TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) SN-18-0005

Number: SN-18-0005
TSCA Section 5(a)(3) Determination: The significant new use is not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Names:
Specific: Butanoic acid, 3-mercapto-,1,1'-[2-(hydroxymethyl)-2-[(3-mercapto-1-oxobutoxy)methyl]-1,3-propanediyl] ester; CASRN: 1027326-93-7; and Butanoic acid, 3-mercapto-,1,1'-[2,2-bis[(3-mercapto-1-oxobutoxy)methyl]-1,3-propanediyl] ester; CASRN: 31775-89-0

Significant New Use: The Significant New Use Rules (SNURs) for these chemical substances at 40 CFR 721.10371 and 40 CFR 721.10372 require notification to EPA for any use of these substances other than as described in PMN P-10-0136, manufacture in the U.S. (excluding import), or release to water resulting in surface water concentrations exceeding 2 ppb.

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic): Import for use as a monomer for industrial adhesives, coatings and inks, consistent with the manufacturing, processing, use, distribution, and disposal information described in the SNUN.

Known conditions of use: Applying such factors as described in footnote 1, EPA evaluated whether there are known conditions of use and identified, based on the previous PMN, P-10-0136, use as a monomer for acryl-based ultra-violet (UV)-curing coatings, inks, and adhesives as a known condition of use.

Reasonably foreseen conditions of use: Applying such factors as described in footnote 1, EPA evaluated whether there are reasonably foreseen conditions of use and identified, based on a patent search and information available in another TSCA submission, the following reasonably foreseen uses: use as a component of cured film in color filter; reactant in laminate for optical member sheet; component in piezoelectric element for ultrasound;

[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.

chain transfer agent; reactant for photocurable ink; additive in curable composition for electroluminescent display device, liquid crystal display device, and touch panel; reactant for adhesion layer for manufacturing optical component, circuit board, and electronic applications; reactant for fire-resistant coatings; and chemical intermediate.

Summary: The significant new use 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. Although EPA estimated that the mixture of the two substances could be very persistent, the mixture has 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 Esters and Thiols[2] and test data on the chemical substances and analogous chemical substances, EPA estimates that the chemical substances have high environmental hazard and potential for the following human health hazards: sensitization, eye irritation, reproductive toxicity, and systemic (liver, kidney, thymus) toxicity. EPA concludes that the significant new use is not likely to present an 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 mixture containing the two chemical substances (CASRN 31775-89-0 and CASRN 1027326-93-7) and of the biodegradation product using data on each substance tested separately, data for the mixture, and EPI (Estimation Program Interface) Suite™ (http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface). In wastewater treatment, the mixture is expected to be removed with an efficiency of 25% to 75% due to sorption and possible biodegradation, and the biodegradation product is expected to be removed with an efficiency of 0% due to low biodegradability, low sorption, and low stripping. Removal of the mixture by biodegradation is negligible to high, and removal of the biodegradation product by biodegradation is negligible. Sorption of the mixture to sludge is expected to be strong and to soil and sediment is expected to be very strong. Sorption of the biodegradation product to sludge, soil, and sediment is expected to be low. Migration of the mixture to groundwater is expected to be negligible due to very strong sorption to soil and sediment, and migration of the biodegradation product to groundwater is expected to be rapid due to low sorption to soil and sediment. Due to low estimated vapor pressure and Henry's law constant, the mixture and the biodegradation product are expected to undergo negligible volatilization to air. Overall, these estimates indicate that the mixture has low potential to volatilize to air or migrate to groundwater and that the biodegradation product has low potential to volatilize to air and high potential to migrate to groundwater.

[2] TSCA New Chemicals Program (NCP) Chemical Categories. https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/chemical-categories-used-review-new.

Persistence[3]: Persistence is relevant to whether a 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 mixture and of the biodegradation product using data on each chemical substance tested separately, data on the mixture, and EPI (Estimation Program Interface) Suite™. EPA estimated an aerobic biodegradation half-life of the mixture is < 2 months to > 6 months, anaerobic biodegradation half-life is > 6 months, and hydrolysis half-life is hours to > months. EPA estimated that the biodegradation product's aerobic biodegradation half-life < 2 months to 6 months and anaerobic biodegradation half-life > 6 months. These estimates indicate that the mixture and the biodegradation product may be very persistent in anaerobic environments (e.g., sediment), that the mixture may be persistent or very persistent in aerobic environments (e.g., surface water), and that the biodegradation product may be persistent in aerobic environments (e.g., surface water).

