TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-16-0422

Number: P-16-0422
TSCA Section 5(a)(3) Determination: Chemical substance not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Specific: 1,2-Cyclohexanedicarboxylic acid, 1-(phenylmethyl) ester, ester with 2,2,4-trimethyl-1,3-pentanediol mono(2-methylpropanoate) (CASRN: 1661012-65-2)

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic): Use as an additive for polymers, 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 has identified, based on changes made to the conditions of use described in the PMN, the following reasonably foreseen conditions of use: manufacture, processing, or use, resulting in releases to water that differ from those from the intended conditions of use described in the PMN.

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 and the terms of the proposed Significant New Use Rule (SNUR) signed by EPA. Although EPA estimated that the new chemical substance could be persistent, the chemical substance has low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative. Based on data on analogous chemical substances, EPA estimates that this new chemical substance has moderate environmental hazard and potential for the following human health

[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. 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.

hazards: irritation, sensitization, and developmental/reproductive toxicity. EPA estimates that the new chemical substance has potential for aquatic toxicity at surface water concentrations exceeding 12 part per billion (ppb). However, risks to the environment would be prevented by either use only as an additive for polymers as described in Part I/Section C of the PMN claimed confidential, or using methods of manufacture, processing, or use that do not result in release to water of the new chemical substance such that surface water concentrations exceed the COC of 12 ppb. The PMN describes conditions of use consistent with these mitigation procedures. Therefore, EPA concludes that the new chemical substance is not likely to present unreasonable risk to human health or the environment under the intended conditions of use.

As set forth below, the information available to EPA is sufficient to permit the Agency to conduct a reasoned evaluation of the health and environmental effects of the chemical substances under the conditions of use that are not subject to the proposed SNUR, in order to determine that the chemical substances are not likely to present an unreasonable risk under those conditions of use. As such, EPA does not need to impose test requirements to conduct this evaluation. Whether testing is needed to evaluate the effects of the intended, known, or reasonably foreseen conditions of use of a chemical substance subject to a PMN is determined on a case-by-case basis. To the extent that testing may be necessary to conduct a reasoned evaluation of the health or environmental effects of the reasonably foreseen conditions of use that are subject to the proposed SNUR, EPA will make the appropriate determination if a SNUN is submitted following finalization of the SNUR.

EPA found no known conditions of use, assessed the intended conditions of use, and addressed reasonably foreseen conditions of use by proposing a SNUR. Therefore, EPA determines the new chemical substances are not likely to present unreasonable risk to human health or the environment.

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 is likely to present an unreasonable risk. EPA estimated physical/chemical and fate properties of the new chemical substance using received data for the new chemical substance and EPI (Estimation Programs Interface) Suite™, a suite of physical/chemical property and environmental fate estimation programs (http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface). In wastewater treatment, the new chemical substance is expected to be removed with 90% efficiency based on sorption and biodegradation. 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, low potential to migrate to groundwater.

Persistence[2]: 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 biodegradation half-lives of the new chemical substance using received data for the new chemical substance and EPI Suite™. EPA estimates indicate that this substance will be persistent in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment).

Bioaccumulation[3]: 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 using EPI Suite™. These estimates indicate that the new chemical substance has low bioaccumulation potential (bioconcentration factor = 350 and bioaccumulation factor = 13). Although EPA estimated that the new chemical substance could be persistent, the substance has a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms.

Human Health Hazard[4]: 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

[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 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)

[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 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)

[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.

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 new chemical substance based on its estimated physical/chemical properties, data on the chemical substance (acute oral toxicity (OECD 423), acute dermal irritation (OPPTS 870.2500), acute eye irritation (OPPTS 870.2400) and dermal sensitization Buehler Test (OECD 406)), and data on an analogue (Ames test (OECD 471), in vitro gene mutation assay (OECD 490), in vitro chromosome aberration test (OECD 473), and a combined repeated dose toxicity with the reproduction/developmental toxicity screening test (OECD 422)).

For this new chemical substance, absorption is estimated to be poor by all routes of exposure based on analogue data. EPA identified dermal irritation, dermal sensitization and developmental toxicity as potential hazards based on submitted test data for the new chemical substance and for an analogue. A LOAEL of 150 mg/kg-bw/day was identified for developmental effects in the offspring of exposed dams in the submitted repeated dose/reproduction/developmental toxicity screening test (OECD 422). This LOAEL was used to derive exposure route- and population-specific points of departure for the quantitative risk assessment of the new chemical substance, described below.

Environmental Hazard[5]: 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 the environmental hazard for this new chemical substance based on submitted toxicity data for an analogous chemical. The acute toxicity values estimated for fish, aquatic invertebrates and algae are: no effects at saturation, 1.1 mg/L and 1.2 mg/L, respectively. The chronic toxicity value for fish was not estimated; the values estimated for aquatic invertebrates and algae are 0.120 mg/L and 1.73 mg/L, respectively. Based on these toxicity values, EPA expects the new chemical substance to have moderate environmental hazard. Application of assessment factors of 5 and 10 to the lowest acute and chronic toxicity values, respectively, results in concentrations of concern (COCs) of 0.22 mg/L (220 ppb) and 0.012 mg/L (12 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.

(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).

EPA estimates occupational exposure and environmental release of new chemical substances under the intended conditions of use described in the PMNs 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 consumer, general population.

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 quantitatively assessed exposure to workers via the dermal route of exposure and to the general population via drinking water. Inhalation exposure is not expected under the conditions of use for either workers or the general population. 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 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. 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 level (i.e., LOAEL) described above. For the new chemical substance, risks were identified for workers for developmental toxicity through dermal exposure (MOE= 5 or 10, depending on the exposure scenario; benchmark MOE = 1000). Risks for dermal irritation and sensitization were not quantified due to a lack of dose-response for these hazards. However, exposures can be controlled by the use of appropriate PPE, including impervious gloves. EPA expects that employers will require and workers will use appropriate personal protective equipment (i.e., impervious gloves), 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 developmental toxicity via drinking water or fish ingestion (MOEs from approximately 15,000-70,000; benchmark MOE = 1000). Risks to consumers were not evaluated because consumer uses were not identified as conditions of use.

Risks to the environment were evaluated by comparing estimated surface water concentrations with the acute and chronic concentrations of concern. Risks to the environment were not identified because estimated maximum surface water concentrations does not exceed the acute COC, and the chronic COC is exceeded fewer than 20 days[6] per year based on information provided in the amended PMN submission. Therefore, risk to the environment is not expected under the intended conditions of use.

It is reasonably foreseen that the manufacture, processing, or use of the new chemical substance could result in releases to water exceeding the chronic COC of 12 ppb. It is reasonably foreseen based on the initial PMN submission that included conditions of use resulting in release to water that posed risk to the environment. The SNUR that has been proposed for this chemical substance defines certain conditions of use as significant new uses. The proposed significant new uses include release of a manufacturing, processing, or use stream associated with any use of the substances, other than the use described in the PMN, into the waters of the United States exceeding a surface water concentration of 12 ppb. Conditions of use that fall under the restrictions of the proposed SNUR are not likely to present unreasonable risk of injury to health or the environment because (1) those conditions of use are not likely to be commenced during the pendency of the proposed SNUR, and (2) upon finalization of the SNUR, those conditions of use would be prohibited unless and until EPA makes an affirmative determination that the significant new use is not likely to present an unreasonable risk or takes appropriate action under section 5(e) or 5(f).

4/15/2019
Date:

/s/
Tala R. Henry, Ph.D.
Acting Deputy Director for Programs
Office of Pollution Prevention and Toxics

[6] 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.