TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-19-0109

Number: P-19-0109
TSCA Section 5(a)(3) Determination: The chemical substances are not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Names:
Specific: Copper, bis[2-(amino-.kappa.N)ethanolato-.kappa.O]- (CASRN 14215-52-2); Copper, [[2,2',2"-(nitrilo-.kappa.N)tris[ethanolato-.kappa.O]](2-)]- (CASRN 21545-60-8)

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic): Manufacture for use and use as components of a cleaning formulation to improve the wettability of the overall cleaning solution on the substrate, consistent with the 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 has identified the following reasonably foreseen conditions of use based on the submitter's amendments to the submission and patents on the new chemical substances: use as a vapor deposition precursor for atomic layer deposition of copper using surface-activating agents, use in the formation of high temperature superconductor thin films by sol-gel techniques, use as a reactant in the formation of copper oxide films, use in two-step preservation and coloring of wood using copper compounds and dithiocarbamates, and alternative conditions of transport and disposal, which could result in releases to water that differ from those under the intended conditions of use, inhalation exposures, and consumer exposures.

Summary: The chemical substances are not likely to present an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors, including an

[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.

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 and the terms of the proposed Significant New Use Rule (SNUR) signed by EPA.[2] EPA estimated that the first anion (ethanolamine) and second anion (triethanolamine) could have limited persistence and the substances have low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Although EPA estimated that the cation could be very persistent, the substance does not bioaccumulate by lipophilic partitioning and there is low concern that it will accumulate in organisms by other mechanisms; thus, repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Based on available data on the new chemical substances and their components and hazard data on analogous chemical substances, EPA estimates that the chemical substances have high environmental hazard and potential for the following human health hazards: acute toxicity, skin irritation, eye irritation, and specific target organ toxicity. The PMN describes conditions of use that mitigate the human health and environmental risks. Therefore, EPA concludes that the new chemical substances are not likely to present unreasonable risk to human health or the environment under the intended conditions of use.

As set forth below, the information available to EPA is sufficient to permit the Agency to conduct a reasoned evaluation of the health and environmental effects of the chemical substances under the conditions of use that are not subject to the proposed SNUR, in order to determine that the chemical substances are not likely to present an unreasonable risk under those conditions of use. As such, EPA does not need to impose testing requirements to conduct this evaluation. Whether testing is needed to evaluate the effects of the intended, known, or reasonably foreseen conditions of use of a chemical substance subject to a PMN is determined on a case-by-case basis. To the extent that testing may be necessary to conduct a reasoned evaluation of the health or environmental effects of the reasonably foreseen conditions of use that are subject to the proposed SNUR, EPA will make the appropriate determination if a Significant New Use Notice (SNUN) is submitted following finalization of the SNUR.

EPA found no known conditions of use, assessed the intended conditions of use, and addressed reasonably foreseen conditions of use by proposing a SNUR. Therefore, EPA determines the new chemical substances are not likely to present unreasonable risk to human health or the

[2] Reasonably foreseen conditions of use subject to a proposed SNUR are not likely to present an unreasonable risk of injury to health or the environment. Based on EPA's experience, it is the Agency's judgment that a new use would not commence during the pendency of a proposed SNUR because web posting of a proposed SNUR serves as the cut-off date for a significant new use. Therefore, manufacturers and processors would not commence a prohibited new use that would be legally required to cease upon the finalization of the SNUR. Once a SNUR is final and effective, no manufacturer or processor – including the PMN submitter – may undertake the conditions of use identified as a significant new use of the PMN substance in the SNUR. EPA must first evaluate the new use in accordance with the requirements of TSCA Section 5 and (a) either conclude that the new use is not likely to present an unreasonable risk under the conditions of use; or (b) take appropriate action under section 5(e) or 5(f). If EPA were not to finalize the proposed SNUR, then that decision would be based on information and data provided to the Agency during the comment period demonstrating that the reasonably foreseen conditions of use subject to the proposed SNUR are not likely to present an unreasonable risk. Under either scenario, the reasonably foreseen condition of use is not likely to present an unreasonable risk.

environment.

