TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-19-0071

Number: P-19-0071
TSCA Section 5(a)(3) Determination: The chemical substance is not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Generic: Trimethylolpropane, alkenoic acid, triester.

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic): Import for processing and use as a physical property modifier 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 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. EPA estimated that the new chemical substance could have limited persistence and a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Based on EPA's TSCA New Chemicals Program Chemical Category for Esters[2] and test data on analogous chemical substances, EPA estimates that the chemical substance has high environmental hazard and potential for the following human health hazards: liver toxicity and developmental toxicity. EPA concludes that the new chemical

[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.
[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.

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 the new chemical substance using data for analogues and EPI (Estimation Program Interface) Suite™ (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 an efficiency of 90% via sorption and possible biodegradation. Removal of the new chemical substance by biodegradation is moderate to high. Sorption of the new chemical substance to sludge, soil, and sediment is 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, has low potential to migrate to groundwater, and is likely to be removed in wastewater treatment.

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. EPA estimated degradation half-lives of the new chemical substance using data for analogues and EPI Suite™. EPA estimated that 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 will have limited persistence in aerobic environments (e.g., surface water) and will be persistent in anaerobic environments (e.g., sediment). Overall the substance's persistence is limited based on a combination of partitioning and the degradation half-lives across environmental media.

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

[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)

[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)

food chains. EPA estimated the potential for the new chemical substance to bioaccumulate using data for analogues and EPI Suite™. EPA estimated that the new chemical substance has low bioaccumulation potential based on bioconcentration and bioaccumulation data reported for an analogue and EPISuite ™ (bioconcentration factor = 1148 (estimated) and bioaccumulation factor = 25 (estimated)). The esters in the molecule are expected to metabolize so the bioaccumulation factor (BAF) model and the analogue data are considered more relevant than the bioconcentration factor (BCF) model. EPA estimated that the new chemical substance could have limited persistence and 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[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, and by comparing it to structurally analogous chemical substances for which there is information on human health hazard. Absorption is expected to be poor via all routes (oral, dermal, and inhalation) based on physical/chemical properties and analogues. For the new chemical substance, EPA identified liver effects based on analogue ([claimed CBI]) data and developmental effects based on a potential metabolite, [claimed CBI]. EPA quantitatively assessed the new chemical substance using a NOAEL of 300 mg/kg-day based on liver effects identified in a 28-day repeated dose study (OECD 407) on [claimed CBI] and a BMDL of 1,100 mg/kg-day based on developmental effects identified in a one-generation reproductive study (OECD 443). These Points of Departure (PODs) were used to derive exposure route- and population-specific points of departure for quantitative risk assessment, described below. Benchmark MOEs of 100 were used.

Environmental Hazard[6]: Environmental hazard is relevant to whether a new chemical substance is likely to present unreasonable risk because the significance of the risk is dependent

[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.

[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

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 based on the Ecological Structure Activity Relationships (ECOSAR) Predictive Model (https://www.epa.gov/tsca-screening-tools/ecological-structure-activityrelationships- ecosar-predictive-model); specifically the QSAR for Esters. This substance falls within the TSCA New Chemicals Category of Esters. Acute toxicity values estimated for fish, aquatic invertebrates, and algae are all no effects at saturation. Chronic toxicity values estimated for fish, aquatic invertebrates, and algae are 0.03 mg/L, no effects at saturation, and no effects at saturation, respectively. These toxicity values indicate that the new chemical substance is expected to have high environmental hazard for fish. Application of an assessment factor of 10 to chronic toxicity values results in a chronic concentration of concern of 0.003 mg/L (3 ppb). An acute COC was not calculated, because the acute toxicity values show no effects at saturation.

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 air, water, and landfill were estimated. General population exposure was assessed via ingestion and fugitive air inhalation (stack air inhalation was not assessed because it is below modeling thresholds). Consumer exposures were not assessed because consumer uses were not identified as conditions of use.

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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).

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 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 and BMDL) described above. Risks were identified for workers for liver effects via dermal exposure based on quantitative hazard data for an analogue, [claimed CBI] (MOE = 51; Benchmark MOE = 100). Risks will be mitigated if exposures are controlled by the use of appropriate PPE, including impervious gloves. EPA expects that employers will require and workers will use appropriate PPE (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 workers for liver effects via inhalation exposure based on quantitative hazard data for an analogue, [claimed CBI] ($MOE_{respirable}$ = 480; MOE_{total} = 160; Benchmark MOE = 100). Risks were not identified for workers for developmental effects via inhalation or dermal route of exposure based on quantitative hazard data for a metabolite of the new chemical substance, [claimed CBI] ([claimed CBI] of the new chemical substance; Inhalation $MOE_{respirable}$ = 2,175; Inhalation MOE_{total} = 725; Dermal MOE = 233; Benchmark MOE = 100).

Risks were not identified for the general population for liver effects via drinking water, fish ingestion, ground water ingestion (from landfill leaching), or fugitive air inhalation exposures based on quantitative hazard data for an analogue, [claimed CBI] (MOEs $\geq$ 351; Benchmark MOE = 100). Risks were not identified for the general population for developmental effects via drinking water, fish ingestion, ground water ingestion (from landfill leaching), or fugitive air inhalation exposures based on quantitative hazard data for a metabolite of the new chemical substance, [claimed CBI] ([claimed CBI] of the new chemical substance; MOEs $\geq$ 1,592; Benchmark MOE = 100). Risks were not assessed for the general population via stack air inhalation because releases were negligible (below modeling thresholds). 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 from acute exposure are not expected at any concentration of the new chemical substance soluble in the

water (i.e., no effects at saturation). Risks to the environment from chronic exposure were not identified because releases to water (surface water concentration = 428 ppb) exceeded the chronic COC of 3 ppb for less than 21 days/year[7] (20/20 days/year during processing of the new chemical substance).

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

6/19/19
Date:

/s/
Jeffery T. Morris
Director
Office of Pollution Prevention and Toxics

[7] 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.