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

Document Type:

☐ **National List Petition or Petition Update**

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

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

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

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

☒ **Technical Report**

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

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

Contractor names and dates completed are available in the report.

Glycolic Acid

Livestock

Identification of Petitioned Substance

Chemical Names:

Glycolic acid; Hydroxyacetic acid; 2-Hydroxyacetic acid; 79-14-1; Hydroxyethanoic acid; Glycollic acid

Other Name:

Glycolate; acetic acid, hydroxy

Trade Names:

Glycoside, Glycopure, Glyclean, Glypure, Glycolic Acid Tech Grade, Glycolic Acid 70% High Purity Solution

CAS Numbers:

79-14-1; 26124-68-5; 26009-03-0

Other Codes:

PubChem: CID 757

InChl: 1S/C2H4O3/c3-1-2(4)5/h3H, 1H2, (H,4,5)

InChl Key: AEMRFAOFKBGASW-UHFFFAOYSA-N

Canonical SMILES: C(C(=O)O)O

EC number: 201-180-5

ICSC Number: 1537

RTECS Number: MC5350000

UN Number: 3261

UNII: OWT12SX38S

Summary of Petitioned Use

A petition was received for the use of glycolic acid as a component of pre and post milking teat dips to control mastitis (205.603(a) Synthetic substances allowed for use in organic livestock production as disinfectants, sanitizer and medical treatment as applicable).

Characterization of Petitioned Substance

Composition of the Substance:

Glycolic acid is a small organic acid. It is not unique to either living organisms or synthetic chemistry. Glycolic acid is produced in many plants from which it can be isolated. Glycolic acid is used industrially for dyeing and tanning, flavoring, cleaning and skin care. Glycolic acid is polymerizable and these polymers are present in several types of biodegradable plastic films and varnishes.

Source or Origin of the Substance:

Glycolic acid is a product of chemical evolution that is likely to have occurred prior to the origin of life. It is well known that single carbon species such as formaldehyde and formic acid were astronomically available. The process going from a one carbon species to a two carbon species can occur in acidic hot water without a catalyst. From glycolic acid, amination likely led to the formation of the amino acid glycine (Morooka et al., 2005). Thus, most living organisms produce glycolic acid metabolically (Greenberg, 2014). Some organisms, mostly plants, e.g. sugar cane, produce isolatable quantities. Ruminant blood contains glycolic acid. Its source may be ingested plants, reduced glyoxic acid in animal tissue or rumen contents or synthetic production from glycine, purines or hydroxyproline (Peters et al., 1971).

Some human skin products contain glycolic acid from natural sources (Firdaus, 2012). However, because of its significance as an industrial chemical, most glycolic acid production is synthetic from formaldehyde. Formaldehyde itself is synthetically produced from methanol. The global glycolic acid market was valued at $159.6 million in 2015 and it is expected to increase driven by personal care, household and industrial uses.

Properties of the Substance:

Glycolic acid (or hydroxyacetic acid) is the smallest alpha-hydroxy acid (AHA). In its pure form, glycolic acid is a colorless crystalline solid. Due to its excellent capability to penetrate skin, glycolic acid finds applications in skin care products, most often as a chemical peel. Glycolic acid is also used for tattoo removal (NCBI, 2017).

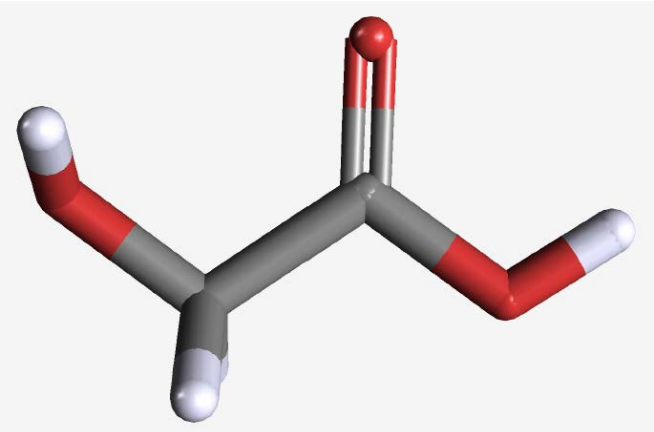

Figure 1 Glycolic Acid (3D) Structure

Carbon=grey; Oxygen=Red; Hydrogen=White (NCBI, 2017)

Table 1 Physical Properties of Glycolic Acid*	
Molecular Formula	$C_2H_4O_3$ or $HOCH_2COOH$
Molecular Weight	76.051 grams/mole
Physical Description	Liquid, Solid, Colorless hygroscopic crystals
Color	Colorless, translucent solid; Solid glycolic acid forms colorless, monoclinic, prismatic crystals; Orthorhombic needles from water; leaves from diethyl ether.
Odor	Odorless
Boiling Point	100 degrees C
Melting Point	79.5 ^{o}C
Solubility	In water: very good; also soluble in ethanol, methanol, acetic acid, acetone and ethyl ether.
Stability	Stable under recommended storage conditions.
Decomposition	When heated emits smoke and irritating fumes.
Corrosivity	Corrosive
PH	pH = 2.5 (0.5%); 2.33 (1.0%); 2.16 (2.0%); 1.91 (5.0%); 1.73 (10.0%)
**From* PubChem (2017)	

