TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-19-0003

Number: P-19-0003
TSCA Section 5(a)(3) Determination: The chemical substance is not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Generic: Polyaromatic ether symmetrical dicarboxylic anhydride

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (specific): Manufacture for use as a monomer for an injection molded resin, 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 product of the new chemical substance could be persistent, it has low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative. Based on EPA's TSCA New Chemicals Program Chemical Category for Anhydrides, Carboxylic Acid[2] and test data on analogous chemical substances, EPA estimates that the chemical substance has moderate environmental hazard and potential for the following human health hazards: cardiac, blood, muscle, reproductive and developmental

[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.

toxicity, skin and eye irritation, and respiratory sensitization. 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 an analogous chemical substance. The chemical substance is expected to be removed with an efficiency of 90 - 99% during wastewater treatment due to rapid hydrolysis of the parent compound, with an estimated hydrolysis half-life of minutes to hours. EPA estimated physical/chemical and fate properties of the hydrolysis product of new chemical substance using 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). The hydrolysis product is expected to be removed with an efficiency of 90% during wastewater treatment due to sorption and biodegradation. Migration of the hydrolysis product to groundwater is expected to be slow due to strong sorption to soil and sediment mitigated by biodegradation. Due to low estimated vapor pressure and Henry's law constant, the hydrolysis product is expected to undergo negligible volatilization to air. Overall, these estimates are indicative of low potential for this chemical substance to volatilize into the air and a low potential for this chemical to 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. EPA estimated persistence of this substance using data on analogous chemical substances, which indicate that the parent compound will rapidly hydrolyze and therefore will not be persistent. EPA estimated biodegradation half-lives of the hydrolysis product using EPI Suite™, a suite of physical/chemical property and environmental fate estimation programs. EPA estimated that the aerobic biodegradation half-life of the hydrolysis product is less than two months and the anaerobic biodegradation half-life is between two and six months. These estimates indicate that this new chemical substance will not be persistent in aerobic environments (e.g., surface water) or anaerobic environments (e.g., sediments), and the hydrolysis product will not be persistent in aerobic environments but may be persistent in anaerobic environments.

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

[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

terrestrial species pose the potential for elevated exposures to humans and other organisms via food chains. EPA estimated the potential for this new chemical substance and its hydrolysis product to bioaccumulate using data on analogous chemical substances and EPI Suite™, a suite of physical/chemical property and environmental fate estimation programs. These estimates indicate that the chemical substance has low bioaccumulation potential based on rapid hydrolysis, and its hydrolysis product also has low bioaccumulation factor (bioconcentration factor = 3, bioaccumulation factor = 250), indicating that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Although EPA estimated that the hydrolysis product of this new chemical substance could be persistent, the substance and its hydrolysis product have 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 of the new chemical substance is estimated to be poor through the skin and lungs and moderate through the GI tract, based on physical/chemical properties. For the new chemical substance, EPA identified cardiac, blood, muscle, and developmental toxicity from potential chelation of nutrient metals by carboxylic moieties; skin and eye irritation based on information for an analogue; and developmental and reproductive toxicity and respiratory sensitization effects based on the New Chemicals Program Chemical Category for Anhydrides, Carboxylic Acid. EPA identified a LOAEL of 1,562 mg/kg-day based on systemic effects in a two-year oral bioassay on a structural component of the new chemical substance, which was used to derive exposure route- and population-specific points of departure for quantitative risk assessment, described below.

---

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.

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 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 the Ecological Structure Activity Relationships (ECOSAR) Predictive Model (https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-releationships-ecosar-predictive-model); specifically the QSAR for neutral organics for the hydrolysis product of the new chemical substance. The new chemical substance falls within the TSCA New Chemicals Category for Anhydrides, Carboxylic Acid. The acute ecotoxicity values estimated for fish, aquatic invertebrates, and algae are 32.75 mg/L, 23.11 mg/L, and 42.23 mg/L, respectively. Chronic toxicity values estimated for fish, aquatic invertebrates, and algae are all >10 mg/L. Based on these toxicity values EPA expects the new chemical substance to have moderate environmental hazard. Application of an assessment factor of 5 and 10 to acute and chronic toxicity values results in a acute and chronic concentration of concern of 4.622 mg/L (4,622 ppb), and 1 mg/L (1,000 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

[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 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).

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 exposure, but not for inhalation exposure since exposure is not expected due to low vapor pressure and no dust formation. Releases to air were estimated. EPA did not assess exposures to the general population because there are no releases to water and releases to air are expected to be negligible (below modeling thresholds). 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., LOAEL) described above. Risks were identified for systemic effects via dermal exposure (MOE = 433; Benchmark MOE = 1000). Irritation and sensitization hazards to workers via dermal contact were identified based on analogue data. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards. Exposures can be mitigated by the use of appropriate personal protective equipment (PPE), including (impervious gloves). EPA expects that employers will require and workers will use appropriate PPE consistent with the Safety Data Sheet prepared by the new chemical submitter, in a manner adequate to protect them.

Risks were not evaluated for the general population because general population exposures are expected to be negligible. Risks to consumers were not evaluated because consumer uses were not identified as conditions of use.

Risks to the environment were not identified because there are no expected releases to water.

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.

04/19/19
Date:

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