

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-23-0068

Number: P-23-0068

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

Chemical Name:

Specific: 1,3-Isobenzofurandione, hexahydro-, polymer with 1,4-cyclohexanedimethanol, isononanoate; CASRN 2773548-84-6

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

Intended conditions of use (specific): Manufacture and process for use as an ingredient in industrial primers and topcoats, 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 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 identified use in a consumer product.

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 very 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 physical/chemical properties and test data for potential hydrolysis products and an anhydride of a potential hydrolysis product, EPA estimates that the chemical substance has low environmental hazard and potential for the following human health hazards: Specific Target Organ Toxicity. EPA concludes that the new 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 any condition of use of a chemical substance that EPA believes is ongoing in the United States at the time of submission of the notification, as well as 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 chemical substance may be manufactured, processed, distributed, used, or disposed of. EPA expects that the identification of “reasonably foreseen” conditions of use will be made on a fact-specific, case-by-case basis. EPA will apply its professional judgment and experience when considering factors such as evidence of current use of the new chemical substance outside the United States, information about known or intended uses of 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 data for analogue(s) (polymers) 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 90% due to sorption. Removal of the new chemical substance by biodegradation is negligible. Sorption of the new chemical substance to sludge is expected to be strong and to soil and sediment is expected to be very strong. Migration of the new chemical substance 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 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 data for analogues (polymers). EPA estimated that the new chemical substance's aerobic and anaerobic biodegradation half-lives are > 6 months. 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).

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 for analogue(s) (polymers) and EPI Suite™. EPA estimated that the new chemical substance has low bioaccumulation potential based on large predicted molecular volume, which limits bioavailability and BCFBAF model result < 1000 for the lower MW fraction (bioconcentration factor = 570 (estimated by linear regression from log Kow) and bioaccumulation factor = 1

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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(estimated by the Arnot-Gobas method (2003))). Although EPA estimated that the new chemical substance 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.⁴

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 the chemical substance based on its estimated physical/chemical properties and test data for potential hydrolysis products and an anhydride of a potential hydrolysis product. Absorption of the parent polymer, low molecular weight (LMW) fraction < 1000 Da (50.00%), and LMW fraction < 500 Da (10.00%) of the new chemical substance is expected to be poor through the skin and nil through the lungs and gastrointestinal (GI) tract based on physical/chemical properties. Absorption of a potential hydrolysis product of the LMW fraction, 3,5,5-trimethylhexanoic acid (3.6%; CASRN 3302-10-1), is expected to be moderate through the skin, moderate through the lungs, and good through the GI tract based on physical/chemical properties. Absorption of both 1,4-cyclohexanedimethanol (27.8%; CASRN 105-08-8) and 1,2-cyclohexanedicarboxylic acid (18.4%; CASRN 1687-30-5), potential hydrolysis products of the LMW fraction, are expected to be nil to poor through the skin when neat, moderate to good through the skin when in solution, good through the lungs, and moderate through the GI tract based on physical/chemical properties. For the new chemical substance, EPA identified respiratory, systemic, reproductive, and developmental effects based on test data for potential hydrolysis products. EPA identified a NOAEL of 100 mg/kg/day based on systemic and developmental effects, which was protective for systemic, reproductive, and developmental effects, and was used to derive exposure route- and population-specific points of departure for quantitative risk assessment, described below.

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.

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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 based on the Log Kow of the new chemical substance. This substance falls within the TSCA New Chemicals Category of Esters. Acute and chronic toxicity values for fish, aquatic invertebrates, and algae are all no effects at saturation. 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.

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 inhalation and dermal routes. Releases to water, landfill, and air were estimated. Exposure to the general population was assessed via drinking water ingestion, fish ingestion, and inhalation of stack and fugitive air. Exposure to the general population was not assessed via groundwater impacted by landfill leachate because releases to landfill were expected to be below modeling thresholds. Consumer

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 no 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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exposures were not assessed because consumer uses were not identified as intended 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 (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 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 were not identified for workers for systemic and developmental effects via dermal contact, based on quantitative hazard data for a hydrolysis product ($MOEDermal = 943$; Benchmark MOE = 100).

Risks were not identified for workers for systemic and developmental effects via inhalation exposure, based on quantitative hazard data for a hydrolysis product ($MOEInhalation = 13,527$; Benchmark MOE = 100).

Risks were not identified for the general population for systemic and developmental effects via exposure to drinking water, fish ingestion, or inhalation of stack or fugitive air, based on quantitative hazard data for a hydrolysis product ($MOEAdultDW > 100,000$; $MOEInfantDW = 36,339$; $MOEFish\ Ingestion = 15,432$; $MOEStack\ Air > 9\ million$; $MOEFugitive\ Air = 12,077$; Benchmark MOE = 100).

Risks were not evaluated for the general population via groundwater impacted by landfill because exposures were expected to be negligible.

Risks to consumers were not evaluated because consumer uses were not identified as intended conditions of use.

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

Because no unreasonable risks were identified for workers, the general population, and the environment for the intended use and because risks to consumers for the reasonably foreseen use are not likely based on high MOEs for workers, who are exposed for longer, more often, and to

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higher concentrations, 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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