Specific Uses of the Substance:

Glycolic acid has been shown to be an effective post-milking teat disinfectant for dairy cows (Godden et al., 2016). Specifically, its petitioned use is as a component in a post milking teat dip to aid in the prevention of bovine mastitis. Teat dips may contain emollients, excipients and other allowed disinfectants. Because glycolic acid conditions the skin by exfoliating cracked skin layers, it removes potential hiding places for mastitis causing bacteria, e.g. *Stapylococcus aureus*.

In addition to its uses in skin care, glycolic acid is used in a broad range of applications. For example glycolic acid is used as a descaler for cutting through hard water salts, as a cleaning agent, as a liquid sour in laundry systems, as a copper and aluminum cleaner including boilers and heat exchangers, and as a dairy and CIP cleaner to dissolve casein as well as hard water deposits.

Glycolic acid is certified by the National Sanitation Foundation (NSF) for use in cleaning potable water wells. It is used widely to rehabilitate the flow efficiency of water wells by enabling water-soluble compounds (chelates) to be easily rinsed away with low corrosion to metal parts. Glycolic acid removes hard water scale (calcium, magnesium, manganese salts), various iron deposits and polysaccharide deposits. Glycolic acid biodegrades rapidly. It is a liquid with low toxicity, low odor, is non-flammable and has negligible fumes.

Approved Legal Uses of the Substance:

The first product containing glycolic acid as an active ingredient was registered by the US Environmental Protection Agency in 2001 as a disinfecting cleaner and a disinfectant/sanitizer for non-food contacting, hard non-porous surfaces in residential and public access premises. Since then, additional products have been registered with the EPA. There are no tolerances, exemptions from tolerances, or tolerance petitions for this antimicrobial pesticide. Glycolic acid is approved by FDA as an indirect food additive for use in food packaging adhesives (§175.105).

Glycolic acid is considered by the FDA to be a human cosmetic that is safe for use by consumers if the concentration is 10 percent or less, the pH is 3.5 or greater and the formulation protects the skin from increased sun sensitivity or the package directions instruct the consumer to use daily protection from the sun (FDA, 2015). Teat dips and udder washes classified as drugs, may currently be marketed without a NADA approval. However, the FDA has developed non-binding guidelines for teat antiseptic product development. The guidelines were assembled to inform the drug industry of the types of data that will demonstrate that a teat antiseptic product: 1) is safe for the cow, 2) is effective and 3) fulfills human food safety, manufacturing and environmental requirements. Products to be marketed must be manufactured according the cGMP regulations (21 CFR Part 211) for pharmaceutical dosage forms under the approved NADA process (FDA, 2016).

The USDA does not regulate glycolic acid for application as a teat dip. However, the USDA regularly reports survey results for the dairy industry including statistics of use and recommendations for pre and post milking teat dips (USDA, 2016).

Action of the Substance:

Glycolic acid is mildly bactericidal. However, its effect on the hyperkeratinization of skin is significant. Hyperkeratinization is a primary event in many skin disorders. It is caused by dying and dead adherent skin cells trapped near a hair follicle in the layers of tightly bound living cells called corneocytes. Normally, the dead cells are sloughed off by the follicles in a process called desquamation, but in the case of hyperkeratinization the dead cells are stuck beneath the tightly bound corneocytes. Dry skin, in wintertime is particularly vulnerable to reduced desquamation and hyperkeratinization. Glycolic acid has a therapeutic effect on hyperkeratinization, and the cohesiveness of corneocytes (Scott and Ruey, 1984). One theory for the mechanism of action of glycolic acid is that it reduces the calcium ion concentration in the epidermis and removes calcium ions from the cell adhesions by chelation. The cell adhesions are thereby disrupted, resulting in desquamation (Wand, 1999).

Glycolic acid reduces cohesiveness in the lower, newly forming layers of corneocytes potentially by inhibition of an enzyme. Glycolic acid does not cause disaggregation of corneocytes of the mature upper layer corneocytes, which would result in damage to the skin. Loosening the corneocytes in the lower layers improves desquamation. Glycolic acid promotes a thinner lower corneocyte layer, which not only

improves the skin surface smoothness because the dead cells can migrate to the follicles, but also to improves the flexibility of the lower corneocyte layers (aka corneum stratum). A thin stratum corneum bends more readily without cracking or fissuring than a thick stratum corneum. Glycolic acid improves desquamation even if the skin is dry (Scott and Ruey, 1984). Bacteria take advantage of hyperkeratinization by entering the skin through cracks and fissures and colonizing the dead cells. The action of routine glycolic acid use is to remove both entry and colonization sites for colonizing bacteria that may lead to mastitis.

