TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0324

Number: P-18-0324
TSCA Section 5(a)(3) Determination: The chemical substance is not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Generic: Organic acid dimethyl ester, polymer with mixed alkanediols and 5-isocyanato-1-(isocyanatomethyl)-1,3,3-trimethylcyclohexane, trimethoxysilylalkylalkanamine-blocked.

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (specific): Imported in solution for use as resin/binder in paint formulations for industrial and architectural applications, 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 hydrolysis products of the new chemical substance could be very persistent, the hydrolysis products of the new chemical substance have low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative. EPA estimated that the new chemical substance could be persistent and has low potential for bioaccumulation.

[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.

Based on EPA's TSCA New Chemicals Program Chemical Category for Alkoxysilanes[2] and test data on analogous chemical substances, EPA estimates that the chemical substance has low environmental hazard and potential for the following human health hazards: lung toxicity (waterproofing), irritation, neurotoxicity and developmental 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 this new chemical substance using data for analogous polymers. The chemical substance is estimated to be removed during wastewater treatment with an efficiency of 90 to 99% via hydrolysis. For the new chemical substance, removal by biodegradation is estimated to be negligible based on high molecular volume. The chemical substance's hydrolysis products are estimated to be removed during wastewater treatment with an efficiency of 90% via sorption. For the hydrolysis products, sorption to soil and sediment is estimated to be very strong, resulting in negligible migration to groundwater. Removal by biodegradation is expected to be negligible. Volatilization to air is estimated to be negligible due to low vapor pressure and a low Henry's Law constant. Overall, these estimates are indicative of low potential for this chemical substance and its hydrolysis products to volatilize into the air or migrate into groundwater.

Persistence[3]: 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. Based on data for analogous polymers, EPA estimated the hydrolysis half-life of the new chemical substance and aerobic and anaerobic biodegradation half-lives of the hydrolysis products. EPA estimated the new chemical substance to rapidly hydrolyze. EPA estimated the aerobic and anaerobic biodegradation half-lives of the hydrolysis products to be greater than six months. These estimates for hydrolysis and biodegradation indicate that the new chemical substance may not be persistent in aerobic environments (e.g., surface water) or anaerobic environments (e.g., sediment), and the hydrolysis products may be very persistent in aerobic and anaerobic environments.

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[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.

[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)

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. The new chemical substance and its hydrolysis products have low bioaccumulation potential based on high molecular volume of the new chemical substance, which limits bioavailability and bioaccumulation. Although EPA estimated that the new chemical substance's hydrolysis products could be very persistent, the new chemical substance and its hydrolysis products have 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 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, data on analogous chemicals, and other structural information. Absorption is estimated to be nil for the fraction of the chemical substance with molecular weight greater than 1000 Daltons and nil to poor for the low molecular weight fraction via all routes, based on physical/chemical properties. There were hazards identified for lung toxicity (waterproofing) and irritation to the eye, skin, mucous membranes, and lung, based on the reaction of alkoxysilanes. Hazards were also identified for neurotoxicity and developmental toxicity by methanol release, and if methanol is released, its absorption is expected to be good via all routes. EPA identified a NOAEL of 11 mg/kg-day for lung toxicity from a 90-day inhalation study on an analogue, [claimed CBI], as described in the TSCA New Chemicals Category for Alkoxysilanes. EPA identified a NOAEL/LOAEL of 2 mg/kg-day for developmental toxicity for methanol, a potential metabolite, in an inhalation study in a

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[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)), structure-activity relationships, and/or structural alerts to support characterizing human health hazards.

toxicological review[6]. These data were used to derive exposure route- and population-specific points of departure for quantitative risk assessment, described below.

Environmental Hazard[7]: 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 predictions based on data on analogous chemicals and the TSCA New Chemical Category for Alkoxysilanes. Hazards from acute and chronic exposures are not expected at concentrations up to the water solubility limit of the new chemical substance (i.e., 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.

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.

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[6] US EPA, Toxicological Review of Methanol (Noncancer) In Support of Summary Information on the Integrated Risk Information System (IRIS), available at https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0305tr.pdf

[7] 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).

For this new chemical assessment, EPA assessed exposure to workers via the dermal and inhalation routes. Releases to water, air, and landfill were estimated and used to assess exposure to the general population. Exposure to the general population was assessed via drinking water, fish ingestion and inhalation. Exposures to consumers 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 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 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., NOAELs) described above. Risks were identified workers for neurotoxicity and developmental effects via inhalation exposure based on methanol (MOE = 0.49; benchmark MOE = 1). Risks were identified workers for neurotoxicity and developmental effects via dermal exposure based on methanol (MOE = 0.1; benchmark MOE = 1). Risks were identified workers for lung effects via inhalation based on quantitative hazard data for an analogue, [claimed CBI], (MOE = 5.9; benchmark MOE = 100; inhalation fold factor = 17). Irritation hazards to workers via dermal contact were identified based on alkoxysilanes. Risks for this hazard endpoint were not quantified due to a lack of dose-response for this hazard. Risks for irritation and systemic toxicity will be mitigated if exposures are controlled by the use of appropriate PPE, including impervious gloves, eye protection and a NIOSH-certified respirator with at least an assigned protection factor of 25. EPA expects that workers will use appropriate personal protective equipment (i.e., impervious gloves, respirator and eye protection), consistent with the Safety Data Sheet prepared by the PMN submitter, in a manner adequate to protect them. Therefore, EPA does not expect unreasonable risk to workers.

Risks were not identified for the general population for neurotoxicity and developmental effects via drinking water and fish ingestion exposure based on methanol release (MOE = 46; benchmark MOE = 1). Risks were not identified for the general population for neurotoxicity and developmental effects via fugitive air inhalation exposure based on methanol release (MOE = 28; benchmark MOE = 1). Risks were not identified for general population for lung toxicity via

fugitive air inhalation based on quantitative hazard data for the analogue [claimed CBI] (MOE = 238; benchmark MOE = 100). Risks were not identified for the general population for irritation effects via drinking water or fish ingestion since these hazards are not expected to result from well-diluted concentrations. Risks to consumers were not evaluated because consumer uses were not identified as conditions of use.

Due to low environmental hazard, EPA believes that this chemical substance is not likely to present an unreasonable risk to the environment even if potential exposures were high.

Because worker exposures can be controlled by PPE, no unreasonable risks to the general population or environment were identified, and there are no expected exposures to consumers, 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.

12/20/2018
Date:

/s/
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