Italy Italy	52 Sunrise Park Road New Hampton, NY 10958 USA
Telephone number:	0039 (0)321 9791	+1 (845) 326-5600
Fax:		+1 (845) 326-5615
Web:	www.balchem.com	www.balchem.com
E-mail:	sds@balchem.com	sds@balchem.com

1.4 Emergency telephone number

An emergency number is not required for this product.

Emergency telephone 24h/24:	001-703-527-3887 – CHEMTREC International 800-424-9300 – CHEMTREC USA
Emergency telephone only during office hours:	0039-(0)321-9791 BALCHEM ITALIA S.r.l.

SECTION 2: HAZARDS IDENTIFICATION

2.1 Classification of the substance or mixture

Classification of the substance according to Directive 67/548/EEC

None: material is not hazardous.

Classification of the substance according to (EC) No 1272/2008

None: material is not hazardous.

2.2 Label elements

None: material is not hazardous

Hazard statement:

None: material is not hazardous

2.3 Other hazards

None

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

Choline Chloride:	99.5 – 100% (up to 0.5% moisture)	CAS# 67-48-1

3.2 Mixtures

See Section 3.1

SECTION 4: FIRST AID MEASURES

4.1 Description of first aid measures

Inhalation: For significant exposure to any nuisance particles (dust or mist), remove to fresh air and, if there is difficulty breathing, get medical attention. Breathing dust from any source may cause respiratory irritation.

Skin: No first aid is required. As a precaution, wash with soap and water. Wash contaminated clothing before reuse.

Eye: To prevent mechanical irritation, flush with clean, low-pressure water.

Ingestion: No first aid required for ingesting small amounts.

4.2 Most important symptoms and effects, both acute and delayed

Symptoms: Acute – None
Chronic – None

4.3 Indication of any immediate medical attention and special treatment needed

There are no adverse effects from exposure to this product.

SECTION 5: FIREFIGHTING MEASURES

5.1 Extinguishing media

Water, Foam, CO_2, Dry Chemical

5.2 Special hazards arising from the substance or mixture

Hazardous Combustion Products: No specific hazards. Combustion will produce compounds of carbon, hydrogen, nitrogen, oxygen and chlorine.

Other Fire and Explosion Hazards: Possible dust explosion. The particle size as produced and the deliquescent nature of the product are expected to limit potential for dust explosion.

5.3 Advice for firefighters

Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source, is a potential dust explosion hazard. This material may present an explosion and deflagration hazard risk when dispersed and ignited in air. Secondary explosions may also pose a risk once an initial explosion occurs with the presence of a combustible dust or powder in the area.

SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

6.1.1 For non-emergency personnel

Dust should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Avoid dispersal of dust in the air (e.g., avoid clearing dust surfaces with compressed air).

6.1.2 For emergency responders

No specific protective equipment is required.

6.2 Environmental precautions

Water runoff can cause environmental damage due to high BOD.

6.3 Methods and material for containment and cleaning up

Vacuum or sweep material and place in a disposal container.

6.4 Reference to other sections

See Section 8: Exposure Controls/ Personal Protection and Section 13: Disposal Considerations

SECTION 7: HANDLING AND STORAGE

7.1 Precautions for safe handling

Avoid contact with eyes, skin and clothing. Wash thoroughly after handling. Avoid breathing dust.

7.2. Conditions for safe storage, including any incompatibilities

Choline chloride is deliquescent (will absorb moisture from air to form a liquid). Ensure containers are properly secured before moving. Minimize dust generation and accumulation. Routine housekeeping should be instituted to ensure that dusts do not accumulate on surfaces. Dry powders can build static electricity charges when subjected to the friction of transfer and mixing operations. Provide adequate precaution, such as electrical grounding and bonding, or inert atmospheres.

7.3. Specific end use(s)

No additional recommendations.

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters

Choline Chloride: OSHA Nuisance Dust PELs (29 CFR 1910.1000): Respirable fraction = 5 mg/m^3; Total = 15 mg/m^3

8.2. Exposure controls

Provide ventilation and particulate control to maintain airborne levels below the exposure guidelines. It is recommended that all dust control equipment such as local exhaust ventilation and material transport systems involved in handling of this product contain explosion relief vents or an explosion suppression system or an oxygen-deficient environment. Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work are (i.e., there is no leakage from the equipment). Use only appropriately classified electrical equipment and powered industrial trucks.

Eye/Face Protection: If there is a potential for exposure to particles (mist or dust) which would cause mechanical injury to the eye, wear chemical goggles.

Skin Protection: No additional precautions.