Combinations of the Substance:

Glycolic acid (3.0%) is used in a teat dip in which it is combined with the humectant/emollient glycerin (5.0%), the crosslinking (thickening) agent xanthan gum, the emulsifying agent C9-11 Pareth-8, a colorant FD&C Blue No. 1, a skin permeant, 1-octanesulfonic acid, a surfactant, sodium C14-16 Olefin sulfonate and sodium hydroxide to adjust pH (OceanBlu®, MSDS).

Status

Historic Use:

Alpha hydroxyl acids are basic chemicals found metabolically in all living organisms. Some agricultural products contain substantial amounts of extractable alpha hydroxyl acids and these have been used for centuries for the cosmetic and medical treatment of the skin. Examples of them include glycolic acid (sugarcane), lactic acid (sour milk), malic acid (apples), citric acid (citrus fruits), and tartaric acid (grapes). Sugar cane is a good natural source containing glycolic acid (Van Scott and Yu, 1984). Glycolic acid only recently began to be used commercially as a teat treatment in regimens to prevent mastitis in dairy cows (Lago et al., 2016).

Organic Foods Production Act, USDA Final Rule:

Glycolic acid is not an explicitly prohibited substance (205.105(a)). However, it is only available as a synthetic substance that does not appear on the National list (205.238(a)(3); 205.603(a)). Because mastitis is difficult to diagnose in its early stage, its prevention is critical and it is difficult to assess that glycolic acid or any teat treatment is administered as a medication in the absence of illness (§6509(d)(1)(c)). Furthermore, therapy to improve keratin dynamics is considered crucial in the milking process when vacuum milking systems are used (National Mastitis Council, 2017).

International

Canada - Canadian General Standards Board Permitted Substances List updated in November 2015 does not list glycolic or hydroxyacetic acid (CAN/CGSB-32.311-2015 — Organic production systems - Permitted substances lists).

CODEX Alimentarius Commission, Guidelines for the Production, Processing, Labelling and Marketing of Organically Produced Foods (GL 32-1999) – Codex guidelines do not explicitly prohibit the use of glycolic acid in a teat dip in ongoing mastitis cases where treatment is required, while its use would be prohibited as a preventative measure (Health Care-line 22). The withholding period would then be doubled or a minimum of 48 hours.

European Economic Community (EEC) Council Regulation, EC No. 834/2007 and 889/2008 – The EC regulations do not explicitly prohibit the use of glycolic acid and provides for cleaning and disinfection products for teats and milking facilities (Article 14(1)(f) of Regulation (EC) No 834/ 2007, only products listed in Annex VII may be used for cleaning (889/2008 *ANNEX VII* Products for cleaning and disinfection referred to in Article 23 (4) and Regulation (EC) No 834/ 2007Article 16).

Japan Agricultural Standard (JAS) for Organic Production—The Japanese Agricultural Standard for Organic Livestock Products (Notification No. 1608 of the Ministry of Agriculture, Forestry and Fisheries of October 27, 2005) does not explicitly prohibit the use of glycolic acid, since it states that in the case of milking, milking equipment and utensils are properly cleaned and disinfected, without using agents other than those for cleaning or disinfecting teats and those indicated in Attached Table 4. Where Table 4 "Agents for cleaning or disinfecting of housing for livestock" lists only the phrase "cleaning agents and disinfectants for milking equipment, rooms and building. Glycolic acid is not listed in table 4.

International Federation of Organic Agriculture Movements (IFOAM) –The IFOAM norms do not explicitly prohibit the use of glycolic acid in teat dips and provide for cleaning and disinfection products for teats and milking facilities (5.1.6d, Appendix 5: Substances for pest and disease control and pest infection in livestock and housing equipment).

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

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

Glycolic acid is mildly bactericidal. It may be considered a medication for hyperkeratinization or prevention of mastitis in dairy cattle.

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

Glycolic acid is a widely used industrial chemical with a large synthetic production footprint. It has commonly been produced by the Dupont process (hydratative carbonylation) from formaldehyde, carbon monoxide and water and in the presence of the catalyst sulfuric acid. The reaction is carried out at high pressure (300-700 bar) and temperature (200-250^{o}C).

$$HCHO + CO + H_2O \xrightarrow{\text{catalyst}} HOCH_2COOH$$

Catalysts such as hydrogen fluoride, hydrogen fluoride/boron trifuoride and strongly acidic (perfluorinated) ion exchangers were subsequently introduced in the Chevron and Mitsubishi processes that are effective at low CO pressure (100 bar). Exxon developed another catalytic method to obtain 70% glycolic acid at 150^{o}C on a strongly acidic ion exchanger made from perfluorosulfonic acid resin (Weisserme and Arpe, 2003).