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 first anion (ethanolamine) using data available for the first anion (ethanolamine, CASRN 141-43-5) and EPI (Estimation Program Interface) Suite™ (http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface), of the second anion (triethanolamine) using data available for the second anion (triethanolamine, CASRN 102-71-6) 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) (metal oxides). In wastewater treatment, the first anion (ethanolamine) is expected to be removed with an efficiency of 75% to 90% due to biodegradation, the second anion (triethanolamine) is expected to be removed with an efficiency of 50% to 90% due to biodegradation, and the cation is expected to be removed with an efficiency of 75% to 90% due to sorption. Removal of the first anion (ethanolamine) by biodegradation is high, removal of the second anion (triethanolamine) by biodegradation is moderate to high and removal of the cation by biodegradation is negligible. Sorption of the first anion (ethanolamine) and the second anion (triethanolamine) to sludge, soil, and sediment is expected to be low, and sorption of the cation to sludge is expected to be strong and to soil and sediment is expected to be very strong. Migration of the first anion (ethanolamine) and second anion (triethanolamine) to groundwater is expected to be moderate due to low sorption to soil and sediment, mitigated by biodegradation, and migration of the cation to groundwater is expected to be negligible due to very strong sorption to soil and sediment. Due to low estimated vapor pressure and Henry's law constant, the first anion (ethanolamine) and the second anion (triethanolamine) are expected to undergo low volatilization to air and the cation is expected to undergo negligible volatilization to air. Overall, these estimates indicate that the first anion (ethanolamine) and the second anion (triethanolamine) have low potential to volatilize to air and moderate potential to migrate to groundwater and that the cation has low potential to volatilize to air or migrate to groundwater.

Persistence[3]: 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 first anion (ethanolamine) using data available for the first anion (ethanolamine, CASRN 141-43-5), of the second anion (triethanolamine) using data available for the second anion (triethanolamine, CASRN 102-71-6) and of the cation using data for analogue(s) (metal oxides). EPA estimated that the first anion (ethanolamine) and second

[3] 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 if 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)

anion (triethanolamine)'s aerobic and anaerobic biodegradation half-lives are < 2 months; and that the cation's aerobic and anaerobic biodegradation half-lives are > 6 months. These estimates indicate that the first anion (ethanolamine) and the second anion (triethanolamine) may have limited persistence in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment). Further, these estimates indicate that the cation may be very persistent in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment).

Bioaccumulation[4]: 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 first anion (ethanolamine) and the second anion (triethanolamine) to bioaccumulate using EPI Suite™; and the potential for the cation to bioaccumulate using data for analogue(s) (metal oxides). EPA estimated that the first anion (ethanolamine) has low bioaccumulation potential based on BCFBAF model result < 1,000 (first anion (ethanolamine) bioconcentration factor = 3.2 [estimated by linear regression from log Kow] and bioaccumulation factor = 0.9 [estimated by the Arnot-Gobas method (2003)][5]), while the second anion (triethanolamine) has low bioaccumulation potential based on BCFBAF model result < 1,000 (second anion (triethanolamine) bioconcentration factor = 0.4 [measured] and bioaccumulation factor = 0.9 [estimated by the Arnot-Gobas method (2003)]). The cation does not bioaccumulate by lipophilic partitioning and there is low concern that it may accumulate in organisms by other mechanisms. EPA estimated that the first anion (ethanolamine) and the second anion (triethanolamine) could have limited persistence and low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Although EPA estimated that the cation could be very persistent, the substance does not bioaccumulate by lipophilic partitioning and there is low concern that it will accumulate in organisms by other mechanisms; thus, repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms.

Human Health Hazard[6]: 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

[4] 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 if 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)

[5] Arnot JA, Gobas FAPC. 2003. A generic QSAR for assessing the bioaccumulation potential of organic chemicals in aquatic food webs. *QSAR and Combinatorial Science* 22: 337-345.

[6] 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

both the hazard (or toxicity) of the chemical substance and the extent of exposure to the substance. EPA estimated the human health hazard of these chemical substances based on their estimated physical/chemical properties, available data on the new chemical substances and their components, and other structural information. Absorption of the new chemical substances is expected to be nil to poor through the skin when neat and good through the skin when in solution based on physical/ chemical properties; absorption is expected to be good through the gastrointestinal (GI) tract and lungs based on physical chemical/properties. For the new chemical substances, EPA identified irritation to skin and eyes and acute toxicity as hazards based on test data for the new chemical substances, systemic effects, blood, liver, kidney, upper respiratory tract effects, lung effects, neurotoxicity, and reproductive and developmental toxicity based on test data for components of the new chemical substances (ethanolamine and triethanolamine). EPA also identified gastrointestinal effects as a hazard based on copper, to the extent that it is bioavailable. Submitted tests on the new chemical substances reported the test substance as moderately irritating to the skin and eyes of rabbits (Organisation for Economic Co-operation and Development (OECD) guideline not specified), non-sensitizing in guinea pigs (Buehler test), moderately toxic via inhalation in rats, and having low toxicity to rats via dermal and oral routes. EPA identified an oral Lowest Observed Adverse effect Level (LOAEL) of 50 mg/kg/day based on developmental toxicity, which was protective for acute toxicity, systemic effects and reproductive toxicity, an inhalation Lowest Observed Adverse Effect Concentration (LOAEC) of 20 mg/m^3 based on upper respiratory tract effects, which was protective for acute toxicity, lung and respiratory tract effects, and an oral NOAEL of 0.0272 mg Cu/kg/day for copper (30-35% of the new chemical substance) based on gastrointestinal effects. These values were used to derive exposure route- and population-specific points of departure for quantitative risk assessment. EPA qualitatively evaluated irritation effects.

