

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0263

Number: P-18-0263

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

Chemical Name:

Generic: Mixed alkyl esters-, polymer with N1-(2-aminoethyl)- 1,2-ethanediamine, aziridine, N-acetyl derivs., acetates (salts)

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

Intended conditions of use (generic): Import and process for use as and use as a solution additive, 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. EPA estimated that the anion (acetate) could have limited persistence and low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Although EPA estimated that the polymeric moieties could be very persistent, the substance has low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms.

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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Based on EPA's TSCA New Chemicals Program Chemical Category for Polycationic Polymers² and test data on analogous chemical substances, EPA estimates that the chemical substance has high environmental hazard and potential for the following human health hazards: Skin Irritation, Eye Irritation, and Specific Target Organ 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 the anion (acetate) using data available for the anion and EPI (Estimation Program Interface) Suite™ (<http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface>) and of the polymeric moieties using data for analogue(s) (polymers). In wastewater treatment, the anion (acetate) is expected to be removed with an efficiency of 90% due to biodegradation and the polymeric moieties are expected to be removed with an efficiency of 90% due to sorption. Removal of the anion (acetate) by biodegradation is high and removal of the polymeric moieties by biodegradation is negligible. Sorption of the anion (acetate) to sludge, soil, and sediment is expected to be low and sorption of the polymeric moieties to sludge is expected to be strong and to soil and sediment is expected to be very strong. Migration of the anion (acetate) to groundwater is expected to be negligible due to biodegradation and migration of the polymeric moieties to groundwater is expected to be negligible due to very strong sorption to soil and sediment. Due to low estimated vapor pressure and Henry's law constant, the anion (acetate) is expected to undergo negligible volatilization to air and the polymeric moieties are expected to undergo negligible volatilization due to low estimated vapor pressure. Overall, these estimates indicate that the anion (acetate) and the polymeric moieties have low potential to volatilize to air and low potential to migrate to groundwater.

Persistence³: 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 degradation half-lives of the anion (acetate) using data available for the anion and of the polymeric moieties using data for analogue(s) (polymers). EPA estimated that the anion's (acetate) aerobic and anaerobic biodegradation half-lives are < 2 months; and that the polymeric moieties' aerobic and anaerobic biodegradation half-lives are > 6 months. These estimates indicate that the anion (acetate) may have limited persistence in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment). Further, these estimates indicate that

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>.

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 if 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 if there are equivalent or analogous data. (64 FR 60194; November 4, 1999)

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the polymeric moieties may be very persistent in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment).

Bioaccumulation⁴: 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 (acetate) to bioaccumulate using EPI Suite™ and of the polymeric moieties to bioaccumulate using data for analogue(s) (polymers). EPA estimated that the anion (acetate) has low bioaccumulation potential based on BCFBAF model result < 1,000 and the polymeric moieties have low bioaccumulation potential based on large predicted molecular volume, which limits bioavailability (anion bioconcentration factor = 3 [estimated by linear regression from log Kow] and bioaccumulation factor = 1 [estimated by the Arnot-Gobas method (2003)]).⁵ EPA estimated that the anion (acetate) could have limited persistence and low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Although EPA estimated that the polymeric moieties could be very persistent, the 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 Hazard⁶: 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

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 if 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 if there are equivalent or analogous data. (64 FR 60194; November 4 1999)

⁵ Arnot JA, Gobas FAPC. 2003. A generic QSAR for assessing the bioaccumulation potential of organic chemicals in aquatic food webs. *QSAR and Combinatorial Science* 22: 337-345.

⁶ 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.

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estimated physical/chemical properties and by comparing it to structurally analogous chemical substances for which there is information on human health hazard. Absorption of the new chemical substance is expected to be nil via all routes based on physical/chemical properties. For the new chemical substance, EPA identified hazards for lung effects and irritation to the skin, eyes, and respiratory tract from cationic binding to lung membranes. EPA identified a corrected Lowest Observed Adverse Effect Concentration (LOAEC) of 587.2 mg/m³ based on cationic lung binding which was protective for pulmonary effects and was used to derive exposure route- and population-specific points of departure for quantitative risk assessment. EPA qualitatively evaluated irritation effects.

Environmental Hazard⁷: 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 determined environmental hazard for this new chemical substance based on Structure Activity Relationships (SAR) predictions for cationic polymers (special class within ECOSAR v2.0). This substance falls within the TSCA New Chemicals Category of Polycationic Polymers. Acute toxicity values estimated for fish, aquatic invertebrates, and algae are 1.34 mg/L, 1.11 mg/L, and 0.20 mg/L, respectively. Chronic toxicity values estimated for fish, aquatic invertebrates, and algae are 0.075 mg/L, 0.079 mg/L, and 0.052 mg/L, respectively. These toxicity values indicate that the new chemical substance is expected to have high environmental hazard. Application of assessment factors of 4 and 10 to acute and chronic toxicity values, respectively, results in acute and chronic concentrations of concern of 0.05 mg/L (50 ppb) and 0.005 mg/L (5 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.

⁷ 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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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 worker exposures via the inhalation and dermal routes. Releases to water, air, and landfill were estimated. Exposure to the general population was assessed via drinking water. Exposures to the general population via fish ingestion were not assessed because bioaccumulation potential was evaluated to be low and exposures via groundwater impacted by landfill leaching and inhalation were not assessed because exposures were expected to be negligible (below modeling thresholds). Consumer exposures were not assessed because consumer uses were not identified as conditions of use.

Risk Characterization: EPA applies a margin of exposure approach to calculate potential human health risks of new chemicals. A benchmark (acceptable) margin of exposure (MOE) is derived by applying uncertainty factors (UF) 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 Lowest Observed Adverse Effect Level (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 1,000 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 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).

Risks to human health for the new chemical substance were evaluated using the route-specific effect levels (i.e., corrected LOAEC) described above. Risks were identified for workers for lung effects via inhalation based on quantitative hazard data for an analogue (MOE = 771; Benchmark MOE = 1,000; Fold Factor = 1). Risks were not evaluated for workers for lung effects via dermal contact because the hazards are not relevant to the exposure route. Irritation hazards to workers via inhalation and dermal contact were identified based on a structural alert for cationic binding. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards. However, exposures can be mitigated by the use of appropriate personal protective equipment (PPE), including impervious gloves, eye protection, and respiratory protection. EPA expects that employers will require and that workers will use appropriate PPE consistent with the Safety Data Sheet (SDS) prepared by the submitter, in a manner adequate to protect them.

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Risks were not evaluated for the general population for lung effects via drinking water because the hazards are not relevant to the exposure route. Risks were not evaluated for the general population via fish ingestion because bioaccumulation potential was evaluated to be low or via groundwater impacted by landfill leaching and inhalation, because exposures were expected to be negligible. Irritation hazards to the general population are not expected via drinking water ingestion due to dilution of the chemical substance in the media. 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 and exceeded the chronic COC of 5 ppb for less than 20 days/year (18 days/year during use 1 of the new chemical substance).⁸

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.

06/29/2020
Date: _____

/s/

Madison H. Le, Director
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⁸ The 20-day criterion for concluding chronic risk is not likely is based on partial life cycle tests (daphnid chronic and fish early life stage tests) that typically range from 21 to 28 days in duration.