Formaldehyde is a naturally occurring substance. It is the smallest aldehyde. Formaldehyde is produced industrially by the catalytic oxidation of methanol. The most common catalysts are silver metal or a mixture of metal oxides. In the commonly used Formox process, methanol and oxygen react at ca. 250–400°C in presence of iron oxide in combination with molybdenum and/or vanadium to produce formaldehyde according to the chemical equation:

$$2\ CH_3OH + O_2 \xrightarrow{\text{catalyst}} 2\ CH_2O + 2\ H_2O$$

A silver-based catalytic process operates at a higher temperature, about 650 °C. Two chemical reactions on it simultaneously produce formaldehyde: that shown above and the dehydrogenation reaction:

$$CH_3OH \xrightarrow{\text{catalyst}} CH_2O + H_2$$

In principle, formaldehyde could be generated by oxidation of methane, but this route is not industrially viable because the methanol is more easily oxidized than methane (Reuss et al., 2000).

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

Glycolic acid is found naturally in sugar beets and sugar cane (Stark et al., 1950; Thangavelu, 2010; Blake et al., 1987). However, this source of glycolic acid has not been capitalized for industrial production. The yeasts, *Saccharomyces cerevisiae* and *Kluyveromyces lactis* are suitable organisms for producing glycolic acid by a fermentation process because they are acid tolerant and can grow in the presence of glycolic acid. *S. cerevisiae* and *K. lactis* were genetically engineered for glycolic acid production by manipulating the reactions of the glyoxylate cycle to produce glyoxylic acid and then reducing it to glycolic acid. Additional deletions in genes encoding malate synthase and the cytosolic form of isocitrate dehydrogenase improved yield. The engineered *S. cerevisiae* and *K. lactis* strains respectively produced up to about 1 and 15 grams per liter of glycolic acid in a medium containing D-xylose and ethanol. Glycolic acid produced by fermentation from lignocellulosic biomass feedstocks like D-xylulose is not yet commercially available. Currently, only glycolic acid manufactured from formaldehyde is available commercially. There are no commercially viable natural sources.

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

Glycolic acid is found in ruminant blood. Studies have shown that it is incorporated into casein, fat and lactose of milk (Peters et al., 1971).

In vitro cultures of the algae, *Chlorella pyrenoidosa* naturally secrete glycolic acid into the surrounding medium to a concentration of up to 3-8 mg/liter of culture. Rapid excretion of glycolate by *Chlorella* is dependent on (a) the presence of bicarbonate, (b) aerobic conditions, (c) light for active photosynthesis, since there must be a net bicarbonate uptake, and (d) the age of the cells, excretion being greatest in the youngest cultures (Tolbert and Zill, 1956). Further studies showed that other algal species also naturally secrete glycolic acid (Cheng et al., 1972). Glycolic acid is also hypothesized as a metabolite of other algal species representing an energy reservoir when conditions were not favorable for photosynthesis and the catalyst for algal blooms (Fogg and Nalewajko, 1963). However, studies of natural waters have subsequently shown that glycolic acid does not accumulate to a great extent in natural waters and there wasn't a verifiable link between glycolic acid and algal bloom formation (Spear and Lee, 1968).

Glycolic acid is registered by the US Environmental Protection Agency (EPA) as an antimicrobial cleaning product in: household disinfecting cleaners for use in cleaning toilet bowls, bathrooms, floors, and other hard non-porous surfaces and disinfecting cleaners for use in agricultural premises and food processing facilities and on food processing equipment. Because glycolic acid is readily degradable (> 90% mineralization in less than 2 weeks) it is not persistent in the environment. The bioconcentration factor (BCF) for glycolic acid is 3.2 (EPA, 2011). In surface water, the BCF is the ratio of a chemical's concentration in an organism to the chemical's aqueous concentration (Arnot and Gobas, 2006). Glycolic acid is not known to be bioaccumulative.

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

In an early report, undiluted glycolic acid administered to rabbits was shown to cause acid-like burns to their skin and eyes (Carpenter and Smyth, 1946). Fifty and 70% Glycolic Acid applied to the backs of minipigs for 15 min caused epidermal necrosis, inflammatory infiltrate and for 70% Glycolic Acid dermal necrosis after one day (Andersen, 1998). Reproductive, gastrointestinal, developmental and renal toxicity in rats, cats and guinea pigs have also been demonstrated with oral administration of high doses (70-100%) of