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 mixture and the biodegradation product to bioaccumulate using EPI Suite™. EPA estimated that the mixture and the biodegradation product have low bioaccumulation potential based on BCFBAF model result < 1000 (parent compound bioconcentration factor = 200 [estimated] and bioaccumulation factor = 7 [estimated]; biodegradation product bioconcentration factor = 3 [estimated] and bioaccumulation factor = 1 [estimated]). Although EPA estimated the mixture and the biodegradation product could be very persistent, it they have 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[5]: Human health hazard is relevant to whether a significant new use of a chemical substance is likely to present an unreasonable risk because the significance of the risk

[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 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)

[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 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] 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

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 these chemical substances based on their estimated physical/chemical properties, structural alerts, and available data on the SNUN substances. Absorption of the SNUN substances is expected to be moderate via all routes based on physical/chemical properties and analogue data. For the SNUN substances, EPA identified skin sensitization, eye irritation, and systemic (liver, kidney, thymus) toxicity as hazards based on data submitted on the chemical substances. In a 2-generation reproduction study on the chemical substances, the reported effects included decreased offspring weight and changes to reproductive organ weights. EPA quantitatively assessed the SNUN substances using test data on the substances and identified a NOAEL of 25 mg/kg-day based on systemic effects in the 28-day oral study (described above), which was protective for reproductive and developmental effects and was used to derive exposure route- and population-specific points of departure for quantitative risk assessment, described below. EPA qualitatively evaluated eye irritation and skin sensitization hazards.

Environmental Hazard[6]: Environmental hazard is relevant to whether a significant new use of a 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 determined the environmental hazard for these chemical substances based on acute toxicity data submitted on the chemical substances. These chemical substances fall within the TSCA New Chemicals Categories of Esters and Thiols. Acute toxicity values measured for fish, aquatic invertebrates, and algae are 0.16 mg/L, 9.0 mg/L, and >0.4 mg/L, respectively. Chronic toxicity values estimated or measured for fish, aquatic invertebrates, and algae are 0.016 mg/L (estimated using an Acute-to-Chronic Ratio (ACR) of 10), 0.9 mg/L (estimated using an ACR of 10), and 0.038 mg/L, respectively. These toxicity values indicate that these chemical substances are expected to have high environmental hazard. Application of assessment factors of 5 and 10 to acute and chronic toxicity values, respectively,

---

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.

[6] 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).

results in acute and chronic concentrations of concern of 0.032 mg/L (32 ppb) and 0.002 mg/L (2 ppb), respectively.

Exposure: The exposure to a chemical substance is potentially relevant to whether a significant new use of that chemical substance is likely to present unreasonable risks under the conditions of use, 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 chemical substances under the intended conditions of use described in the SNUN 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 and inhalation exposure. Releases to water, air, and landfill were estimated. Exposure to the general population was assessed via drinking water and fish ingestion. Exposures to the general population via groundwater ingestion and inhalation were not assessed because releases to air or landfill were expected to be negligible (below modeling thresholds). Consumer exposures were not assessed because consumer uses were not identified as conditions of use.

Risk Characterization: EPA applies a margin of exposure approach to calculate potential human health risks of significant new use of a chemical substance. 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 significant new use of a chemical substance is not likely to present an unreasonable risk. EPA assesses risks to workers considering engineering controls described in the SNUN, but unless otherwise noted, 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 chemical substances were evaluated using the route-specific effect level (i.e., NOAEL) described above. Risks were not identified for workers for systemic or reproductive effects via inhalation exposure based on quantitative data for the chemical substances (MOE = 122; Benchmark MOE = 100). Risks were identified for workers for systemic effects via dermal exposure based on quantitative data for the chemical substances (MOE = 1-5; Benchmark MOE = 100). Irritation and sensitization hazards to workers via inhalation and dermal contact were identified based on data submitted for a same-as substance. 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, 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 systemic or reproductive effects via exposure from drinking water or fish ingestion based on quantitative data on the chemical substances (MOE_{Adult} = 710, MOE_{Infant} = 169, MOE_{Fish}=192; Benchmark MOE = 100). Risks were not evaluated for the general population via inhalation routes because exposures are negligible (below modeling thresholds). Sensitization and irritation hazards to the general population are not expected via drinking water due to dilution of the chemical substances 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 COCs. Acute and chronic risks to the environment were identified for the significant new use based on the acute COC of 32 ppb being exceeded during processing, and the chronic COC of 2 ppb being exceeded for 42 days/yr (estimated surface water concentration = 2.2 ppb) during use.

Although models used by EPA to estimate surface water concentrations from environmental releases of the chemical substances predicted that the acute COC of 32 and the chronic COC of 2 ppb would be exceeded, these are based on worst-case assumptions. Since the existing SNURs for these chemical substances mitigate ecotoxicity risks by limiting the releases to surface water to a maximum concentration of 2 ppb, acute and chronic risk concerns are not expected.

It is reasonably foreseen, based on a patent search and a previous TSCA submission that these substances could be used other than as described in the SNUN and previously submitted PMN. However, the existing SNURs for these chemical substances define certain conditions of use as significant new uses. Conditions of use that fall under the restrictions of the SNURs are not likely to present unreasonable risk of injury to health or the environment because 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).

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

9/25/2019
Date:

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