TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-14-0482

Number: P-14-0482
TSCA Section 5(a)(3) Determination: The chemical substance is not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Generic: Organic salt.

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic): Manufacture for processing and use as an industrial chemical, 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 has identified the following reasonably foreseen conditions of use: use for [claimed CBI] based on conditions of use specified in the initial PMN that were subsequently amended and use as a [claimed CBI] 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 and the terms of the proposed Significant New Use Rule (SNUR) signed by EPA.[2] Although EPA

[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] 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

estimates that the new chemical substance's cation could be very persistent, the chemical substance's anion and cation both have low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative (the anion is not estimated to be persistent). Based on test data on the new chemical substance and analogous chemical substances, EPA estimates that the chemical substance has moderate environmental hazard and the potential for the following human health hazards: developmental toxicity, neurotoxicity, and skin sensitization. The PMN describes conditions of use that mitigate both ecological and human health risks. Therefore, EPA concludes that the new chemical substance is not likely to present an unreasonable risk 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 chemical may present an unreasonable risk. EPA estimated physical/chemical and fate properties of the anion and cation components using data for analogous chemical substances. The anion component of the chemical substance is expected to be removed with an efficiency of 90 - 99% during wastewater treatment via sorption and the cation component is expected to be removed with an efficiency of 0 - 50% during wastewater treatment via possible biodegradation. For both the anion and the cation, sorption to sludge is estimated to be low, and sorption to soils and sediments is also estimated to be low. Migration to groundwater for the anion component is negligible but migration to ground water for the cation

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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

is rapid. Time for complete ultimate aerobic biodegradation for the anion is days while for the cation it is months. Due to low volatility for highly soluble salts, this new chemical substance is estimated to undergo negligible volatilization to air. Overall, these estimates are indicative of low potential for the anion of the chemical substance to volatilize into the air and low potential for it to migrate into groundwater. However, for the cation, estimates are indicative of low potential to volatilize into the air and high potential 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 the anion using data for acetate. EPA estimated that the aerobic and anaerobic biodegradation half-lives of the anion are less than 2 months. These estimates indicate that the anion will not be persistent in aerobic environments (e.g., surface water) or anaerobic environments (e.g., sediment). EPA estimated biodegradation half-lives of the cation using data for analogous chemical substances, *i.e.*, [claimed CBI]. EPA estimated that the aerobic and anaerobic biodegradation half-lives of the cation will be more than 6 months. These estimates indicate that the cation will be persistent in aerobic environments (e.g., surface water) and 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 anion to bioaccumulate using data for acetate. These estimates indicate that the anion has low bioaccumulation potential based on high water solubility. EPA estimated that the anion could have low persistence and a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. EPA estimated the potential for the cation to bioaccumulate using data for analogous chemical substances, *i.e.*, [claimed CBI]. These estimates indicate that the cation has low bioaccumulation potential based on high water solubility. Although EPA estimated that the cation could be very 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.

[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)

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 health hazard of this chemical substance based on data submitted on the new chemical and comparison to structurally analogous chemical substances for which there is information on human health hazard. For this new chemical substance, absorption is estimated to be poor through the skin based on data on the new chemical and good through the lung and gastrointestinal tract based on analogue data. EPA identified developmental toxicity and neurotoxicity based on a component of the new chemical substance [claimed CBI]. EPA also identified skin sensitization based on positive results in a study submitted on the new chemical (OECD 429). Submitted test data for the new chemical indicate it does not cause serious eye damage or irritation (OECD 437 and EpiOcular™ Eye Irritation Test), does not show corrosive potential (EpiDerm™ Skin Corrosion Test), is not mutagenic (with or without metabolic activation) (OECD 471), and not acutely toxic via oral exposure (OECD 423).

EPA quantitatively assessed this new chemical substance using data on a component of the new chemical [claimed CBI]. A NOAEL of 60 mg/kg/day was identified based on developmental toxicity in a Prenatal Developmental Toxicity Study (OECD 414). This NOAEL was used to derive exposure route- and population-specific points of departure for quantitative risk assessment, described below.

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

[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] 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).

upon both the hazard (or toxicity) of the chemical substance and the extent of exposure to the substance. EPA determined environmental hazard for this new chemical substance based on SAR predictions for [claimed CBI] (special class within ECOSAR) and test data on the new chemical substance. Acute toxicity values estimated for fish, aquatic invertebrates and algae are greater than 100 mg/L (SAR predictions for [claimed CBI]), 25.8 mg/L (test data on the new chemical substance), and 27.8 mg/L (test data on new chemical), respectively. Chronic toxicity values estimated for fish, aquatic invertebrates, and algae are greater than 10 mg/L (SAR predictions for [claimed CBI]), 0.368 mg/L (ACR of 70 supported by scientific literature on [claimed CBI]), and 3.8 mg/L (test data on the new chemical) for fish, aquatic invertebrates, and algae. These toxicity values indicate that the new chemical substance is expected to have moderate environmental hazard. Application of assessment factors of 5 and 10 to acute and chronic toxicity values results in an acute concentration of concern (COC) of 5.160 mg/L (5,160 ppb) and a chronic COC of 0.037 mg/L (40 ppb).

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 dermal exposure to workers. Inhalation exposures to workers were estimated to be negligible. Releases to water and air were estimated. EPA assessed exposure to the general population via drinking water and fish ingestion. EPA did not estimate exposures for consumers as no consumer uses are expected.

Risk Characterization: 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 in the absence of personal protective equipment such as gloves and respirators and 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 substance were evaluated using the point of departure (i.e., NOAEL) described above. Sensitization hazard via dermal contact was identified for workers based on data on the new chemical. Risks were also identified for workers for developmental toxicity via dermal exposure (MOE = 29; benchmark MOE = 100). Risks would be mitigated if exposures can be controlled by the use of appropriate PPE, including impervious gloves. EPA expects that employers will require and workers will use appropriate personal protective equipment (i.e., impervious gloves, chemically protective clothing), 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 developmental toxicity via drinking water (MOE_{Adult} = 2,010 and MOE_{Infant} =480; benchmark MOE =100) or fish ingestion (MOE = 5,460; benchmark MOE =100). Risks to consumers were not evaluated because consumer uses were not identified as conditions of use.

Risks to the environment were evaluated by comparing estimated surface water concentrations with the acute and chronic concentrations of concern. Risks to the environment were not identified due to releases to water that did not exceed the acute COC of 5,160 ppb and did not exceed the chronic COC of 40 ppb.

It is reasonably foreseen, based on a patent search and the assessment conducted on the initial PMN submission that was subsequently amended, that increased production volume and uses other than those described in the amended PMN could result in greater exposures and thus unreasonable human health and ecological risk. The SNUR that has been proposed for this chemical substance defines certain condition of use as significant new uses. The proposed significant new uses are: annual production volume greater than [claimed CBI] and any use other than the use described in the PMN. 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).

04/15/19 /s/

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