glycolic acid (NIOSH, 2017). Glycolic acid is known to cause enhanced sensitivity to UV light. Short-term application of 10% glycolic acid sensitizes the skin to UV light. However, this photosensitivity is reversed within a week of terminating treatments (Kaidbey et al., 2003). Glycolic acid is an important metabolite of ethylene glycol. Increased glycolic acid in the blood correlates directly with acute ethylene glycol toxicity and renal failure (Hewlett et al., 1986). Glycolic acid has been widely studied because it is used in health products and cosmetics. However, many of the conclusions of these studies have been equivocal or even contradictory. Varying or unreported conditions, parameters and criteria such as the concentration and grade of glycolic acid used and duration of exposure have made it difficult to assess and compare them. The primary areas of concern for glycolic acid however, are its dermal irritation potential and its potential to increase sensitivity to sunlight. Both of these factors result from glycolic acid's ability to partially remove the stratum corneum layer of skin. Generally, for leave on products, glycolic acid concentrations not greater than 10% at pH no less than 3.0 will not produce unacceptable irritation. Glycolic acid does increase sensitivity to sunlight which should be considered in treatment (Andersen, 1998).

In six studies presented by the US Environmental Protection Agency, glycolic acid was noted to be slightly toxic to bluegill sunfish (Effective Concentration $(EC)_{50}$=93 ppm), and practically non-toxic to bobwhite quail (Lethal Concentration $(LC)_{50}$=>5000 ppm), Mallard duck (LC_{50}=>5000 ppm), fathead minnow (LC_{50}=164 ppm) and daphnia (EC_{50}=141 ppm). In this same review, glycolic acid was noted to be only slightly toxic to mammals with an LC 50 of 1938 ppm (EPA, 2011).

Glycolic acid as glycolate is an important intermediary molecule in plant photorespiration, but in excess it is toxic and can inhibit photosynthesis (Ogren, 2003; Dellero et al., 2016).The degree of inhibition and toxicity both depend on the particular species and variety of affected plant. In maize, for example, the accumulation of glycolate provokes the inhibition of ribulose bisphosphate carboxylase (RUBISCO) and the subsequent decrease in CO_2 assimilation (Gonzalez-Moro et al., 1997). Because it can inhibit photorespiration glycolic acid may be algistatic for some algal species , e.g. *Selenastrum capricornutum*, but since CO_2 absorption pathways may vary between algal species, e.g. *Chlorella* spp., the appearance of toxicity is likely to be dependent upon glycolic acid concentration (EPA, 2011; Fogg and Nalewajko, 1963; Raven et al., 2012).

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

Most of the glycolic acid is manufactured at a chemical production plant in Belle, West Virginia. This chemical plant is located in the Kanawha Valley which is known for its many chemical manufacturing facilities. There have not been any major spills or accidents at this plant since 2010, when the release of phosgene gas into the atmosphere caused the death of an employee. The State of West Virginia provided the plant operator with a permit to operate and produce glycolic acid in 2015 (West Virginia Department of Environmental Protection, 2015). The permit expires in 2020 and permits respectively maxima of 1.9, 15.5, 15.2 8.14 and 5.85 tons/year of formaldehyde, methanol, formic acid, carbon monoxide and NOx to be released to the atmosphere from the plant's thermal oxidizer.

The US EPA has not received any guideline environmental fate studies on glycolic acid, and has not required studies to be done. Since a toxicological concern has not been identified, the US EPA believes that, based on the currently registered use pattern of glycolic acid for household use as a disinfectant/sanitizer for hard non-porous surfaces in homes, guideline environmental fate or ecological effects studies are not necessary (EPA, 2011).

Various synthetic process are available for preparing glycolic acid. Contaminants potentially found in downstream products are formaldehyde and monochloroacetic acid which are the starting materials. Residual reagents include sodium chloride, formic acid, methoxyacetic acid which are byproducts from the synthesis process. These impurities must be controlled for safety and the physical and chemical characteristics of the product (Liedtka, 2016). Glycolic Acid is available as a technical grade 70% solution and as higher purity grade solutions of 70% (Glypure 70) and 99% (Glypure 99) (Chemours, 2015). Because of the amount of impurities, technical-grade Glycolic Acid is not used in personal care applications (Andersen, 1998, Table 2). The US FDA found no concerns about the physical and chemical characterization when potential impurities, such as formaldehyde are controlled at acceptable levels.

Glycolic acid is a well-characterized small molecule that is likely to be stable under ordinary storage conditions (Liedtka, 2016).

Table 2 Typical Analysis of Glycolic Acid*

	Glypure @99%	Glypure @70	Technical (70%)
Total acid (%)	99.8–100.5	69.7–72.0	70.0–72.2
Heavy metals (ppm)	<4	<4	<4
Sulfates (ppm)	<100	<25	<150
Formic acid (ppm)	<10	<150	<3800
Turbidity (ntu)	N/A	N/A	<2.3
Formaldehyde (ppm)	<3.5	<15 (as made)	<750
Iron (ppm)	<1.0	<1.0	<7.0
Chloride (ppm)	<1.0	<1.0	<1.7
Sodium (ppm)	<10	<2.5	<32
Ammonia (ppm)	<5.0	<3.9	<110
Diglycolic acid	<115 ppm	<140 ppm	<1.1%
Methoxyacetic acid	<170 ppm	<190 ppm	<1.9%
Free acid (%)	>95.0	64.0–67.0	62.8–65.2