Respiratory Protection: In dusty atmospheres, use an approved dust respirator. In confined or poorly ventilated areas or emergency and other conditions where the exposure guidelines may be greatly exceeded, use an approved positive pressure self-contained breathing apparatus.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Product:	Choline Chloride
Appearance:	Clear
Physical state:	Liquid
Chemical Family:	Aliphatic amines
Odor:	Slight amine odor; threshold not determined
Specific Gravity:	Not determined
pH:	Choline chloride: 4.5-7.5 for a 25% wt/vol solution
Melting Point:	Choline chloride: decomposes 247°C (477°F)
Boiling Point:	Not available
Flash Point:	None
Evaporation Rate:	Not available (assumed equal to water)
Flammability:	Not flammable
Flammability Limits:	Not flammable
Vapor Pressure:	Not available (assumed equal to water)
Vapor Density (air=1):	Not available (assumed equal to water)
Bulk Density:	Not determined
Solubility:	Choline chloride: 370 g/100 mL water @ 50 ^{o}F (10 ^{o}C)
Octanol/Water Partition Coefficient	Not available
Autoignition Temperature:	Not available
Viscosity:	Not available
Explosive Properties:	Dry choline chloride for particles > 500 micron diameter and 2.3 wt% moisture is classified as ST1 dust explosion and has a lower explosion limit of 125 g/m^3, overpressure of 3.5 bar, Kst of 4 bar-m/s, a minimum ignition energy > 10^6 mJ and an ignition temperature of 430 ^{o}C. For particles < 63 um, choline chloride is classified as ST1 dust explosion.
Oxidizing Properties:	Not an oxidizer
Volatile Organic Chemical Content:	Not available (assumed to be essentially zero)

9.2. Other information

No additional information.

SECTION 10: STABILITY AND REACTIVITY

10.1. Reactivity

Not considered reactive.

10.2. Chemical stability

Stable

10.3. Possibility of hazardous reactions

No hazardous reactions expected.

10.4. Conditions to avoid

Do not heat to boiling or decomposition in sealed container.

10.5. Incompatible materials

Avoid contact with strong acids and bases as well as iron, mild steel and galvanized steel.

10.6. Hazardous decomposition products

Compounds of carbon, hydrogen, nitrogen, oxygen, chlorine.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information on toxicological effects

100% Choline Chloride: LD_{50} – 3400 mg/kg oral (rat)

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity

100% Choline Chloride: 10,000 mg/L 24 weeks (mortality) coho salmon, silver salmon.

12.2. Persistence and degradability

Readily biodegradable.

12.3. Bioaccumulative potential

Not bioaccumulative.

12.4. Mobility in soil

Not determined.

12.5. Results of PBT and vPvB assessment

Not determined.

12.6. Other adverse effects

Not determined.

SECTION 13: DISPOSAL CONSIDERATIONS

13.1. Waste treatment methods

Product: Not considered a hazardous waste under US Federal Hazardous Waste Regulations (40 CFR 261) or EU Directive 91/689/EEC. Consult local regulations regarding proper disposal as they may be more restrictive or otherwise different from Federal/International regulations.

Packaging: Dispose of packaging contaminated by product in accordance with regulations.

SECTION 14: TRANSPORT INFORMATION

14.1. UN number

Not hazardous.

14.2. UN proper shipping name

Not hazardous.

14.3. Transport hazard class(es)

Not hazardous.

14.4. Packing group

Not hazardous.

14.5. Environmental hazards

Not hazardous.

14.6. Special precautions for user

Not hazardous.

14.7. Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

Not hazardous.

SECTION 15: REGULATORY INFORMATION

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

U.S. Federal Regulations

OSHA: This product is not hazardous under the criteria of the Federal OSHA Hazard Communication Standard 29 CFR 1910.1200.
PSM: This product is not subject to Process Safety Management (29 CFR 1910.119).
FIFRA: Not applicable
TSCA: On TSCA inventory
CERCLA: Reportable Quantity – None (40 CFR 302.4)

SARA TITLE III: Section 302 Extremely Hazardous Substances – None (40 CFR 355)
Section 311/312 Hazard Categories – None (40 CFR 370.2)
Section 313 Toxic Chemicals – None (40 CFR 372.65)

RMP: Not listed under the Risk Management Plan (40 CFR 68).
RCRA: If discarded in purchased form, this product is not a listed or characteristic hazardous waste. However, under RCRA, it is the responsibility of the product user to determine at the time of disposal whether a material containing the product or derived from the product should be classified as a hazardous waste (40 CFR 261.20-24).
CWA: Release into a waterway may require reporting to the National Response Center @ 800-424-8802 (40 CFR 116.4).
FDA/USDA: Follow Good Manufacturing Practice (GMP). GRAS per 21 CFR 182.8252.

International Regulations

Canadian Dangerous Substance List (DSL): Listed (published 5 April 1994)
European Inventory of Existing Commercial Chemical Substances (EINECS): No. 200-655-4
Australian Inventory of Chemical Substances (AICS): Listed.
Korean Existing Chemicals List (ECL): No. KE-20909
Japan ENCS: 2-341X; 9-1994X
German Water Class (WKG): 0 (Internal assessment)
EU Regulations:
Food law: Regulation (EC) 178/2002
Food hygiene law: Regulation (EC) 852/2004
Food contaminates: Regulation (EC) 1881/2006
Microbiological in Food: Regulation (EC) EC 2073/2005
REACH: Regulation (EC) No 1907/2006 Registration, Evaluation, Authorisation and Restriction of Chemicals does not apply to food.
Safety Data Sheets: Regulation (EU) No 453/2010 does not apply to non-hazardous materials.
CLP: Regulation (EC) No 1272/2008 Classification, Labeling and Packaging does not apply to non-hazardous materials.
Hazardous Waste: Directive (EU) 91/689/EEC - If discarded in purchased form, this product is not a hazardous waste

USA State Regulations

This product is not subject to California Proposition 65. There are no known additional requirements necessary for compliance with state right-to-know regulations.

15.2. Chemical safety assessment

Not completed.

SECTION 16: OTHER INFORMATION

Reason for Issue: Updated to format of EU 453/2010.

