**TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0221**

**Number: P-18-0221**
**TSCA Section 5(a)(3) Determination**: The chemical substance is not likely to present an unreasonable risk (5(a)(3)(C))

**Chemical Name:**
Generic: Polyglycerol reaction product with acid anhydride, etherified

**Conditions of Use (intended, known, or reasonably foreseen)[1]:**
Intended conditions of use (specific): Manufacture for use as a binder for wood panels, 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 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 EPA's TSCA New Chemicals Program Chemical Category for Esters[2] and test data on analogous chemical substances, EPA estimates that the chemical substance has low environmental hazard and potential for the following human health hazards:

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[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.

skin and lung sensitization, mutagenicity, carcinogenicity, and developmental, reproductive, liver, and kidney toxicity. 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 based on data for analogous soluble polymers. The chemical substance is estimated to be removed during wastewater treatment with an efficiency of 90% via sorption and biodegradation. Removal by biodegradation is estimated to be moderate to high. Sorption to sludge is estimated to be low to strong, and sorption to soil and sediment is estimated to be strong, resulting in slow migration to groundwater. Volatilization to air is expected to be negligible because the substance is estimated to have a low vapor pressure and a low Henry's law constant. Overall, these estimates are indicative of low potential for this chemical substance to volatilize into the air and a low potential for this chemical substance 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 the biodegradation half-lives of this new chemical substance using data on analogous soluble polymers and 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 estimated the aerobic biodegradation half-life to be less than two months to two to six months and the anaerobic biodegradation half-life to be greater than six months. These biodegradation half-lives indicate that the new chemical substance may have limited to moderate persistence in aerobic environments (e.g., surface water) and may be very persistent in anaerobic environments (e.g., sediment). However, based on the high water solubility and low log$K_{OW}$ for this new chemical substance, it is not likely that this substance will accumulate 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

[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)

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 data for analogous soluble polymers and EPI Suite™. EPA estimated that the new chemical substance has low bioaccumulation potential (bioconcentration factor = 3, bioaccumulation factor = 1). EPA estimated that the new chemical substance would be of limited to moderate persistence, and the new chemical substance has low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative.

**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, identified structural alerts (epoxide-forming double bonds), analogue data and QSAR predictions identified in the Sustainable Futures submission. Absorption of the low molecular weight fractions ([claimed CBI] < 500 and [claimed CBI] < 1000) is estimated to be good through the GI tract and nil to poor through the skin and lungs based on physical/chemical properties. EPA identified skin and lung sensitization, germ cell mutagenicity, carcinogenicity and developmental, reproductive, liver, kidney toxicity as hazards based on potential epoxide formation via metabolic oxidation of the [claimed CBI]. The submitter provided a Sustainable Futures analysis predicting low concern for acute and systemic toxicity based on QSAR models; however, enzymatic or acid ester hydrolysis of the new chemical substance in the body may release [claimed CBI], with subsequent concern for adverse systemic effects (growth retardation, kidney toxicity, mortality).

EPA identified a LOAEL of 250 mg/kg/day and a LOAEC of 720 mg/m$^3$ as points of departure (POD) for oral and inhalation exposure, respectively, based on potential release of [claimed CBI]. EPA did not identify a POD for potential formation of the epoxide oxidation product.

EPA qualitatively assessed sensitization because dose-response information is not available for this endpoint.

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[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 QSARs for esters and vinyl/allyl/propargyl ethers (assessed using [claimed CBI] and [claimed CBI] MW; ECOSAR V2.0). Acute toxicity values estimated for fish, aquatic invertebrates, and algae are >100 mg/L. Chronic toxicity values estimated for fish, aquatic invertebrates, and algae are >10 mg/L. These toxicity values indicate that the new chemical substance is expected to have low environmental hazard. Application of assessment factors of 5 and 10 to acute and chronic toxicity values, respectively, results in acute and chronic concentrations of concern 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 estimated occupational exposure and environmental release of the 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 used 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 dermal exposure to workers, and inhalation exposure to workers is not expected. EPA assessed exposure to the general population via

[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).

drinking water exposures from landfill releases. Exposure to the general population via inhalation was not assessed because releases to air were 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, which compares an effect level to an estimated exposure concentration, 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. 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 considers whether the risks would be mitigated by the use of PPE (e.g., impervious gloves, respirator).

Human health risks were evaluated qualitatively and quantitatively. Quantitative risks from exposure to the new chemical substance were evaluated using the route-specific effect levels described above (i.e., LOAEL and LOAEC). Risks were identified for workers for adverse systemic effects via dermal exposure based on quantitative hazard data for the analogue, [claimed CBI] (MOE = 194; benchmark MOE = 1000). EPA also identified worker risks for skin sensitization, mutagenicity, carcinogenicity, and developmental, reproductive, liver, and kidney toxicity via dermal exposure based on potential epoxide formation. These risks were not quantified due to a lack of dose-response (sensitization) and a lack of suitable toxicity data for these hazards. Risks will be mitigated if exposures are controlled by the use of appropriate PPE, including impervious gloves. EPA expects that workers will use appropriate personal protective equipment (i.e., impervious gloves), consistent with the Safety Data Sheet prepared by the PMN submitter, in a manner adequate to protect them.

Risks were not identified for the general population for systemic toxicity via oral exposure based on quantitative hazard data for the analogue, [claimed CBI] ($MOE_{adult}$ = 170,000; $MOE_{infant}$ = 42,000; benchmark MOE = 1000). Although general population risks for skin sensitization, mutagenicity, carcinogenicity and liver, kidney and reproductive toxicity were identified via oral exposure based on the potential for epoxide formation in the body, these risks are unlikely to be unreasonable given the low exposures from estimated for ground water and the very high allyl FGEW [claimed CBI].

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. 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.

12/21/2018
Date:

/s/
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