**from* Andersen, 1998

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

Over the counter non-wipe post milking dairy teat dips containing three percent glycolic acid (e.g. Ocean Blue Barrier®) are also likely to contain 5% glycerol, 5% sorbitol, xanthan gum, povidone k30, c9-11 Pareth-8, FD&C Blue No. 1, sodium hydroxide, water and sodium C14-16 olefin sulfonate. Package instructions do not suggest the use of one post-milking teat dip with another. The glycolic acid used for this formulation may be technical grade. Glycerin, an emollient, does not enhance the absorption of glycolic acid into the skin (Andersen, 1998). Sodium hydroxide is added to raise the pH of the teat dip. Low pH is a potential source of skin irritation when using glycolic acid to treat skin (FDA, 2015). Other ingredients used in teat dips include additional emollients, surfactants, colorants and plasticizers that permit adherence and identification of treated skin. Although there is general acceptance for the use of post milking teat dips, no advantage has been described for the use of multiple teat dip products in the same application (The National Mastitis Council, 2017).

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

The chemomechanic action of alphahydroxy acids (AHAs) in exfoliation is to reduce calcium ion concentration in the epidermis and remove calcium ions from the cell adhesions by chelation causing disruption in cell adhesions and desquamation. Glycolic acid can also suppress melanin formation by inhibition of tyrosinase activity. Intraperitoneal administration of 1000 mg/kg glycolic acid inhibits oxygen consumption and glucose metabolism in rat liver and myocardium *in vivo*, but does not affect brain oxygen consumption. Glycolic acid in high concentrations (70% solution and pure) causes local effects typical of a strong acid, such as dermal and eye irritation. In a 3-week dermal toxicity study in hairless guinea pigs, erythema and/or flaking of the skin were noted at 5% and 10% concentrations of glycolic acid. Glycolic acid induced calculi formation in rats in a 4- to 12-week repeat dose oral toxicity which also disclosed increased renal oxalate and nephrotoxic effects have been observed. In a 2 week study in rats, respiratory tract irritation, hepatocellular degeneration and thymus atrophy were observed. Glycolic acid was negative for mutagenicity in the Ames test and the mouse lymphoma assay and not considered genotoxic. Glycolic acid was negative for clastogenicity in an *in vitro* chromosome aberration assay and an *in vivo* micronucleus assay in mice.

Table 3 Plants Naturally Containing Glycolic Acid

Genus species	**Common name**	**Part**
Allium cepa	Onion	Bulb
Apium graveolens	Celery	Root
Arbutus unedo	Strawberry Tree	Leaf
Cynara cardunculus subsp cardunculus	Artichoke	Flower
Glycine max	Soybean	Root; seed; sprout seedling
Hibiscus sabdariffa	Jamaica Sorrel	Flower
Juniperus communis	Common Juniper	Fruit
Lupinus albus	White Juniper	Seed
Lycopersicon esculentum	Tomato	Fruit
Malus domestica	Apple	Plant
Musa x paradisiaca	Banana	Leaf
Petroselinum crispum	Parsley	Root; seed
Pisum sativum	Pea	Seed
Ricinus communis	Castorbean	Seed
Rosmarinus officinalis	Rosemary	Plant
Ruscus aculeatus	Box-holly	Root
Theobroma caco	Cacao	Leaf
Zea mays	Corn	Silk; stigma; style

from NCBI (2017)

Carcinogenicity from glycolic acid exposure has not been demonstrated. Oral (gavage) doses of glycolic acid up to 600 mg/kg/day were administered to female rats during gestation days 7-21 – Maternal toxicity was seen at doses ≥ 300 mg/kg/day – Developmental toxicity was also noted at doses ≥ 300 mg/kg/day, including fetal weight reduction and increases in skeletal malformation (FDA, 2005). Glycolic acid post milking treatment can affect keratin dynamics (The National Mastitis Council, 2017). Glycolic acid is non-toxic in dogs up to 100 milligrams/kilogram, but nephrotoxic effects result from doses of 250 mg/kg, and

fatality occurs if greater than 500 mg/kg is ingested. Glycolic acid is also nephrotoxic to cats (Krop and Gold, 1944).

Glycolic acid is found in the fruit, leaf, stem and root portions of all plants. Glycolic acid is found naturally in extractable amounts in sugar cane and sugar beets (Thangaevelu, 2010; Stark et al., 1950). It is also excreted naturally by several algal species (Tolbert and Zill, 1956). Commonly consumed fruits and vegetables are reported to contain from 0.45-7.4 milligrams glycolic acid per 100 grams fresh wet weight. Tea, coffee, fruit juice and other beverages derived from plant sources may contain 5-7 mg glycolic acid per 100 mL. Foods of animal origin are generally low in glycolic acid, with milk and beef reported to contain 0.06-0.12 mg per 100 g (NICNAS, 2000). It is readily biodegradable in soil and water. A list of common plants that contain glycolic acid is provided (Table 3).

