TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-16-0354 & P-16-0355

Number: P-16-0354 & P-16-0355
TSCA Section 5(a)(3) Determination: The chemical substances are not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Generic (P-16-0354 and P-16-0355): Esteramine

Conditions of Use (intended, known, or reasonably foreseen) [1]**:**
Intended conditions of use (generic): Manufacture for use as and use as chemical intermediates, consistent with manufacturing, processing, use, distribution, and disposal information described in the PMNs.
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 PMNs, 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 PMNs.

Summary: The chemical substances are 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

[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.

the terms of the proposed Significant New Use Rule (SNUR) signed by EPA.[2] Although EPA estimates that the new chemical substances could be very persistent, the chemical substances have low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative. Based on data on analogous chemical substances, EPA estimates that these new chemical substances have potential for the following human health hazards: irritation and developmental/reproductive toxicity. EPA expects that workers will use appropriate personal protective equipment (i.e., dermal and ocular protection) in a manner adequate to protect them. EPA also estimates that the new chemical substances have high environmental hazard with potential for aquatic toxicity at surface water concentrations exceeding 1 part per billion (ppb). However, risks to the environment would be prevented by either use only as chemical intermediates for the use described in Part I/Section C of the PMNs claimed confidential, or using methods of manufacture, processing, or use that do not result in release to water of the new chemical substances such that surface water concentrations exceed the COC of 1 ppb. The PMNs describe conditions of use consistent with these mitigation procedures. Therefore, EPA concludes that the new chemical substances are 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.

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[2]Reasonably foreseen conditions of use subject to a proposed SNUR are not likely to present an unreasonable risk of injury to health or the environment. Based on EPA's experience, it is the Agency's judgment that a new use would not commence during the pendency of a proposed SNUR because web posting of a proposed SNUR serves as the cut-off date for a significant new use. Therefore, manufacturers and processors would not commence a prohibited new use that would be legally required to cease upon the finalization of the SNUR. Once a SNUR is final and effective, no manufacturer or processor – including the PMN submitter – may undertake the conditions of use identified as a significant new use of the PMN substance in the SNUR. EPA must first evaluate the new use in accordance with the requirements of TSCA Section 5 and (a) either conclude that the new use is not likely to present an unreasonable risk under the conditions of use; or (b) take appropriate action under section 5(e) or 5(f). If EPA were not to finalize the proposed SNUR, then that decision would be based on information and data provided to the Agency during the comment period demonstrating that the reasonably foreseen conditions of use subject to the proposed SNUR are not likely to present an unreasonable risk. Under either scenario, the reasonably foreseen condition of use is not likely present an unreasonable risk.

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 new chemical substance is likely to present an unreasonable risk. EPA estimated physical/chemical and fate properties of these new chemical substances 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 chemical substances are estimated to be removed with an efficiency of 90% during wastewater treatment due to strong sorption to sludge and to biodegradation. The chemical substances are estimated to have strong sorption to soil and sediments, resulting in negligible migration to groundwater. Volatilization to air is estimated to be negligible because the substances have low vapor pressures and low Henry's Law constants. Overall, these estimates are indicative of low potential for these chemical substances to volatilize into the air and a low potential for these chemicals 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 biodegradation half-lives of these new chemical substances 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). EPA estimates the aerobic biodegradation half-lives to be less than two months, which indicates that the chemical substances may be of low persistence in aerobic environments (e.g., surface water). The anaerobic biodegradation half-lives are estimated to be greater than six months, which indicates that the chemical substances may be very persistent in anaerobic environments (e.g., sediment).

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. EPA estimated the potential for the new chemical substances to bioaccumulate using EPI Suite™. These estimates indicate that the chemical substances have low