Environmental Hazard[7]: 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 substances using hazard

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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.

[7] 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).

data on analogous chemicals. Acute toxicity values estimated for fish, aquatic invertebrates, and algae are 0.9 mg/L, 0.078 mg/L, and 0.11 mg/L, respectively. Chronic toxicity values estimated for fish, aquatic invertebrates, and algae are 0.078 mg/L, 0.051 mg/L, and 0.029 mg/L, respectively. These toxicity values indicate that the new chemical substances are expected to have high environmental hazard. Application of assessment factors of 5 and 10 to acute and chronic toxicity values, respectively, results in acute and chronic concentrations of concern of 0.016 mg/L (16 ppb) and 0.003 mg/L (3 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 release of the new 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-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 assessment, EPA assessed worker exposure via dermal exposure; worker inhalation exposures are not expected. Releases to air and landfill were estimated. Exposure to the general population was assessed via ingestion of groundwater impacted by landfill leaching. Exposures to the general population were not assessed via drinking water or fish ingestion because no releases to surface water are expected, or via stack and fugitive air inhalation because those releases are expected to be negligible (below modeling thresholds). Consumer exposure is not a condition of use and was not assessed.

Risk Characterization: EPA applies a margin of exposure approach to calculate potential human health risks of new chemicals. A benchmark (acceptable) margin of exposure (MOE) is derived by applying uncertainty factors (UF) 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 1,000 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 route-specific effect levels (i.e., NOAEL, LOAEL, or LOAEC) described above. Risks were identified for workers for developmental toxicity via dermal exposure based on quantitative hazard data for a component of the new chemical substances (MOE = 5; Benchmark MOE = 1,000). Irritation hazards to workers via dermal contact were identified based on test data for the new chemical substances, structural alert for aliphatic amines, and information provided in the SDS. 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 impervious gloves and eye 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 assessed for workers via inhalation exposure because exposures are expected to be negligible.

Risks were not identified for the general population for developmental toxicity via ingestion of groundwater impacted by landfill leaching based on quantitative hazard data for a component of the new chemical substances ($MOE_{Landfill}$ = 92,593; Benchmark MOE = 1,000). Risks were not identified for the general population for gastrointestinal symptoms via ingestion of groundwater impacted by landfill leaching based on quantitative hazard data for the copper component of the new chemical substances ($MOE_{Landfill}$ = 144; Benchmark MOE = 3). Risks were not evaluated for the general population via ingestion of drinking water or fish because no releases to surface water are expected, or via inhalation of stack or fugitive air because releases are expected to be negligible (below modeling thresholds). Irritation hazard to the general population is not expected via ingestion of groundwater impacted by landfill leaching due to dilution of the chemical substance in the media. Consumer use is not an intended or reasonably foreseen condition of use.

Risks to the environment were not identified due to no releases to water.

It is reasonably foreseen, based on the submitter's amendments to the submission and patents on the new chemical substances, that the new chemical substances could be used for different applications or under different conditions of use, leading to inhalation exposure, higher releases to the environment, and consumer exposures. The SNUR that has been proposed for these chemical substances defines certain conditions of use as significant new uses. The proposed significant new uses include releases to water resulting in surface water concentrations above 3 ppb, modification of the manufacturing, processing, or use that results in inhalation exposure, and use in consumer products. Conditions of use that fall under the restrictions of the proposed SNUR are not likely to present unreasonable risk of injury to health or the environment because (1) those conditions of use are not likely to be commenced during the pendency of the proposed

SNUR, and (2) upon finalization of the SNUR, those conditions of use would be prohibited unless and until EPA makes an affirmative determination that the significant new use is not likely to present an unreasonable risk or takes appropriate action under section 5(e) or 5(f).

5/29/2020
Date:

/s/
Tala R. Henry, Ph.D.
Deputy Director for Programs
Office of Pollution Prevention and Toxics