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

There have not been any reports of adverse environmental events related to glycolic acid release. Approximately 0.15 ml of glycolic acid (3%) is used per udder quarter in a post milking test dip (Matti and Tinnis, 2015). Glycolic acid at a concentration of 70% is approved for use as an acid non-food cleaning agent for removal of rust, corrosion, scale or other deposits that are not readily removed by alkaline cleaners in dairies.

Glycolic acid is a significant industrial chemical (EPA, 2011). If released to air at an extrapolated vapor pressure of 0.02 mm Hg at 25 ◦C, glycolic acid will exist solely as a vapor. Vapor-phase glycolic acid will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 3.4 days. Glycolic acid does not contain chromophores that absorb at wavelengths >290 nm and, therefore, is not expected to be susceptible to direct photolysis by sunlight. If released into soil, glycolic acid is expected to have very high mobility based upon an estimated Koc of 0.14. Koc is a measure of the tendency of a chemical to bind to soils, corrected for soil organic carbon content. The pKa of glycolic acid is 3.6, indicating that this compound will exist almost entirely in anion form in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts. Volatilization of glycolic acid from moist soil surfaces is not expected to be an important fate process because the compound exists as an anion and ions do not volatilize. Glycolic acid is not expected to volatilize from dry soil surfaces based upon its vapor pressure. Tests for inherent biodegradability showed 86% of the theoretical BOD was reached in 2 weeks. This indicates that biodegradation is an important environmental fate process in soil and water. If released into water, glycolic acid is not expected to adsorb to suspended solids and sediment based upon the estimated low Koc. A pKa of 3.6 indicates glycolic acid will exist almost entirely in the anion form at pH values of 5 to 9 and, therefore, volatilization from water surfaces is not expected to be an important fate process. An estimated BCF of 3 suggests the potential for bioconcentration in aquatic organisms is low. Hydrolysis is not expected to be an important environmental fate process since this compound lacks functional groups that hydrolyze under environmental conditions.

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

Labels for products containing 3% glycolic acid for use as a pre and post milking teat dip indicate only that the substance can cause eye irritation (MSDS, OceanBlu Barrier, deLaval). Glycolic acid at different concentrations is used for a number of human medical procedures as a keratolytic agent. Glycolic acid at 57-70% is corrosive to the skin and eyes. Ingestion of substantial amounts at this concentration may result in kidney failure (Pubchem, 2017). Glycolic acid in cosmetic products used by the general public may cause skin and eye irritation when present at high concentrations and low pH values. In addition, manufacturers, importers and suppliers of consumer products should inform consumers that the use of skin exfoliant cosmetic products may result in an enhanced sensitivity to sunburn, and that use of sunscreen protection is advised (NICNAS, 2000).

Occupational exposure to glycolic acid may occur through inhalation and dermal contact with this compound at workplaces where glycolic acid is produced or used. Monitoring and use data indicate that the general population may be exposed to glycolic acid via inhalation of ambient air, ingestion of food and dermal contact with consumer products containing glycolic acid (NCBI, 2017).

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

The pathogens that cause mastitis inhabit many locations throughout the dairy cow environment and infect multiple tissues in the udder. As a result, effective prevention and treatments for mastitis in the organic dairy a can range from surface sanitation to parenteral administration of homeopathic medicines, but each alone may not be 100% effective. Thus, there are many possible substances that may serve in place of glycolic acid. Glycolic acid represents a unique approach to bovine teat health, inasmuch as the net effect is to prevent hyperkeratosis, although there is additionally some microbiocidal activity associated with its application.

Vitamin A is similar to glycolic acid in its action, however; the subset of skin cells that are affected are not the same (Scott and Ruey, 1984). Thus, vitamins and minerals to supplement nutrition such as vitamin, selenium, copper, zinc, vitamin A and β-carotene are important to both bolster both cellular and humoral immune response and to maintain skin and udder health (Heinrichs et al., 2009). Low blood plasma concentrations of vitamin A and β-carotene are directly associated with the severity of mastitis in cows (Chew et al., 1982).

