

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0150

Number: P-18-0150

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

Chemical Name:

Generic: Tertiary amine, compounds with amino sulfonic acid blocked aliphatic isocyanate homopolymer

Conditions of Use (intended, known, or reasonably foreseen)¹:

Intended conditions of use (generic): Import as a solution for use as a component of an industrial coating, 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 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 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 Category for Diisocyanates², estimated physical/chemical properties, available data on the new chemical substance, and by comparing it to structurally analogous chemical substances,

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.

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>.

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EPA estimates that the chemical substance has low environmental hazard and potential for the following human health hazard: specific target organ toxicity. EPA concludes that the new chemical substance 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 anion using data for analogue(s) (polymers with isocyanate groups) and data submitted for analogue(s) ([claimed CBI]); of the hydrolysis product using data for analogue(s) (polymers), data submitted for analogue(s) ([claimed CBI]), and data submitted for the new chemical substance; and of the cation using data for analogue(s) ([claimed CBI]) and EPI (Estimation Program Interface) Suite™ (<http://www.epa.gov/tsc-screening-tools/epi-suitetm-estimation-programinterface>). In wastewater treatment, the anion is expected to be removed with an efficiency of 90% to 99% due to rapid hydrolysis; the hydrolysis product is expected to be removed with an efficiency of 90% due to sorption; and the cation is expected to be removed with an efficiency of 90% due to biodegradation and sorption. Removal of the hydrolysis product by biodegradation is negligible and removal of the cation by biodegradation is high. Sorption of the hydrolysis product to sludge is expected to be strong and to soil and expected to be low to moderate. Migration of the hydrolysis product to groundwater is expected to be negligible due to very strong sorption to soil and sediment while, migration to the cation to groundwater is expected to be negligible due to low to moderate sorption to soil and sediment, mitigated by biodegradation. The hydrolysis product and the cation are expected to undergo negligible volatilization due to low estimated vapor pressure and Henry's law constant. Overall, these estimates indicate that the hydrolysis product and cation have low potential to volatilize to air or migrate to groundwater.

Persistence³: 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) (polymers with isocyanate groups) and data submitted for the analogue(s) ([claimed CBI]); of the hydrolysis product using data for analogue(s) (polymers) and data submitted for analogue(s) ([claimed CBI]); and of the cation using data for analogue(s) ([claimed CBI]). EPA estimated that the anion's hydrolysis half-life is hours; that the hydrolysis product's aerobic and anaerobic biodegradation half-lives are > 6 months; and that the cation's aerobic and anaerobic biodegradation half-lives are < 2 months. These estimates indicate that the anion may have limited persistence in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediments) due to rapid hydrolysis. Further, these estimates indicate that the hydrolysis

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)

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product may be very persistent in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment). These estimates also indicate that the cation may have limited persistence in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment).

Bioaccumulation⁴: 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 data for analogues (polymers with isocyanate groups); of the hydrolysis product to bioaccumulate using data for analogues (polymers); and of the cation to bioaccumulate using data for analogue(s) ([claimed CBI]). EPA estimated that the anion has low bioaccumulation potential based on rapid hydrolysis; the hydrolysis product has low bioaccumulation potential based on large predicted molecular volume, which limits bioavailability; and the cation has low bioaccumulation potential based on high water solubility, which increases elimination. EPA estimated that the anion 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 hydrolysis product could be very persistent, the substance has 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 low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms.

Human Health Hazard⁵: 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 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 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](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.

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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, available data on the new chemical substance, 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 nil to poor for all routes based on physical/chemical properties. For the new chemical substance, EPA identified systemic toxicity as a hazard based on test data for the cationic component and respiratory effects as a hazard based on analogue data for the low molecular weight (LMW) species [claimed CBI]. For the hydrolysis product of the residual, EPA identified systemic effects as hazards. The available studies were conducted on a mixture of the new chemical substance, which contained the residual. The results were negative for skin and eye irritation (OECD 405, 431, 439), negative for skin sensitization (OECD 429), negative for mutagenicity (OECD 471), and had low acute toxicity via the oral (OECD 423) and inhalation (OECD 403) routes. EPA identified a NOAEL of 30 mg/kg-bw/day based on systemic effects for the cationic component of the new chemical substance and an oral NOAEL of 59 mg/kg-bw/day based on the potential hydrolysis product. For the residual, EPA identified a BMCL of 0.14 mg/m³ based on respiratory effects via inhalation exposure which was used to derive exposure route- and population-specific points of departure (POD) for quantitative risk assessment. EPA considered these PODs protective for the identified hazards in the lung and systemic toxicity.

Environmental Hazard⁶: 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 determined environmental hazard for this new chemical substance based on SAR predictions for isocyanates. This substance falls within the TSCA New Chemicals Category of Diisocyanates. Acute and chronic toxicity values estimated for fish, aquatic invertebrates, and algae are all no effects at saturation. These toxicity values indicate that the new chemical substance is expected to have low environmental hazard. Because hazards are not expected up to the water solubility limit, acute and chronic concentrations of concern are not identified.

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.

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>).

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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 the dermal and inhalation routes. Releases to water, air, and landfill were estimated. Exposure to the general population was assessed via ingestion of drinking water and fish. Exposure to the general population was not assessed via ingestion of ground water (due to landfill leaching) or inhalation because releases are 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 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 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 and BMCL) described above. Risks were identified for workers for respiratory effects via inhalation exposures based on quantitative hazard data for an analogue of the LMW species (MOE = 6; Benchmark MOE = 30, Fold Factor = 5). Risks were not identified for workers for systemic effects via dermal exposure based on quantitative hazard data for a component of the new chemical substance (MOE = 13,468; Benchmark MOE = 100). EPA

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expects that employers will require and workers will use appropriate PPE (i.e., respiratory protection with an APF of 10), consistent with the Safety Data Sheet prepared by the PMN submitter, in a manner adequate to protect them.

Risks were not identified for the general population for systemic effects via drinking water or fish ingestion exposure based on quantitative hazard data for an analogue of the hydrolysis product of the residual (MOE > 6,000,000; Benchmark MOE = 100). Risks were not evaluated for the general population via ingestion of ground water (due to landfill leaching) or inhalation because all predicted environmental releases to air, incineration, or landfill are expected to be negligible (below modeling thresholds). Risks to consumer were not evaluated because consumer uses were not identified as conditions of use.

Risk from acute and chronic exposures to the environment are not expected at any concentration of the new chemical substance soluble in the water (i.e., no effects at saturation).

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.

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Date:

/s/
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