Risk Phrases Used: None used

Hazard Ratings – The following NFPA hazard ratings are recommended for this product:
Fire - 1; Health – 0; Reactivity – 0; Specific Hazard - None

For safe handling, refer to NFPA 654, *Standard for the prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids***.**

The following abbreviations may be used in this document:

% - percent
μg/kg - micrograms per kilogram
g/kg – grams per kilogram
lb/ft^3 – pounds per cubic foot
mg/kg – milligrams per kilogram
mg/m^3 – milligrams per cubic meter
mmHg – millimeters of mercury
ppm – parts per million
w/w – Weight per weight
ACGIH – American Council of Governmental Industrial Hygienists
AICS – Australian Inventory of Chemical Substances
CAS – Chemical Abstract Service
CERCLA – Comprehensive Emergency Response, Compensation and Liability Act
CFR – Code of Federal Regulations
CWA – Clean Water Act
D.O.T. – Department of Transportation
DSL – Domestic Substance List (Canada)
ECL – Existing Chemicals List (Korea)
EINECS – European Inventory of Existing Commercial Substances
FDA – Food and Drug Administration
FIFRA – Federal Insecticide, Fungicide and Rodenticide Act
IDLH – Immediately Dangerous to Life and Health
LD_{50} – Lethal dose for 50% mortality of subject species
LD_{LO} – Lethal dose low; the lowest dose of a substance introduced by any route other than inhalation reported to have caused death in humans or animals.
LFL – Lower Flammable Limit
MSHA – Mine Safety Health Administration
NFPA – National Fire Protection Association
NIOSH – National Institute of Occupational Safety and Health
OSHA – Occupational Safety and Health Administration
PEL – Permissible Exposure Limit (default 8-hour day, 40-hour week TWA)
PSM – Process Safety Management
RCRA – Resource Conservation and Recovery Act
REL – Recommended Exposure Limit (default 10-hour day, 40-hour week TWA)
RMP – Risk Management Plan
SARA – Superfund Amendment and Reauthorization Act
STEL – Short Term Exposure Limit (default 15-minute TWA)
TD_{LO} – Lowest dose to which humans or animals have been exposed and reported to produce a toxic effect other than cancer
TSCA – Toxic Substance Control Act
TWA – Time Weighted Average
UFL – Upper Flammable Limit
USDA – United States Department of Agriculture

Choline Chloride C-Salt™ FP&N MSDS - English
Revised: 9 September 2010
Supersedes: 28 July 2010

MATERIAL SAFETY DATA SHEET

According to OSHA Regulation 29 CFR 1910.1200 and Regulation (EC) No. 1907/2006

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME: C-Salt™
SYNONYMS: Choline Chloride
2-Hydroxy-N,N,N-trimethylethanaminium chloride
TYPICAL USES: Ingredient in foods and dietary supplements

MANUFACTURER / SUPPLIER:	USA	Europe
	Balchem Corporation 52 Sunrise Park Road New Hampton, NY 10958 Phone : +1 (845) 326-5600 Fax: +1 (845) 326-5615 Web: www.balchem.com E-mail: sds@balchem.com	Balchem Italia Srl, Via del Porto, snc 28040 Marano Ticino (NO), Italy +39-(0)321-9791

24h EMERGENCY PHONE: Not required. If needed, call CHEMTREC at + 1-703-527-3887 [USA]

2. HAZARDS IDENTIFICATION

Emergency Overview

White crystalline powder with faint amine (fish-like) odor. Not classified as hazardous according to US Hazard Communication Regulation (29 CFR 1910.1200), the EEC Dangerous Substance Directive and Dangerous Preparation Directive (67/548/EEC and 1999/45/EC). No risk to the environment expected. Warning! May form combustible dust concentrations in air (during processing).

Potential Health Effects

Eye: Dust may cause mechanical eye irritation.
Inhalation: No adverse effects anticipated by breathing small amounts.
Skin: No hazard expected.
Ingestion: No hazard expected.
Systemic: No known physiological hazards.
Medical Conditions Aggravated by Exposure: None determined

3. COMPOSITION/INFORMATION ON INGREDIENTS

Also see Section 15.

Product	Components	Weight %	CAS #	IUPAC Name
C-Salt™	$C_5H_{14}ClNO$	97 – 98.5 %	67-48-1	Trimethyl (2-hydroxyethyl) ammonium chloride, or 2-hydroxy-*N*,*N*,*N*-trimethylethanaminium chloride
	$(C_{17}H_{35}COO)_2Mg$	1.5 – 2.5 %	557-04-0	Magnesium octadecanoate
	H_2O	0 – 0.5 %	7732-18-5	Water

Exposure Limits

OSHA Nuisance Dust PELs (29 CFR 1910.1000): Respirable fraction = 5 mg/m^3; Total = 15 mg/m^3
ACGIH Total Dust for Stearates: 10 mg/m^3
Risk Phrases and Symbols: None

4. FIRST AID MEASURES

Symptoms: Acute – None expected; Chronic – None expected
Eye: To prevent mechanical irritation, flush with clean, low-pressure water.

Inhalation: For significant exposure to any nuisance dust, remove to fresh air and, if there is difficulty breathing, get medical attention.
Skin: No first aid should be required. As a precaution, wash with soap and water. Wash contaminated clothing before reuse.
Ingestion: No first aid should be required for ingesting small amounts.
Note to Physician: There are no adverse effects expected from exposure to this product.