Homeopathic pharmacies can provide pre-prepared remedies for mastitis in dairy cows. Udder liniments, containing mint or anti-inflammatory agents are often used as support therapy with homeopathy (Hovi and Roderick, 1998). More examples include Belladonna for acute postpartum mastitis; Aconitum for routine treatment for all acute cases, particularly those that develop rapidly after exposure to cold dry wind; Apis Mellifica is indicated for first calving, heifers with edema of and around the udder; Bryonia Alba is indicated for swollen and very hard udders; Arnica Montana for mastitis resulting from udder injuries; Belia Perennis for deeper injuries (e.g., neglected milkers); Phytolacca for clinical and chronic cases with sour, coagulated milk, small clots at mid-lactation; Urtica Ulens for clinical cases where edema forms plaques sometimes up to perineum; mixtures of Sulphur, Silica and Carbo Vegetabilis for clinical and subclinical cases; Hepar Sulphuris to aid suppuration and cleaning of udder in summer mastitis cases; Silicea for summer mastitis cases with purulent abscess and Ipeca for treating internal bleeding that produces pink or bloody milk (MacLeod, 1981). Homeopathic remedies used to treat mastitis also include: Belladonna, Lachesis, Vipera Reddi, Conium maculatum + Plumbum iodanum, Phytolacca, Bryon and Silicea (Quiquandon, 1982). Homeopathic remedies are not regulated for efficacy and quality as are veterinary drugs, therapies and medications. Furthermore, some research indicates that homeopathic approaches are not effective therapies for bovine mastitis (Ebert et al., 2017).

Currently only iodine (§205.603(a)(13) and §205.603(b)(3)), chlorhexidine §205.603(a)(6), glycerin §205.603(a)(11), and hydrogen peroxide §205.603(a)(12), are allowed to be used in organic dairy production for mastitis prevention and therapy. Teat dips containing the disinfectants iodine and chlorhexidine are effective in reducing intra-mammary infections (Enger et al., 2016). Iodine is effective as a pre and post milking teat dip or spray, however, small increases in milk iodide concentration can be expected with its use. Where sprays usually produce a larger increase than dip cup preparations (French et al., 2016). Chlorine materials (§205.603(a)(7)) and phosphoric acid (§205.603(a)(19)) are allowed for sanitizing equipment and facilities. Vaccines, anti-inflammatory drugs (e.g., aspirin and flunixin), electrolytes, and furosemide (with double the milk withholding period) can also be used for the treatment of clinical mastitis (Ruegg, 2014).

Post-milking teat disinfectants need to be persistent and effective in killing bacteria. They must also leave teats in good condition. Preservation of healthy teat skin is essential for maintaining its natural defense against infection because sore, dry, cracked teats may harbor mastitis-causing pathogens (Hogan et al., 1990; National Mastitis Council, 2017). Barrier type teat disinfectants have been developed to extend the

germicidal properties of the disinfectant after the cow leaves the milking parlor. These products contain components that can provide a protective film and seal the teat from mastitis-causing bacteria (Lago et al., 2016). Glycerin is a humectant that is allowed for use as a skin conditioner in teat dips. Aloe is a naturally derived products with skin healing properties that may also be included in teat dips (Fox et al., 2006).

Teat irritation can be caused by interaction between teat dip and management or environmental factors in a herd. Teat dips may promote chapping during extremely cold weather especially with windy conditions. Emollients are incorporated such as glycerin or lanolin to minimize irritation and condition skin, however, the germicidal effectiveness of the teat dip may be diminished with too much emollient (Pankey, 1984). Emollients and humectants do not affect bacterial colonization of the skin (Rasmussen and Larsen, 1998).

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

The USDA reports that premilking teat disinfectants (predips) are used to reduce bacterial contamination on teat ends before milking. Using predips can reduce the amount of bacteria that enter the milk line and can also reduce exposure to mastitis pathogens. The majority of all operations (95.7 percent) used a premilking teat disinfectant; 55.5 percent of operations used iodophors. Postmilking teat disinfectants (postdips) are applied to the part of the teat that was covered in milk residue during milking. Postdipping is important in preventing transmission of contagious mastitis pathogens, since milk is one of the methods of pathogen transmission. Overall, 96.8 percent of operations used a postmilking teat disinfectant. The primary postmilking teat disinfectants used were iodophors (69.4 percent of operations). Barrier teat dips are meant to create an impermeable barrier at teat ends to prevent new intramammary (IMM) infections. The majority of operations (58.1 percent) did not use a barrier teat dip. Almost one-third of operations (30.1 percent) used a barrier teat dip on all cows all the time (USDA, 2016).

Successful control of mastitis requires the application of many practices that decrease the exposure of the teat end to pathogens and enhance the cow's natural immunity to infection. Often infections vary in control methods and may be chronic or persistent. Different methods of mastitis control are necessary between lactation and the dry period. Prevention is very important. Teats should be maintained as clean and as dry as possible. Cloths and sponges should be cleaned or disposable. Milking machines should be scrupulously cleaned to avoid cross contamination. Post milking teat dips and barrier treatments are useful and effective. Anti-bacterial vaccines are available, but may not always be effective. Infected animals should be segregated if possible. Clean bedding and good nutrition are also very important (The National Mastitis Council, 2017).

Suckling may also improve udder health. Some farmers have reported improvement while suckling that allowed cows to return to milk production (Hamilton et al., 2006; Rasmussen and Larsen, 1998).

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