

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0174

Number: P-18-0174

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

Chemical Name:

Generic: Enzyme

Conditions of Use (intended, known, or reasonably foreseen)¹:

Intended conditions of use (generic): Import for use in oilfield 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 use as an enzyme in chemical synthesis to be a reasonably foreseen use based on a patent search.

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 new chemical substance could be persistent, the new chemical substance has low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative. Based on test data on analogous chemical substances and physical/chemical properties, EPA estimates that the chemical substance has low environmental hazard and potential for the following human health hazards: skin and respiratory sensitization, skin irritation. EPA concludes that the new chemical substance is not likely to present an unreasonable risk under the conditions of use.

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.

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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 biological compounds and submitted data for the new chemical substance. The chemical substance is estimated to be removed with an efficiency of 90% during wastewater treatment due to sorption and biodegradation. Removal by biodegradation is estimated to be moderate. Sorption of the new chemical substance to sludge is estimated to be moderate to strong, and sorption to soil and sediment is also expected to be moderate to strong, resulting in slow migration of the substance to groundwater. Volatilization to air is estimated to be negligible, based on the low reported vapor pressure. Overall, these estimates are indicative of low potential for this chemical substance to volatilize into the air and a low to moderate potential for this chemical substance to migrate into groundwater.

Persistence²: 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 biological compounds and submitted data for the new chemical substance, EPA estimated the aerobic biodegradation half-life of this substance to be less than two months and the anaerobic biodegradation half-life to be two to six months. These estimates indicate that this substance is not expected to be persistent in aerobic environments (e.g., surface water) and may be persistent in anaerobic environments (e.g., sediment).

Bioaccumulation³: 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 that the new chemical substance has low potential to bioaccumulate using data for analogous biological compounds and submitted data for the new chemical substance. Although EPA estimated that this 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.

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)

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Human Health Hazard⁴: 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 structure and physical/chemical properties and data on analogous substances. Absorption of the new chemical substance is estimated to be nil neat and poor all routes in solution based on physical/chemical properties. EPA identified skin and respiratory sensitization hazards based on the allergenic properties of the new chemical substance (i.e., enzyme allergy) and skin irritation hazard based on analogue data. Due to a lack of dose-response information, EPA qualitatively assessed risk for the identified hazards, as discussed below.

Environmental Hazard⁵: 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 hazard data on an analogous chemical and SAR predictions for amphoteric polymers (special class within ECOSAR v.2.0). The acute ecotoxicity values estimated for fish, aquatic invertebrate and algae are greater than 100 mg/L. Chronic ecotoxicity values (ChV) estimated for fish, aquatic invertebrates, and algae are greater than 10 mg/L. Based on these toxicity values, EPA expects the new chemical substance to have low environmental hazard. Application of acute and chronic assessment factors of 5 and 10 to the acute and chronic values, respectively, results in

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. ([http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono\(2014\)4&doclanguage=en](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>).

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concentrations of concern (COCs) of 20 mg/L (20,000 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 basis of greater exposure potential compared to the general population who do not use specific products.

For this new chemical assessment, EPA assessed inhalation and dermal exposures to workers. Releases to water and air were estimated. Exposure to the general population was assessed via inhalation exposure to fugitive emissions. Exposure to the general population via ingestion of drinking water or fish was not assessed because the new chemical substance is expected to be digested in the gastrointestinal tract. Exposures to consumers were not assessed because consumer uses were not identified as conditions of use.

Risk Characterization: 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).

EPA qualitatively assessed the new chemical substance due to the lack of dose-response information for the identified hazards (sensitization and irritation). As no systemic hazards were identified for this new chemical substance and no effects were identified in the available repeated dose studies for an analogue, a quantitative human health risk assessment was not conducted. Sensitization and irritation hazards to workers via inhalation and dermal contact were not quantified due to a lack of dose-response information, however, hazards will be mitigated if exposures are controlled by the use of appropriate PPE, including impervious gloves, clothing which covers any exposed areas of the arms, legs and torso, and a full-face NIOSH-certified particulate-filter respirator. EPA expects that workers will use appropriate personal protective equipment (i.e., impervious gloves, clothing, and a respirator), consistent with the Safety Data Sheet provided by the PMN submitter, in a manner adequate to protect them.

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Sensitization and irritation hazards to the general population via exposures to fugitive air releases were not quantified due to a lack of dose-response information; however, hazards are expected to be mitigated by dilution of the new chemical substance upon release into environmental media. Risks were not assessed for general population via drinking water or fish ingestion as the new chemical substance is expected to be digested in the gastrointestinal tract. 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.

EPA also identified based on a patent search that a reasonably foreseen use of this chemical substance is as an enzyme in chemical synthesis. EPA expects exposures to be similar or lower than those assessed for the intended conditions of use; therefore, EPA concludes that the reasonably foreseen conditions of use are not likely to present unreasonable risk.

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.

04/16/19

Date:

/s/

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