TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0302

Number: P-18-0302
TSCA Section 5(a)(3) Determination: The chemical substance is not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Specific: D-Glucaric acid, ammonium salt (1:1); 6614-39-7

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic): Manufacture for use as a chemical intermediate, consistent with manufacturing, processing, use, distribution, and disposal information described in the PMN.
Known conditions of use: Applying such factors as described in footnote 1, EPA evaluated whether there are known conditions of use and found none.
Reasonably foreseen conditions of use: Applying such factors as described in footnote 1, EPA evaluated whether there are reasonably foreseen conditions of use and found none.

Summary: The chemical substance is not likely to present an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant by the Administrator under the conditions of use, based on the risk assessment presented below. EPA estimated that the new chemical substance could have limited persistence and a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms.. Based on EPA's TSCA New Chemicals Program Chemical Categories for Neutral Organics, physical/chemical properties and test data on the new chemical substance and on analogous chemical substances, EPA estimates that the

[1] Under TSCA § 3(4), the term "conditions of use" means "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." In general, EPA considers the intended conditions of use of a new chemical substance to be those identified in the section 5(a) notification. Known conditions of use include activities within the United States that result from manufacture that is exempt from PMN submission requirements. Reasonably foreseen conditions of use are future circumstances, distinct from known or intended conditions of use, under which the Administrator expects the chemical substance to be manufactured, processed, distributed, used, or disposed of. The identification of "reasonably foreseen" conditions of use will necessarily be a case-by-case determination and will be highly fact-specific. Reasonably foreseen conditions of use will not be based on hypotheticals or conjecture. EPA's identification of conditions of use includes the expectation of compliance with federal and state laws, such as worker protection standards or disposal restrictions, unless case-specific facts indicate otherwise. Accordingly, EPA will apply its professional judgment, experience, and discretion when considering such factors as evidence of current use of the new chemical substance outside the United States, evidence that the PMN substance is sufficiently likely to be used for the same purposes as existing chemical substances that are structurally analogous to the new chemical substance, and conditions of use identified in an initial PMN submission that the submitter omits in a revised PMN. The sources EPA uses to identify reasonably foreseen conditions of use include searches of internal confidential EPA PMN databases (containing use information on analogue chemicals), other U.S. government public sources, the National Library of Medicine's Hazardous Substances Data Bank (HSDB), the Chemical Abstract Service STN Platform, REACH Dossiers, technical encyclopedias (e.g., Kirk-Othmer and Ullmann), and Internet searches.

chemical substance has moderate environmental hazard and has identified the following human health hazards: lung toxicity, systemic toxicity, and eye irritation. EPA concludes that the new chemical substance is not likely to present unreasonable risk under the conditions of use.

Fate: Environmental fate is the determination of which environmental compartment(s) a chemical moves to, the expected residence time in the environmental compartment(s) and removal and degradation processes. Environmental fate is an important factor in determining exposure and thus in determining whether a chemical may present an unreasonable risk. EPA estimated physical/chemical and fate properties of the anion using data for analogue(s) (tartaric acid, CASRN 526-83-0 and D,L-tartaric acid, CASRN 133-37-9) and EPI (Estimation Program Interface) Suite™ (http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface) and of the cation using data for analogue(s) (ammonium and ammonia). In wastewater treatment, the anion is expected to be removed with an efficiency of 95% to 99.9% due to biodegradation and the cation is expected to be removed with an efficiency of 60% due to biodegradation. Removal of the anion by biodegradation is high, destruction (mineralization) of the anion by biodegradation is complete, and removal of the cation by biodegradation is moderate. Sorption of the anion and the cation to sludge, soil, and sediment is expected to be low. Migration of the anion to groundwater is expected to be negligible due to low sorption to soil and sediment, mitigated by biodegradation, and migration of the cation to groundwater is expected to be slow due to low sorption to soil and sediment, mitigated by biodegradation. Due to low estimated vapor pressure and Henry's law constant, the anion and the cation are expected to undergo negligible volatilization to air. Overall, these estimates indicate that the anion and the cation have low potential to volatilize to air and low potential to migrate to groundwater.

