TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-16-0532

Number: P-16-0532
TSCA Section 5(a)(3) Determination: Chemical substance not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Generic: Substituted heteromonocycle

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic): Imported ingredient used in fertilizer manufacturing.
Known conditions of use: Chemical intermediate.
Reasonably foreseen conditions of use: Chemical intermediate. Two patents were found in the public domain for use of the PMN substance as a chemical intermediate.

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 estimates that the new chemical substance could be very persistent, the chemical substance has low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative. Based on test data on the PMN substance and analogous chemical substances, EPA estimates that the chemical substance has low human health hazard and low environmental hazard, and is therefore not likely to present an 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 may present an unreasonable risk. EPA estimated physical/chemical and fate properties of this new chemical substance using EPI

[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.

(Estimation Programs Interface) Suite™, a suite of physical/chemical property and environmental fate estimation programs (https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface). Based on these estimates, the chemical substance is expected to be removed with an efficiency of 90% during wastewater treatment due to biodegradation. Volatilization to air is expected to be negligible, and migration to groundwater is expected to be rapid.

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 this 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). EPA estimates the aerobic biodegradation half-life to be less than two months, which indicates that the chemical substance is expected to be of low persistence in aerobic environments (e.g., surface water). The anaerobic biodegradation half-life is estimated to be greater than six months, which indicates that the chemical substance may be very persistent in 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 to bioaccumulate 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). These estimates indicate that the chemical substance has low bioaccumulation potential (bioconcentration factor = 3.2; bioaccumulation factor = 0.89). Although EPA estimates that the new chemical substance could be very persistent, the chemical substance has low potential for bioaccumulation, such that repeated exposures are not expected to cause food chain effects via accumulation in exposed organisms.

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[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)

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 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 test data on the new chemical substance and on analogous chemicals. Based on physical/chemical properties, EPA estimates absorption of the neat material to be nil through the skin and poor through the skin when in solution. Absorption is estimated to be good from the lung based on physical/chemical properties and good from the GI tract based on analogue data. Test data available for the PMN chemical indicate it is not an irritant to skin or eyes. Potential for sensitization was identified based on physical-chemical properties; however, EPA concludes that the substance is unlikely to be a sensitizer based on results of multiple tests for an analogous chemical. Testing of the PMN substance in a bacterial reverse mutation test yielded negative results. Potential concern for developmental toxicity was identified based on a structural alert ([claimed CBI]). A NOAEL of 1,000 mg/kg/day for developmental toxicity for an analogous chemical was identified in a Reproduction/Developmental Toxicity Screening Test (OECD TG 421) and indicates the PMN substance is expected to have low human health hazard with respect to developmental toxicity. This NOAEL was used for quantitative risk assessment of the PMN substance. Overall, EPA expects human health hazard associated with the PMN substance to be low.

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

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[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)), 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)

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-relationships-ecosar-predictive-model). ECOSAR predicts fish, daphnid, and algae LC_{50} values to be greater than 100 mg/L, and fish and daphnid chronic values to be greater than 10 mg/L, indicating the new chemical substance is expected to have low environmental hazard. Application of acute and chronic assessment factors of 5 and 10, results in estimated acute and chronic concentrations of concern of 20,000 and 1,000 ppb, respectively.

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. Due to low hazard, EPA expects that this chemical substance is not likely to present an unreasonable risk even if potential exposures were high.

Potentially Exposed or Susceptible Subpopulation(s) (PESS): EPA considers workers to be a PESS on the basis of greater exposure potential compared to the general population. EPA has assessed risks to workers under the conditions of use of the PMN substance and concludes that workers are not expected to be exposed to the PMN substance at levels that would present an unreasonable risk. EPA assessed risks to the general population under the conditions of use and concludes that, due to low hazard, risks to the general population are not likely. 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. Consumer exposures were not assessed for this PMN substance because consumer uses were not identified as intended, known, or reasonably foreseen uses.

9/6/18
Date:

/s/
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