5. FIRE FIGHTING MEASURES

Flammable Properties: Flash point – not applicable
Flammable Limits: not applicable
A**utoignition Temperature:** Not available
Hazardous Combustion Products: No specific hazards. Combustion will produce compounds of carbon, hydrogen, nitrogen, oxygen and chlorine.
Other Fire and Explosion Hazards: Possible dust explosion. The particle size as produced and the deliquescent nature of the product are expected to limit potential for dust explosion. Choline chloride for particles > 500 micron diameter and 2.3 wt% moisture is classified as ST1 dust explosion and has a lower explosion limit of 125 g/m^3, overpressure of 3.5 bar, Kst of 4 bar-m/s, a minimum ignition energy > 10^6 mJ and an ignition temperature of 430 ^oC. For particles < 63 um, choline chloride is classified as ST1 dust explosion.
Extinguishing Media: Water, Foam, CO_2, Dry Chemical
Fire Fighting Equipment: Full protective equipment (Bunker Gear) and NIOSH/MSHA approved SCBA should be used for all indoor and any significant outdoor fires.
Fire Fighting Instructions: Water run off can cause environmental damage. Dike and collect water used to fight fires. Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source, is a potential dust explosion hazard. This material may present an explosion and deflagration hazard risk when dispersed and ignited in air. Secondary explosions may also pose a risk once an initial explosion occurs with the presence of a combustible dust or powder in the area.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions: See Section 8.
Environmental Precautions: As good practice, prevent material from entering waterways.
Cleaning Method: Vacuum or sweep material and place in a disposal container. Dust should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Avoid dispersal of dust in the air (e.g., avoid clearing dust surfaces with compressed air).

7. HANDLING AND STORAGE

General Handling Precautions
Avoid contact with eyes, skin and clothing. Wash thoroughly after handling. Avoid breathing dust. Ensure containers are properly secured before moving. Minimize dust generation and accumulation. Routine housekeeping should be instituted to ensure that dusts do not accumulate on surfaces. Dry powders can build static electricity charges when subjected to the friction of transfer and mixing operations. Provide adequate precaution, such as electrical grounding and bonding, or inert atmospheres.
Storage Information
Storage temperature: Ambient recommended. Keep containers closed and away from moisture.
Shelf Life: Use within one year recommended.
Special Sensitivity: None
Miscellaneous: Choline chloride is deliquescent (will absorb moisture from air to form a liquid).
Specific Use: No special requirements apply to expected use as a food ingredient.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Exposure Limits: See Section 3.
Engineering Controls: Provide ventilation and particulate control to maintain airborne levels below the exposure guidelines. It is recommended that all dust control equipment such as local exhaust

ventilation and material transport systems involved in handling of this product contain explosion relief vents or an explosion suppression system or an oxygen-deficient environment. Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work are (i.e., there is no leakage from the equipment). Use only appropriately classified electrical equipment and powered industrial trucks.

Eye Protection: Use safety glasses. If there is a potential for exposure to particles which would cause mechanical injury to the eye, wear chemical goggles.

Respiratory Protection: In dusty atmospheres, use an approved dust respirator. In confined or poorly ventilated areas or emergency and other conditions where the exposure guidelines may be greatly exceeded, use an approved positive pressure self-contained breathing apparatus.

Hand and Skin Protection: Use gloves. No additional precautions other than clean body-covering clothing should be needed.

9. PHYSICAL AND CHEMICAL PROPERTIES

Also see Section 5

Product:	Choline Chloride
Appearance:	White crystal
Physical state:	Solid
Chemical Family:	Aliphatic amines
Odor:	Slight amine odor
Molecular Formula:	$C_5H_{14}ClNO$ (choline chloride)
Molecular Weight:	139.6 (choline chloride)
Specific Gravity:	Not determined
Bulk Density:	Not determined
Solubility:	Choline chloride: 370 g/100 mL water @ 50 ^{o}F (10 ^{o}C)
Octanol/Water Partition Coefficient	Not available
pH:	Choline chloride: 4.5-7.5 for a 25% wt/vol solution
Melting Point:	Choline chloride: Decomposes @ 477°F (247°C)
Boiling Point:	Not available
Evaporation Rate:	Not available (assumed to be essentially zero)
VOC Content:	Not available (assumed to be essentially zero)
Vapor Pressure:	Not available (assumed to be very low)
Vapor Density (air=1):	Not available
Viscosity:	Not available

10. STABILITY AND REACTIVITY

Chemical Stability: Stable under normal conditions

Material Incompatibility: Avoid contact with strong acids and bases as well as iron, mild steel and galvanized steel.

Hazardous Decomposition Products: Compounds of carbon, hydrogen, nitrogen, oxygen, chlorine.

Hazardous Polymerization: None

11. TOXICOLOGICAL INFORMATION (100% Choline Chloride)

LD_{50} – 3400 mg/kg oral (rat)

12. ECOLOGICAL INFORMATION (100% Choline Chloride)

10,000 mg/L 24 weeks (mortality) coho salmon, silver salmon. Readily biodegradable.

13. DISPOSAL CONSIDERATIONS

Product: Not considered a hazardous waste under Federal Hazardous Waste Regulations (40 CFR 261). Consult state and local regulations regarding proper disposal as they may be more restrictive or otherwise different from Federal regulations.

Packaging: Dispose of packaging contaminated by product in accordance with regulations.