Persistence[2]: Persistence is relevant to whether a new chemical substance is likely to present an unreasonable risk because chemicals that are not degraded in the environment at rates that prevent substantial buildup in the environment, and thus increase potential for exposure, may present a risk if the substance presents a hazard to human health or the environment. EPA estimated degradation half-lives of the anion using data for analogue(s) (tartaric acid, CASRN 526-83-0 and D,L-tartaric acid, CASRN 133-37-9) and EPI Suite™ and of the cation using data for analogue(s) (ammonium and ammonia). EPA estimated that the anion's aerobic and anaerobic biodegradation half-lives are < 2 months; and that the cation's aerobic and anaerobic biodegradation half-lives are < 2 months. These estimates indicate that the anion and the cation may have limited persistence in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment). The cation is utilized in the biogeochemical cycle and is expected to be transformed.

[2] Persistence: A chemical substance is considered to have limited persistence if it has a half-life in water, soil or sediment of less than 2 months or there are equivalent or analogous data. A chemical substance is considered to be persistent if it has a half-life in water, soil or sediments of greater than 2 months but less than or equal to 6 months or if there are equivalent or analogous data. A chemical substance is considered to be very persistent if it has a half-life in water, soil or sediments of greater than 6 months or there are equivalent or analogous data. (64 FR 60194; November 4, 1999)

Bioaccumulation[3]: Bioaccumulation is relevant to whether a new chemical substance is likely to present an unreasonable risk because substances that bioaccumulate in aquatic and/or terrestrial species pose the potential for elevated exposures to humans and other organisms via food chains. EPA estimated the potential for the anion to bioaccumulate using EPI Suite™ and of the cation to bioaccumulate using data for analogue(s) (ammonium and ammonia). EPA estimated that the anion has low bioaccumulation potential based on BCFBAF model result < 1000 and the cation has low bioaccumulation potential based on high water solubility, which increases elimination (anion bioconcentration factor = 3 [estimated] and bioaccumulation factor = 0.89 [estimated]). EPA estimated that the anion could have limited persistence and a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. EPA estimated that the cation could have limited persistence and a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms.

Human Health Hazard[4]: Human health hazard is relevant to whether a new chemical substance is likely to present an unreasonable risk because the significance of the risk is dependent upon both the hazard (or toxicity) of the chemical substance and the extent of exposure to the substance. EPA estimated the human health hazard of this chemical substance based on its estimated physical/chemical properties and by comparing it to structurally analogous chemical substances for which there is information on human health hazard. Absorption of the new chemical substance is expected to be poor to moderate via the skin, good via the GI tract, and

[3] Bioaccumulation: A chemical substance is considered to have a low potential for bioaccumulation if there are bioconcentration factors (BCF) or bioaccumulation factors (BAF) of less than 1,000 or there are equivalent or analogous data. A chemical substance is considered to be bioaccumulative if there are BCFs or BAFs of 1,000 or greater and less than or equal to 5,000 or there are equivalent or analogous data. A chemical substance is considered to be very bioaccumulative if there are BCFs or BAFs of 5,000 or greater or there are equivalent or analogous data. (64 FR 60194; November 4 1999)

[4] A chemical substance is considered to have low human health hazard if effects are observed in animal studies with a No Observed Adverse Effect Level (NOAEL) equal to or greater than 1,000 mg/kg/day or if there are equivalent data on analogous chemical substances; a chemical substance is considered to have moderate human health hazard if effects are observed in animal studies with a NOAEL less than 1,000 mg/kg/day or if there are equivalent data on analogous chemical substances; a chemical substance is considered to have high human health hazard if there is evidence of adverse effects in humans or conclusive evidence of severe effects in animal studies with a NOAEL of less than or equal to 10 mg/kg/day or if there are equivalent data on analogous chemical substances. EPA may also use Benchmark Dose Levels (BMDL) derived from benchmark dose (BMD) modeling as points of departure for toxic effects. See https://www.epa.gov/bmds/what-benchmark-dose-software-bmds. Using this approach, a BMDL is associated with a benchmark response, for example a 5 or 10 % incidence of effect. The aforementioned characterizations of hazard (low, medium, high) would also apply to BMDLs. In the absence of animal data on a chemical or analogous chemical substance, EPA may use other data or information such as from in vitro assays, chemical categories (e.g., Organization for Economic Co-operation and Development, 2014 Guidance on Grouping of Chemicals, Second Edition. ENV/JM/MONO(2014)4. Series on Testing & Assessment No. 194. Environment Directorate, Organization for Economic Co-operation and Development, Paris, France. (http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2014)4&doclanguage=en)), structure-activity relationships, and/or structural alerts to support characterizing human health hazards.

