TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-16-0575

Number: P-16-0575
TSCA Section 5(a)(3) Determination: Chemical substance not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Specific: Glucosyltransferase (International Union of Biochemistry and Molecular Biology (IUBMB) enzyme nomenclature recommendations: IUBMB Number 2.4.1.5, CASRN: 9032-14-8)

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic): Imported for use in the polymerization of glucose, application methods that do not result in worker inhalation exposure 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 described in footnote 1, EPA has identified manufacture (including import), processing, or use that results in worker inhalation as a reasonably foreseen condition of use based on information provided by the submitter indicating manufacturing, processing and/or use in another country that may result in worker inhalation exposure.

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 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 substance could be persistent, the chemical substance has low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative. Based on data on analogous chemicals, EPA estimates that the chemical substance has low environmental hazard and potential for the following human health hazard: respiratory sensitization. EPA did not identify risks to health or the environment when the methods described in the PMN, which prevent inhalation exposure to workers, are used. Therefore, EPA concludes that the new chemical is 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 substance under the conditions of use that are not subject to the proposed SNUR, in order to determine that the chemical substance is 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 substance is 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 new chemical substance is likely to present an unreasonable risk. EPA estimated physical/chemical and fate properties of this new chemical substance using data for analogous chemicals. The chemical substance is estimated to be removed with an efficiency of 90% during wastewater treatment due to strong sorption to sludge

[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.

and partial destruction by biodegradation. Sorption to sludge, soil and sediment are all estimated to be strong, resulting in negligible migration to groundwater. Volatilization to air is estimated to negligible based on high molecular volume. 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. Based on data for analogous chemicals, EPA estimated the aerobic biodegradation half-life and anaerobic biodegradation to be between greater than 2 months to less than 6 months. These estimates for biodegradation indicate that the chemical substance may be persistent in aerobic environments (e.g., surface water) and 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. The chemical substance has low bioaccumulation potential based on data on analogous substances and high molecular volume, which limit bioavailability and bioaccumulation. Although EPA estimated that the new chemical substance could be 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.

Human Health Hazard[5]: Human health hazard is relevant to whether a new chemical substance

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[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)

[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,

is likely to present an unreasonable risk because the significance of the risk is dependent upon both the hazard (toxicity) of the chemical substance and the extent of exposure to the substance. EPA estimated the human health hazard of the new 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. For this new chemical substance, absorption is estimated to be nil through the skin, lung and GI tract based on physical/chemical properties. EPA identified respiratory sensitization hazard if inhaled, based on potential allergenic properties of foreign enzymes. No other hazards were identified.

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 new chemical substance and the extent of exposure to the substance. EPA estimated environmental hazard of this new chemical 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 QSAR for the class of phenols. ECOSAR predicted acute toxicity values for fish, daphnid, and algae of >100 mg/L and chronic toxicity values for fish, daphnia, and algae of >10 mg/L. These toxicity values indicate the new chemical substance is expected to have low hazard. Application of assessment factors of 5 and 10 to acute and chronic toxicity values results in estimated acute concentration of concern (COCs) of 20 mg/L (20,000 ppb) and chronic COC of 1 mg/L (1,000 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 releases 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-

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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 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).

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 assessment, EPA qualitatively assessed worker exposure via dermal contact, and inhalation exposure is not expected under the intended conditions of use for workers. General population exposure was not assessed because environmental releases are expected to be low (below modeling thresholds). Consumer exposures were not assessed because consumer uses were not identified as conditions of use.

Under the conditions of use described in the PMN, worker inhalation exposure is expected to be negligible, and therefore inhalation risks are also negligible. Risks were not identified for workers for respiratory sensitization based specifically on the exposure controls in place that are expected to prevent inhalation exposures. Risks were not evaluated for workers via dermal contact because hazards for this route of exposure were not identified, although EPA expects that workers will use appropriate personal protective equipment, including dermal protection consistent with the Safety Data Sheet submitted with the PMN, in a manner adequate to protect them.

Risks were not evaluated for the general population via inhalation because air releases of the new chemical substance are expected to be low (below modeling thresholds). Risks were not evaluated for the general population via drinking water based on no identified hazards for this route of exposure. Risks were not evaluated for consumers because consumer uses were not identified as a conditions of use. Under the intended conditions of use, the chemical substance is not likely to present an unreasonable risk to human health.

Risks to the environment are evaluated by comparing the estimated surface water concentrations with the estimated acute and chronic concentrations of concern. Risks to the environment were not identified for this new chemical substance due to no releases to water associated with the conditions of use. Due to low hazard, EPA believes that this chemical substance would be unlikely to present an unreasonable risk even if exposures were high.

It is reasonably foreseen that manufacture (including import), processing, or use could occur such that workers are exposed via the inhalation route. It is reasonably foreseen based on information provided by the submitter indicating manufacturing, processing or use in another country that may result in worker inhalation exposure. The SNUR that has been proposed for this chemical substance defines certain conditions of use as significant new uses. The proposed significant new use is manufacture, processing, or use of the substance that results in inhalation exposures to the new chemical substance. 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/
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