14. TRANSPORT INFORMATION

EU: As produced, this product is not subject to hazardous material transport regulations in Europe.
US: Not a D.O.T. Hazardous Material (49 CFR 172.101).
Labeling: Containers of this product need no special warning labels. Only a product identity label is needed.

15. REGULATORY INFORMATION

U.S. Federal Regulations

OSHA: This product is not hazardous under the criteria of the Federal OSHA Hazard Communication Standard 29 CFR 1910.1200.
PSM: This product is not subject to Process Safety Management (29 CFR 1910.119).
FIFRA: Not applicable
TSCA: On TSCA inventory
CERCLA: Reportable Quantity – None (40 CFR 302.4)

SARA TITLE III: Section 302 Extremely Hazardous Substances – None (40 CFR 355)
Section 311/312 Hazard Categories – None (40 CFR 370.2)
Section 313 Toxic Chemicals – None (40 CFR 372.65)

RMP: Not listed under the Risk Management Plan (40 CFR 68).
RCRA: If discarded in purchased form, this product is not a listed or characteristic hazardous waste. However, under RCRA, it is the responsibility of the product user to determine at the time of disposal whether a material containing the product or derived from the product should be classified as a hazardous waste (40 CFR 261.20-24).
CWA: Release into a waterway may require reporting to the National Response Center @ 800-424-8802 (40 CFR 116.4).
FDA/USDA: Follow Good Manufacturing Practice (GMP). GRAS per 21 CFR 182.8252.

International Regulations

Canadian Dangerous Substance List (DSL): Listed (published 5 April 1994)
European Inventory of Existing Commercial Chemical Substances (EINECS): No. 200-655-4
Australian Inventory of Chemical Substances (AICS): Listed.
Korean Existing Chemicals List (ECL): No. KE-20909
Japan ENCS: 2-341X; 9-1994X
German Water Class (WKG): 0 (Internal assessment)

State Regulations
This product is not subject to California Proposition 65. There are no known additional requirements necessary for compliance with state right-to-know regulations.

16. OTHER INFORMATION

For safe handling, refer to NFPA 654, *Standard for the prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids***.**

Reason for Issue: Updated to simplify information including describing only a single product.
Risk Phrases Used: None used
Hazard Ratings – The following NFPA hazard ratings are recommended for this product:
Fire - 1; Health – 0; Reactivity – 0; Specific Hazard - None

BALCHEM ANIMAL NUTRITION & HEALTH

Choline Chloride Dry and Aqueous Prouducts ANH MSDS - English

Revised: 20 December 2010
Supersedes: 7 December 2010

MATERIAL SAFETY DATA SHEET

According to OSHA Regulation 29 CFR 1910.1200 and Regulation (EC) No. 1907/2006
[as amended by (EU) No. 453/2010]

SECTION 1: IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/UNDERTAKING

1.1 Product identifier

Chemical name: Choline Chloride

Product label name:

Dry Products
60% Choline Chloride – Dry
70% Choline Chloride – Dry
75% Choline Chloride – Dry
Choline chloride, 50% on vegetable carrier
Choline chloride, 60% on vegetable carrier
Choline chloride, 70% on vegetable carrier
Choline chloride, 50% on silica carrier
Choline chloride, 35% on silica carrier

Aqueous Products
70% Choline Chloride – Aqueous
75% Choline Chloride – Aqueous

Other names or synonyms of identification: 2-Hydroxy-N,N,N-trimethylethanaminium chloride
Number of Registration: Feed Registry # not available
C.A.S. Registry number: 67-48-1 (choline chloride)
EINECS number: 200-655-4
EINECS name: Choline Chloride
Molecular weight: 139.6 (choline chloride)
Molecular formula: $C_5H_{14}ClNO$ (choline chloride)

1.2 Relevant identified uses of the substance or mixture and uses advised against

Nutritional additive for feed

1.3 Details of the supplier of the safety data sheet

Supplier:	Balchem Italia Srl,	Balchem Corporation
Address:	Via del Porto, snc 28040 Marano Ticino (NO) – Italy Italy	52 Sunrise Park Road New Hampton, NY 10958 USA
Telephone number:	0039 (0)321 9791	+1 (845) 326-5613
Fax:		+1 (845) 326-5800
Web:	www.balchem.com	www.balchem.com
E-mail:	sds@balchem.com	sds@balchem.com

1.4 Emergency telephone number

An emergency number is not required for this product.

Emergency telephone 24h/24:	001-703-527-3887 – CHEMTREC International 800-424-9300 – CHEMTREC USA
Emergency telephone only during office hours:	0039-(0)321-9791 BALCHEM ITALIA S.r.l.

SECTION 2: HAZARDS IDENTIFICATION

2.1 Classification of the substance or mixture

Classification of the substance according to Directive 67/548/EEC

None: material is not hazardous.

Classification of the substance according to (EC) No 1272/2008

None: material is not hazardous.