good via the lungs based on physical/chemical properties. The new chemical substance is expected to produce ammonia gas in a pH- and temperature-dependent manner. Absorption of ammonia gas is nil through the skin and GI tract and good through the lungs based on physical/chemical properties. For the new chemical substance, EPA identified lung toxicity, systemic toxicity, and severe eye irritation as hazards. EPA identified a NOAEL of 1,696 mg/kg/day based on systemic toxicity and a NOAEC of 13.6 mg/m^3 based on lung toxicity, which were used to derive exposure route- and population-specific points of departure for quantitative risk assessment.

Environmental Hazard[5]: Environmental hazard is relevant to whether a new chemical substance is likely to present unreasonable risk because the significance of the risk is dependent upon both the hazard (or toxicity) of the chemical substance and the extent of exposure to the substance. EPA estimated environmental hazard of this new chemical substance using hazard data on an analogous chemical. This substance falls within the TSCA New Chemicals Category of neutral organics. The acute toxicity values estimated for fish, aquatic invertebrates and algae are > 100 mg/L, 93.3 mg/L, and 51.4 mg/L, respectively. The chronic toxicity values estimated for fish, aquatic invertebrates and algae are > 10 mg/L (ACR of 10), 9.33 mg/L (ACR of 10), and 4.42 mg/L, respectively. These toxicity values indicate that the new chemical substance is expected to have moderate environmental hazard. Application of assessment factors of 4 and 10 to acute and chronic toxicity values, respectively, results in acute and chronic concentrations of concern of 12.85 mg/L (12,850 ppb) and 0.442 mg/L (442 ppb), respectively.

Exposure: The exposure to a new chemical substance is potentially relevant to whether a new chemical substance is likely to present unreasonable risks because the significance of the risk is dependent upon both the hazard (or toxicity) of the chemical substance and the extent of exposure to the substance.

EPA estimates occupational exposure and environmental releases of the chemical substance under the intended conditions of use described in the PMN using ChemSTEER (Chemical Screening Tool for Exposures and Environmental Releases; https://www.epa.gov/tsca-screening-tools/chemsteer-chemical-screening-tool-exposures-and-environmental-releases). EPA uses EFAST (the Exposure and Fate Assessment Screening Tool; https://www.epa.gov/tsca-

[5] A chemical substance is considered to have low ecotoxicity hazard if the Fish, Daphnid and Algae LC50 values are greater than 100 mg/L, or if the Fish and Daphnid chronic values (ChVs) are greater than 10.0 mg/L, or there are not effects at saturation (occurs when water solubility of a chemical substance is lower than an effect concentration), or the log Kow value exceeds QSAR cut-offs. A chemical substance is considered to have moderate ecotoxicity hazard if the lowest of the Fish, Daphnid or Algae LC50s is greater than 1 mg/L and less than 100 mg/L, or where the Fish or Daphnid ChVs are greater than 0.1 mg/L and less than 10.0 mg/L. A chemical substance is considered to have high ecotoxicity hazard, or if either the Fish, Daphnid or Algae LC50s are less than 1 mg/L, or any Fish or Daphnid ChVs is less than 0.1 mg/L (Sustainable Futures https://www.epa.gov/sustainable-futures/sustainable-futures-p2-framework-manual).

screening-tools/e-fast-exposure-and-fate-assessment-screening-tool-version-2014) to estimate general population, consumer, and environmental exposures.
EPA considers workers to be a potentially exposed or susceptible subpopulation (PESS) on the basis of greater exposure potential compared to the general population. EPA also considers PESS in conducting general population drinking water exposures by evaluating risks associated with water intake rates for multiple age groups, ranging from infants to adults. EPA considers consumers of specific products to be a potentially exposed or susceptible subpopulation on the basis of greater exposure potential compared to the general population who do not use specific products.