[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)

bioaccumulation potential based on estimated bioaccumulation factor (BAF) of 5. The BAF was considered a better indicator of bioaccumulation potential than the estimated bioconcentration factor (BCF) as the BAF model incorporates a calculated metabolism rate for these specific chemical substances. Although EPA estimated that the new chemical substances could be very persistent, the chemical substances 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. Although absorption is expected to be poor by all routes of exposure based on physical/chemical properties of the chemical substances, there is concern for irritation at portals of entry (eyes, skin, and respiratory tract) based on data for analogous amines. If absorbed, the new chemical substances can be metabolized to release triethanolamine. For systemic toxicity, hazard potential is low based on a 90-day repeated-dose oral toxicity study on triethanolamine demonstrating no effects at 1000 mg/kg-day, the highest dose tested. EPA identified toxicity data for diethanolamine, an analogue of triethanolamine, including a dermal LOAEL = 150 mg/kg-day for maternal reproductive toxicity from a dermal prenatal developmental toxicity study and an oral NOAEL = 50 mg/kg-day for maternal and postnatal developmental toxicity from a developmental toxicity study (OECD SIDS 2007)[6]. EPA quantitatively assessed the new chemical substances using the dermal LOAEL with a benchmark MOE of 1000 and oral NOAEL with a benchmark MOE of 100 for diethanolamine to derive exposure route- and population-specific points of departure for quantitative risk assessment of the chemical substance.

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

[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] OECD SIDS Initial Assessment Profile, SIAM 24, April 17-20, 2007.

[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

upon both the hazard (or toxicity) of the chemical substance and the extent of exposure to the substance. The new chemical substances fall within the TSCA New Chemicals Program Chemical Category of Aliphatic Amines[8] which indicates potential toxicity to all groups of freshwater organisms (i.e., fish, aquatic invertebrates and green algae). Consistent with the category document EPA estimated environmental hazard of these new chemical substances using the Ecological Structure Activity Relationships (ECOSAR) Predictive Model (https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model); specifically, the SAR for the class of aliphatic amines. ECOSAR estimates indicate that the chemical substances would not cause acute toxicity at concentrations up to their water solubility limit (i.e., no effects at saturation). However, the chronic toxicity values are estimated to be 0.001 mg/L. Based on the estimated chronic toxicity values, EPA concludes that these chemical substances have high environmental hazard. An acute concentration of concern is not identified due to no effects expected at saturation. The chronic concentration of concern is 0.001 mg/L (i.e., 1 ppb).

Exposure and Risk Characterization: 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 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 and exposure to the general population via drinking water and fish ingestion. Inhalation exposure is

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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).

[8] 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.

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.

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 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 levels (i.e., LOAEL or NOAEL) described in the above human health hazard section. Risk to consumers was not evaluated because use by consumers was not an identified condition of use. The LOAEL from the dermal study with diethanolamine was used to assess worker risk and the NOAEL from the oral study with diethanolamine was used to assess general population risk. These effect levels were compared to estimated exposure concentrations to determine the MOE. Risk to workers for irritation/corrosion via dermal and ocular exposure based on analogue data was identified, but not quantified due to a lack of dose-response data. Risk to workers for developmental/reproductive toxicity via dermal exposure was identified (MOE = 36, benchmark MOE = 1000). Dermal and ocular risk would be mitigated with the use of dermal and eye protection. EPA expects that workers will use appropriate personal protective equipment (i.e., impervious gloves and chemical goggles or equivalent eye protection), consistent with the Safety Data Sheet prepared by the PMN submitter, in a manner adequate to protect them. Therefore, EPA finds that the new chemical substances are not likely to present an unreasonable risk to workers under the intended conditions of use. EPA did not identify risk to the general population for developmental/reproductive toxicity because the MOEs (MOE= 3,226 for adults; MOE = 774 for infants; MOE = 37,879 for fish ingestion) exceeded the benchmark MOE of 100. Risks to consumers were not evaluated because consumer uses were not identified.

Risks to the environment are estimated by comparing the 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 chemical substances soluble in water (i.e., no effects at saturation). The chronic concentration of concern (1 ppb) is exceeded for fewer than

20 days[9] per year based on information provided in the amended PMN submission. Therefore, risk to the environment from chronic exposure is not expected under the intended conditions of use.

It is reasonably foreseen that the manufacture, processing or use of the new chemical substances could result in releases to water exceeding the 1 ppb COC. 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 these chemical substances 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 PMNs, into the waters of the United States exceeding a surface water concentration of 1 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).

10/9/18
Date:

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

[9] The 20-day criterion for no chronic risk is derived from partial life cycle tests (daphnid chronic and fish early life stage tests) that typically range from 21 to 28 days in duration.