2.2 Label elements

None: material is not hazardous

Hazard statement:

None: material is not hazardous

2.3 Other hazards

None

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

See Section 3.2

3.2 Mixtures

Product	Components	Weight %	CAS #
CC 35% and 50% on Silica	$C_5H_{14}ClNO$	35-50	67-48-1
	$SiO_2 \bullet xH_2O$	50-65	7631-86-9
	H_2O	< 0.5	7732-18-5
Other Dry Products	$C_5H_{14}ClNO$	50-70	67-48-1
	Carrier	30-50	Not applicable
	$SiO_2 \bullet xH_2O$	0-2	63231-67-4
	H_2O	< 0.5	7732-18-5
Aqueous Products	$C_5H_{14}ClNO$	70-75	67-48-1
	H_2O	25-30	7732-18-5

SECTION 4: FIRST AID MEASURES

4.1 Description of first aid measures

Inhalation: For significant exposure to any nuisance particles (dust or mist), remove to fresh air and, if there is difficulty breathing, get medical attention. Breathing dust from any source may cause respiratory irritation. Breathing large amounts of dust from any source may cause injury.

Skin: No first aid is required. As a precaution, wash with soap and water. Wash contaminated clothing before reuse.

Eye: To prevent mechanical irritation, flush with clean, low-pressure water.

Ingestion: No first aid required for ingesting small amounts.

4.2 Most important symptoms and effects, both acute and delayed

Symptoms: Acute – None
Chronic – None

4.3 Indication of any immediate medical attention and special treatment needed

There are no adverse effects from exposure to this product.

SECTION 5: FIREFIGHTING MEASURES

5.1 Extinguishing media

Water, Foam, CO_2, Dry Chemical.

5.2 Special hazards arising from the substance or mixture

Hazardous Combustion Products: No specific hazards. Combustion will produce compounds of carbon, hydrogen, nitrogen, chlorine and oxygen.

Other Fire and Explosion Hazards: Possible dust explosion. The particle size as produced and the deliquescent nature of the product are expected to limit potential for dust explosion. Aqueous products support combustion only after evaporation of the water content.

5.3 Advice for firefighters

Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source, is a potential dust explosion hazard. This material may present an explosion and deflagration hazard risk when dispersed and ignited in air. Secondary explosions may also pose a risk once an initial explosion occurs with the presence of a combustible dust or powder in the area.

SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

6.1.1 For non-emergency personnel

Dust should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Avoid dispersal of dust in the air (e.g., avoid clearing dust surfaces with compressed air).

6.1.2 For emergency responders

No specific protective equipment is required.

6.2 Environmental precautions

None.

6.3 Methods and material for containment and cleaning up

Vacuum or sweep material and place in a disposal container.

6.4 Reference to other sections

See Section 8: Exposure Controls/ Personal Protection and Section 13: Disposal Considerations

SECTION 7: HANDLING AND STORAGE

7.1 Precautions for safe handling

Avoid contact with eyes, skin and clothing. Wash thoroughly after handling. Avoid breathing dust.

7.2. Conditions for safe storage, including any incompatibilities

Choline chloride is deliquescent (will absorb moisture from air to form a liquid). Ensure containers are properly secured before moving. Minimize dust generation and accumulation. Routine housekeeping should be instituted to ensure that dusts do not accumulate on surfaces. Dry powders can build static electricity charges when subjected to the friction of transfer and mixing operations. Provide adequate precaution, such as electrical grounding and bonding, or inert atmospheres.

7.3. Specific end use(s)

No additional recommendations.

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control parameters

Choline Chrloride: OSHA Nuisance Dust PELs (29 CFR 1910.1000):
Respirable fraction = 5 mg/m^3; Total = 15 mg/m^3

Silicon dioxide / Precipitated synthetic amorphous silica (Italy): Respirable dust = 2.4 mg/m^3; Inhalable dust = 6 mg/m^3. Note SiO_2 is a carrier for CC 35% and 50% CC on Silica, and is added as a flow agent to conditioned product only. This silica gel is synthetic amorphous silica not to be confused with crystalline silica. Epidemiological studies indicate low potential for adverse health effects from amorphous silica.

8.2. Exposure controls

Provide ventilation and particulate control to maintain airborne levels below the exposure guidelines. It is recommended that all dust control equipment such as local exhaust ventilation and material transport systems involved in handling of this product contain explosion relief vents or an explosion suppression system or an oxygen-deficient environment. Ensure that dust-handling systems (such as exhaust ducts, dust collectors, vessels, and processing equipment) are designed in a manner to prevent the escape of dust into the work area (i.e., there is no leakage from the equipment). Use only appropriately classified electrical equipment and powered industrial trucks.

Eye/Face Protection: If there is a potential for exposure to particles (mist or dust) which would cause mechanical injury to the eye, wear chemical goggles.

Skin Protection: No additional precautions.

Respiratory Protection: In dusty atmospheres, use an approved dust respirator. In confined or poorly ventilated areas or emergency and other conditions where the exposure guidelines may be greatly exceeded, use an approved positive pressure self-contained breathing apparatus.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on basic physical and chemical properties

Product:	Dry Products	Aqueous Products
Appearance:	Pale yellow / tan to light brown, dark brown or off-white granule or powder	Clear to light amber / pale yellow
Physical state:	Solid	Liquid
Chemical Family:	Aliphatic amines	Aliphatic amines
Odor:	Odorless to slight grain odor; threshold not determined	Faint amine odor; threshold not determined
Specific Gravity:	0.46	1.1
pH:	Choline chloride: 4.5-7.5 for a 25% wt/vol solution in water	5 - 8 at 10 g/l water @ 20^{o}C
Melting Point:	Choline chloride: decomposes 247°C (477°F)	-0.4^{o}F (-18^{o}C)
Boiling Point:	Choline choride: decomposes	>125°C (>257 ^{o}F)
Flash Point:	Choline chloride: not applicable	Not applicable
Evaporation Rate:	Not available (assumed to be essentially zero)	Not available
Flammability:	Not flammable	Not flammable
Flammability Limits:	Not flammable	Not flammable
Vapor Pressure:	Not available (assumed to be essentially zero)	Only water vapor is present.