For this new chemical, EPA assessed worker exposure via inhalation and dermal contact. Releases to water, air, and landfill were estimated. Exposure to the general population was assessed via drinking water, fish ingestion, and fugitive air inhalation. Exposure to the general population via groundwater ingestion (landfill leachate) and stack air inhalation were not assessed, because releases to landfill and stack air were expected to be negligible (below modeling thresholds).

Risk Characterization: EPA applies a margin of exposure approach to calculate potential human health risks of new chemicals. A benchmark (acceptable) margin of exposure is derived by applying uncertainty factors for the following types of extrapolations: intra-species extrapolation (UF_H = 10 to account for variation in sensitivity among the human population), inter-species extrapolation (UF_A = 10 to account for extrapolating from experimental animals to humans) and LOAEL-to-NOAEL extrapolation (UF_L = 10 to account for using a LOAEL when a NOAEL is not available). Hence, in the New Chemicals Program, a benchmark MOE is typically 100 and 1000 when NOAELs and LOAELs, respectively, are used to identify hazard. When allometric scaling or pharmacokinetic modeling is used to derive an effect level, the UF_H may be reduced to 3, for a benchmark MOE of 30. The benchmark MOE is used to compare to the MOE calculated by comparing the toxicity NOAEL or LOAEL to the estimated exposure concentrations. When the calculated MOE is equal to or exceeds the benchmark MOE, the new chemical substance is not likely to present an unreasonable risk. EPA assesses risks to workers considering engineering controls described in the PMN but in the absence of personal protective equipment (PPE) such as gloves and respirators. If risks are preliminarily identified, EPA then considers whether the risks would be mitigated by the use of PPE (e.g., impervious gloves, respirator).

Risks to human health for the new chemical substances were evaluated using the points of departure (i.e., NOAEL and NOAEC) described above. Risks were identified for workers for lung toxicity via inhalation exposure to total, but not respirable particulates, based on quantitative hazard data for the ammonia component (MOE_{total} = 6; $MOE_{respirable}$ = 18; benchmark MOE = 10; inhalation fold factor of 2 for total particulates). Risks were not identified for workers for systemic effects via dermal exposure based on quantitative hazard data for an analogue, ammonium chloride (MOE = 106; benchmark MOE = 100). Irritation hazards to workers via inhalation and dermal contact were identified based on analogue data. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards. However,

exposures can be mitigated by the use of appropriate personal protective equipment (PPE), including eye protection and respiratory protection. EPA expects that employers will require and that workers will use appropriate PPE consistent with the Safety Data Sheet prepared by the new chemical submitter, in a manner adequate to protect them.

Risks were not identified for the general population for lung toxicity via fugitive air inhalation based on quantitative hazard data for the ammonia component (MOE = 32; benchmark MOE = 10). Risks were not identified for the general population for systemic toxicity via oral (drinking water and fish ingestion) or fugitive air inhalation based on quantitative hazard data for an analogue (all MOEs > 1000; benchmark MOE = 100). Irritation hazards to the general population are not expected via drinking water or stack air releases due to dilution of the chemical substance in the media. Risks to consumers were not evaluated because consumer uses were not identified as conditions of use.

Risks to the environment were evaluated by comparing estimated surface water concentrations with the acute and chronic concentrations of concern. Risks from acute exposure to the environment were not identified due to releases to water that did not exceed the acute COC. Risks from chronic exposure to the environment were not identified since the chronic COC is exceeded less than 20 days[6] per year.

Because worker exposures can be controlled by PPE, no unreasonable risks to the general population or environment were identified, and there are no expected consumer exposures, EPA has determined that the new chemical substance is not likely to present unreasonable risk to human health or the environment under the conditions of use.

9/30/19
Date:

/s/
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[6] The 20-day criterion for concluding chronic risk is not likely is based on partial life cycle tests (daphnid chronic and fish early life stage tests) that typically range from 21 to 28 days in duration.