

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-21-0012

Number: P-21-0012

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

Chemical Name:

Generic: Multialkylbicycloalkenyl substituted propanenitrile

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

Intended conditions of use (generic): Import and process for use as and use as a fragrance ingredient, 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. 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. Based on test data on the PMN, EPA estimates that the 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 new chemical substance is not likely to present an unreasonable risk under the conditions

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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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 new chemical substance using data submitted for the new chemical substance and 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 50% to 75% due to sorption and stripping. Removal of the new chemical substance by biodegradation is negligible. 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 moderate reported vapor pressure, the new chemical substance is expected to undergo low to moderate volatilization to air. Overall, these estimates indicate that the new chemical substance has low to moderate potential to volatilize to air and has low potential to 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 data submitted for the new chemical substance. EPA estimated that the new chemical substance's aerobic and anaerobic biodegradation half-lives are > 6 months, atmospheric oxidation by hydroxyl radical (OH•) is rapid, and atmospheric oxidation by ozone (O₃) is rapid. These estimates indicate that the new chemical substance may be very persistent in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment). However, the new chemical substance is expected to be persistent due to rapid degradation by atmospheric oxidation.

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 data submitted for the new chemical substance. EPA estimated that the new chemical substance

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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has low bioaccumulation potential based on submitted data (bioconcentration factor = 210 (measured)). 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 Hazard⁴: 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, available data on the new chemical substance, and other structural information. Absorption of the new chemical substance is expected to be nil to poor through the skin when neat, poor through the skin when in solution or as a liquid, and poor through the lungs and gastrointestinal (GI) tract based on physical/chemical properties. For the new chemical substance, EPA identified hazards including eye irritation and liver effects based on test data for the new chemical substance. EPA identified a NOAEL of 104.01 mg/kg-bw/day which is protective for systemic effects and was used to derive exposure route- and population-specific points of departure for quantitative risk assessment. EPA qualitatively evaluated irritation effects.

Environmental Hazard⁵: 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

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

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

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acute toxicity data submitted for the new chemical substance. This substance falls within the TSCA New Chemicals Category of Neutral Organics.⁶ Acute toxicity values measured for fish, aquatic invertebrates, and algae are 2.48 mg/L (test data), 2.5 mg/L (test data), and 1.9 mg/L (test data), respectively. Chronic toxicity values for fish, aquatic invertebrates, and algae are 0.25 mg/L (Acute-to-Chronic Ratio (ACR)10), 0.25 mg/L (ACR10), and >1.4 mg/L (test data). 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 0.475 mg/L (475 ppb) and 0.025 mg/L (25 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 new chemical assessment, EPA assessed worker exposure via dermal and inhalation exposures. Releases to water, air, and landfill were estimated. Exposure to the general population was assessed via drinking water, fish ingestion, and groundwater impacted by landfill leachate. Exposures to the general population via stack air or fugitive air inhalation were not assessed because releases to these media were expected to be negligible (below modeling thresholds). Exposure to consumers was assessed via inhalation and dermal exposures.

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

⁶ 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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experimental animals to humans) and Lowest Observed Adverse Effect Level (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 substance were evaluated using the route-specific effect levels (i.e., NOAEL) described above. Risks were identified for workers for liver effects via dermal exposures based on quantitative hazard data for the new chemical substance ($MOE_{Dermal} = 35$; Benchmark MOE = 100). Risks were not identified for workers for liver effects via inhalation exposures based on quantitative hazard data for the new chemical substance ($MOE_{Inhalation} = 1,421$; Benchmark MOE = 100). Irritation hazards to workers via dermal contact were identified based on test data for the new 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 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 submitter, in a manner adequate to protect them.

Risks were not identified for the general population for liver effects via drinking water, fish ingestion, or groundwater impacted by landfill leachate based on quantitative hazard data for the new chemical substance ($MOE_{Adult\ Drinking\ Water\ (DW)} = 82,5438$; $MOE_{InfantDW} = 19,654$; $MOE_{Fish\ Ingestion} = 9,455$; $MOE_{Landfill\ Leachate} > 2$ million; Benchmark MOE = 100). Irritation hazards to the general population are not expected via ingestion of drinking water, fish, or groundwater impacted by landfill leachate due to dilution of the chemical substance in the media. Risks were not evaluated for the general population via stack air or fugitive air inhalation because exposures were expected to be negligible. Risks were not identified for consumers for liver effects via inhalation exposures to [claimed CBI] based on quantitative hazard data for the new chemical substance ($MOE_{[claimed\ CBI]} = 6,353$; $MOE_{[claimed\ CBI]} = 29,310$; $MOE_{[claimed\ CBI]} = 7,820$; Benchmark MOE = 100). Risks were not identified for consumers for liver effects via dermal exposures to [claimed CBI] based on quantitative hazard data for the new chemical substance ($MOE_{[claimed\ CBI]} = 56,440$; $MOE_{[claimed\ CBI]} = 177,665$; $MOE_{[claimed\ CBI]} = 8,456$; Benchmark MOE = 100). Although the new chemical substance is an eye irritant, EPA assumes that eye irritation is not likely from exposure to the new chemical substance in a consumer product as long as the concentration in the consumer product is maintained below 3% ([claimed CBI]%) and to the extent that remaining unknown components do not exhibit irritating properties.⁷

⁷ 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

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Risks to the environment were evaluated by comparing estimated surface water concentrations with the acute and chronic concentrations of concern. Risks from acute exposure to the environment were not identified due to releases to water that did not exceed the acute COC. Risks from chronic exposure to the environment were not identified since the chronic COC is exceeded less than 20 days per year.⁸

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 new chemical substance is not likely to present unreasonable risk to human health or the environment under the conditions of use.

1/25/2021
Date:

/s/
Madison H. Le, Director
New Chemicals Division
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency

value for the new chemical substance's skin and eye irritation effects in consumer products. EPA will consider a new chemical substance in a mixture to be irritating to the skin or eye when intended to be used at a concentration \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, for instance where an ingredient contributes to the overall irritation properties of the mixture to a greater extent than its proportion would suggest (e.g., synergy). 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.⁸ The 20-day criterion for concluding chronic risk is not likely is based on partial life cycle tests (daphnid chronic and fish early life stage tests) that typically range from 21 to 28 days in duration.