Product:	Dry Products	Aqueous Products
Vapor Density (air=1):	Not available (assumed to be essentially zero)	Not available
Bulk Density:	450-650 kg/m^3	Not applicable
Solubility:	Choline chloride: 370 g/100 mL water @ 50 ^oF (10 ^oC)	Completely miscible in water
Octanol/Water Partition Coefficient	Not available	Log Pow < 0
Autoignition Temperature:	Choline chloride: Not available	Not available
Viscosity:	Not available	26 mPa.s @ 20°C
Explosive Properties:	Based on minimal samples with vegetable carrier, material as produced is 0-2 wt% of particle size 70 microns or less. While not fully evaluated for dust explosion properties, material is expected to be classified as ST2 for dry particles less than 75 micron diameter. Literature reports choline chloride for particles < 63 micron diameter and 2.3 wt% moisture is classified as ST1 dust explosion and has a lower explosion limit of 125 g/m^3, overpressure of 3.5 bar, Kst of 4 bar-m/s, a minimum ignition energy (MIE) > 10^6 mJ and an ignition temperature of 430 ^oC (806 ^oF). One sample of 70% choline chloride on vegetable carrier at 0.6 wt% moisture and particle size < 70 micron diameter had the following properties: Layer Ignition Test (LIT): No ignition up to 400 ^oC (752 ^oF) of 5 mm dust layer, minimum ignition temperature (MIT) of 300 ^oC (572 ^oF), MIE = 30 mJ, Charge Relaxation Time <0.01 seconds yielding classification as quick which implies rapid elimination of charge buildup when grounded / earthed, Powder Volume Resistivity = 2.6 x 10^4 classified as low implying grounding/earthing is likely effective at preventing charge buildup, Pmax = 6.8 bar, Kst=245 bar-m/s and ST=2 (for dust cloud composed of particle 70 micron or less under high turbulence).	Material not tested as mist. Water content must first evaporate before dust formation occurs. Choline chloride for particles > 500 micron diameter and 2.3 wt% moisture is classified as ST1 dust explosion and has a lower explosion limit of 125 g/m^3, overpressure of 3.5 bar, Kst of 4 bar-m/s, a minimum ignition energy > 10^6 mJ and an ignition temperature of 430 ^oC. For particles < 63 um, choline chloride is classified as ST1 dust explosion.
Oxidizing Properties:	Not an oxidizer	
Volatile Organic Chemical Content:	Not available (assumed to be essentially zero)	

9.2. Other information

No additional information.

SECTION 10: STABILITY AND REACTIVITY

10.1. Reactivity

Not considered reactive.

10.2. Chemical stability

Stable.

10.3. Possibility of hazardous reactions

No hazardous reactions expected.

10.4. Conditions to avoid

Do not heat to boiling or decomposition in sealed container.

10.5. Incompatible materials

Avoid contact with strong acids and bases as well as iron, mild steel and galvanized steel.

10.6. Hazardous decomposition products

Compounds of carbon, hydrogen, nitrogen, oxyen, chlorine.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information on toxicological effects

100% Choline Chloride: LD_{50} – 3400 mg/kg oral (rat)
LD_{50} – 450 mg/kg intraperitoneal (rat)
LD_{50} – 3900 mg/kg oral (mouse)
LD_{50} – 320 mg/kg intraperitoneal (mouse)
LD_{LO} – 735 mg/kg subcutaneous (mouse)
LD_{50} – 53 mg/kg intravenous (mouse)
LD_{LO} – 5 mg/kg intravenous (dog)
LD_{LO} – 25 mg/kg intravenous (cat)
LD_{LO} – 500 mg/kg intraperitoneal (rabbit)
LD_{LO} – 1 g/kg subcutaneous (rabbit)
LD_{LO} – 1100 μg/kg intravenous (rabbit)
LD_{LO} – 1 g/kg rectal (rabbit)
LD_{LO} – 1500 mg/kg (frog)
TD_{LO} – 331 mg/kg/14 weeks continuous oral (rat)
TD_{LO} – 4950 mg/kg/30 days intermittent intraperitoneal (rat)
TD_{LO} – 6250 mg/kg/10 weeks intermittent intraperitoneal (rat)
TD_{LO} – 3564 mg/kg/5 weeks intermittent intraperitoneal (rat)

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity

100% Choline Chloride: 10,000 mg/L 24 weeks (mortality) coho salmon, silver salmon.
.

12.2. Persistence and degradability

Expected to be readily biodegradable.

12.3. Bioaccumulative potential

Not bioaccumulative.

12.4. Mobility in soil

Not determined.

12.5. Results of PBT and vPvB assessment

Not determined.

12.6. Other adverse effects

Not determined.

SECTION 13: DISPOSAL CONSIDERATIONS

13.1. Waste treatment methods

Product: Not considered a hazardous waste under US Federal Hazardous Waste Regulations (40 CFR 261) or EU Directive 91/689/EEC. Consult local regulations regarding proper disposal as they may be more restrictive or otherwise different from Federal/International regulations.

