

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0380

Number: P-18-0380

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

Chemical Name:

Generic: Butanoic acid ethyl amine

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

Intended conditions of use (generic): Import in solution and process for use for, and use for automotive brake parts 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 identified the same use as the intended use based on a previous TSCA submission for this chemical substance.

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. Although EPA estimated that the new chemical substance could be persistent, the new chemical substance has low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Based on test data on analogous chemical substances and physical/chemical properties, EPA estimates that the new chemical substance has moderate environmental hazard and potential for the following human health hazards: eye irritation and specific target organ toxicity. EPA concludes that the chemical substance is not likely to present an unreasonable risk under the conditions of use.

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.

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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 new chemical substance using EPI (Estimation Program Interface) Suite™ (<http://www.epa.gov/tsca-screening-tools/epi-suite-estimation-program-interface>). In wastewater treatment, the new chemical substance is expected to be removed with an efficiency of 90% due to sorption and possible biodegradation. Removal of the new chemical substance by biodegradation is negligible to high and destruction (mineralization) of the new chemical substance by biodegradation is partial. Sorption of the new chemical substance to sludge, soil, and sediment is expected to be strong. Migration of the new chemical substance to groundwater is expected to be slow due to strong sorption to soil and sediment. Due to low estimated vapor pressure and Henry's law constant, the new chemical substance is expected to undergo negligible volatilization to air. Overall, these estimates indicate that the new chemical substance has low potential to volatilize to air or migrate to groundwater.

Persistence²: 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 new chemical substance using EPI Suite™. EPA estimated that the new chemical substance's aerobic biodegradation half-life is < 2 months and anaerobic biodegradation half-life is 2 to 6 months. These estimates indicate that the new chemical substance may have limited persistence in aerobic environments (e.g., surface water) and may be persistent in anaerobic environments (e.g., sediment).

Bioaccumulation³: 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 new chemical substance to bioaccumulate using EPI Suite™. EPA estimated that the new chemical substance has low bioaccumulation potential based on BCFBAF model result < 1000 (bioconcentration factor = 10 [estimated by linear regression from log Kow] and bioaccumulation factor = 840 [estimated by the Arnot-Gobas

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 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 if there are equivalent or analogous data. (64 FR 60194; November 4, 1999)

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 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 if there are equivalent or analogous data. (64 FR 60194; November 4 1999)

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method (2003)⁴). Although EPA estimated that the new chemical substance could be 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.

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 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 through the skin and moderate through the lungs and gastrointestinal (GI) tract based on physical/chemical properties. For the new chemical substance, EPA identified hazards for surfactant effects on the lung and irritation to eyes based on analogue data. EPA identified an inhalation benchmark concentration lower bound (BMCL) that was dosimetrically adjusted to a human equivalence concentration (BMCL_{HEC}) of 0.6 mg/m³ based on lung effects. EPA qualitatively evaluated eye irritation effects.

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 estimated environmental hazard of this new chemical substance using hazard

⁴ 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.

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.

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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data on an analogous chemical. This substance falls within the TSCA New Chemicals Category of [claimed CBI]⁷. Acute toxicity values estimated for fish, aquatic invertebrates, and algae are 120 mg/L, 100 mg/L, and 40 mg/L, respectively. Chronic toxicity values estimated for fish, aquatic invertebrates, and algae are all 20 mg/L. 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 10 mg/L (10,000 ppb) and 2 mg/L (2,000 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 the dermal route; inhalation exposures to workers are not expected. Releases to water, air, and landfill were estimated. Exposures to the general population were assessed via ingestion of drinking water, fish, and groundwater impacted by landfill leaching. Exposure to the general population via inhalation was not assessed because releases to air were expected to be negligible (below modeling thresholds). Consumer exposures were assessed via the inhalation and dermal routes.

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 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

⁷ 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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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 chemical substance were evaluated using a route-specific effect level (i.e., $BMCL_{HEC}$) described above. Based on the hazard determination and available quantitative and qualitative risk information, EPA did not identify risks for the chemical substance. Risks were not evaluated for workers for lung effects via inhalation exposure because exposures are expected to be negligible. Risks were not evaluated for workers for lung effects via dermal exposure because the hazard is not relevant to the exposure route. Eye irritation hazards to workers were identified based on information in the Safety Data Sheet (SDS), prepared by the submitter, and surfactant properties of the chemical 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 PPE, including eye protection. EPA expects that employers will require and that workers will use appropriate PPE, consistent with the SDS prepared by the submitter, in a manner adequate to protect them.

No oral hazards were identified for the chemical substance; therefore, risks were not quantified for ingestion of drinking water, fish, or groundwater impacted by landfill leaching. Based on no identified oral hazards, risks are not expected. Risks were not evaluated for the general population via inhalation exposures because exposures are expected to be negligible. Eye irritation hazards to the general population are not expected via drinking water, fish, or groundwater impacted by landfill leachate due to dilution of the chemical substance in the media.

Risks were not identified for consumers for lung effects via inhalation exposure based on quantitative hazard data for an analogue (MOE = 12,058; Benchmark MOE = 30). EPA assumes that eye irritation is possible from exposure to the consumer product because the chemical substance is an ingredient in the consumer product at concentration levels $\geq 3\%$, and therefore, its irritating properties are assumed to persist even in the presence of other unknown components⁸. Although eye irritation is possible from exposure to the consumer product, the

⁸ EPA is using the *Globally Harmonized System of Classification and Labelling of Chemicals (GHS): Eighth Revised Edition* (UN, New York, <https://doi.org/10.18356/f8fbb7cb-en>, Chapter 3.2 and 3.3), to establish the cut-off value for a new chemical substance's skin and eye irritation effects in consumer products. EPA will consider a mixture to be irritating to the skin or eye when the concentration of the new chemical substance is $\geq 3\%$ in the mixture. When selecting the cut-off value, EPA assumes that a mixture containing irritant ingredients cannot be classified based on the additivity approach. The theory of additivity assumes that each ingredient contributes to the overall irritant properties of the mixture in proportion to its potency and concentration. However, there are types of chemicals that the theory of additivity might not apply.

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final product contains only [claimed CBI] of the chemical substance, which is very close to the cut off value of $\geq 3\%$ in formulation for eye irritation effects in consumer products. The chemical substance is non-volatile, and spray applications are not expected under the intended, known, and reasonably foreseen conditions of use. Therefore, consumer eye contact with the chemical substance is expected to be minimal, and EPA concludes that unreasonable risk to consumers from eye irritation is not likely.

Risks to the environment were evaluated by comparing estimated surface water concentrations with the acute and chronic concentrations of concern. Risks from acute and chronic exposures to the environment were not identified due to releases to water that did not exceed the acute or chronic COC.

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

5/29/2020
Date:

/s/
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Annex 5 of the GHS document states “[e]stimates of possible exposures and risk to consumers should be based on conservative, protective assumptions to minimize the possibility of underestimating exposure or risks [Section A5.2.1(c)].” Thus, EPA selected the cut-off value ($\geq 3\%$) under the assumption that the additivity approach does not apply for the new chemical substance in relation to the other ingredients in the consumer product.