Packaging: Dispose of packaging contaminated by product in accordance with regulations.

SECTION 14: TRANSPORT INFORMATION

14.1. UN number

Not hazardous.

14.2. UN proper shipping name

Not hazardous.

14.3. Transport hazard class(es)

Not hazardous.

14.4. Packing group

Not hazardous.

14.5. Environmental hazards

Not hazardous.

14.6. Special precautions for user

Not hazardous.

14.7. Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

Not hazardous.

SECTION 15: REGULATORY INFORMATION

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

U.S. Federal Regulations

OSHA: This product is not hazardous under the criteria of the Federal OSHA Hazard Communication Standard 29 CFR 1910.1200.
PSM: This product is not subject to Process Safety Management (29 CFR 1910.119).
FIFRA: Not applicable
TSCA: On TSCA inventory
CERCLA: Reportable Quantity – None (40 CFR 302.4)

SARA TITLE III: Section 302 Extremely Hazardous Substances – None (40 CFR 355)
Section 311/312 Hazard Categories – None (40 CFR 370.2)
Section 313 Toxic Chemicals – None (40 CFR 372.65)

RMP: Not listed under the Risk Management Plan (40 CFR 68).
RCRA: If discarded in purchased form, this product is not a listed or characteristic hazardous waste. However, under RCRA, it is the responsibility of the product user to determine at the time of disposal whether a material containing the product or derived from the product should be classified as a hazardous waste (40 CFR 261.20-24).
CWA: Release into a waterway may require reporting to the National Response Center @ 800-424-8802 (40 CFR 116.4).
FDA/USDA: Follow Good Manufacturing Practice (GMP). Choline chloride is GRAS per 21 CFR 581.5252. IFN 7-01-228.

International Regulations

Canadian Dangerous Substance List (DSL): Listed (published 5 April 1994)
European Inventory of Existing Commercial Chemical Substances (EINECS): No. 200-655-4
EU Regulations:
- **Reregistration of Feed Additives**: Regulation (EC) 1831/2003) – Feed Registry # not available.
- **REACH:** Regulation (EC) No 1907/2006 Registration, Evaluation, Authorisation and Restriction of Chemicals does not apply to feed.
- **Safety Data Sheets:** Regulation (EU) No 453/2010 does not apply to non-hazardous materials.
- **CLP:** Regulation (EC) No 1272/2008 Classification, Labeling and Packaging does not apply to non-hazardous materials.
- **Hazardous Waste:** Directive (EU) 91/689/EEC - If discarded in purchased form, this product is not a hazardous waste.

Australian Inventory of Chemical Substances (AICS): Listed
Korean Existing Chemicals List (ECL): No. KE-20909
Japan ENCS: 2-341X; 9-1994X
German Water Class (WKG): 0 (Internal assessment)

USA State Regulations

This product is not subject to California Proposition 65. There are no known additional requirements necessary for compliance with state right-to-know regulations.

15.2. Chemical safety assessment

Not completed.

SECTION 16: OTHER INFORMATION

Reason for Issue: Updated to format of EU 453/2010.

Risk Phrases Used: None used

Hazard Ratings – The following NFPA hazard ratings are recommended for this product:
Fire - 1; Health – 0; Reactivity – 0; Specific Hazard - None

For safe handling, refer to NFPA 654, *Standard for the prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids***.**

The following abbreviations may be used in this document:

% - percent
μg/kg - micrograms per kilogram
g/kg – grams per kilogram
lb/ft^3 – pounds per cubic foot
mg/kg – milligrams per kilogram
mg/m^3 – milligrams per cubic meter
mmHg – millimeters of mercury
ppm – parts per million
w/w – Weight per weight
ACGIH – American Council of Governmental Industrial Hygienists
AICS – Australian Inventory of Chemical Substances
CAS – Chemical Abstract Service
CERCLA – Comprehensive Emergency Response, Compensation and Liability Act
CFR – Code of Federal Regulations
CWA – Clean Water Act
D.O.T. – Department of Transportation
DSL – Domestic Substance List (Canada)
ECL – Existing Chemicals List (Korea)
EINECS – European Inventory of Existing Commercial Substances
FDA – Food and Drug Administration
FIFRA – Federal Insecticide, Fungicide and Rodenticide Act
IDLH – Immediately Dangerous to Life and Health
LD_{50} – Lethal dose for 50% mortality of subject species
LD_{LO} – Lethal dose low; the lowest dose of a substance introduced by any route other than inhalation reported to have caused death in humans or animals.
LFL – Lower Flammable Limit
MSHA – Mine Safety Health Administration
NFPA – National Fire Protection Association
NIOSH – National Institute of Occupational Safety and Health
OSHA – Occupational Safety and Health Administration
PEL – Permissible Exposure Limit (default 8-hour day, 40-hour week TWA)
PSM – Process Safety Management
RCRA – Resource Conservation and Recovery Act
REL – Recommended Exposure Limit (default 10-hour day, 40-hour week TWA)
RMP – Risk Management Plan
SARA – Superfund Amendment and Reauthorization Act
STEL – Short Term Exposure Limit (default 15-minute TWA)
TD_{LO} – Lowest dose to which humans or animals have been exposed and reported to produce a toxic effect other than cancer
TSCA – Toxic Substance Control Act
TWA – Time Weighted Average
UFL – Upper Flammable Limit
USDA – United States Department of Agriculture