

## TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-19-0028

**Number: P-19-0028**

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

**Chemical Name:**

Generic: Alkyl salicylate, metal salts

**Conditions of Use (intended, known, or reasonably foreseen)<sup>1</sup>:**

Intended conditions of use (generic): Import for use as a lubricating oil 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. Although EPA estimated that the new chemical substance could be very persistent, the new chemical substance has low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative. Based on negligible water solubility and submitted test data on analogous chemical substances, EPA estimates that the chemical substance has low environmental hazard and potential for the following human health hazards: irritation, sensitization, and lung surfactancy. EPA concludes that the new chemical substance is not likely to present an unreasonable risk under the conditions of use.

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<sup>1</sup> 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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**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 new chemical substance using submitted data for the new chemical substance and an analogous chemical substance. In wastewater treatment, the new chemical substance is expected to be removed with 90% efficiency based on sorption. Migration of the new chemical substance to groundwater is expected to be negligible due to very strong sorption to soil and sediment. Due to low estimated vapor pressure, the new chemical substance is expected to undergo negligible volatilization to air. Overall, these estimates indicate that the new chemical substance has low potential to volatilize to air and low potential to migrate to groundwater.

**Persistence<sup>2</sup>:** 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 new chemical substance using submitted data for the new chemical substance and an analogue. EPA estimated that the aerobic biodegradation half-life of this substance is two to greater than six months and the anaerobic biodegradation half-life is greater than six months. These estimates indicate that this substance will partition primarily to soil and sediment, where it will be very persistent, depending on alkyl chain length and degree of branching.

**Bioaccumulation<sup>3</sup>:** 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 data submitted on analogous chemical substances. Based on the submitted data and on expected metabolism of the new chemical substance, EPA estimates that the new chemical substance has low bioaccumulation potential. Although EPA estimated that the new chemical substance 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.

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<sup>2</sup> 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)

<sup>3</sup> 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)

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**Human Health Hazard<sup>4</sup>:** EPA estimated the human health hazard of this chemical substance based on its estimated physical/chemical properties, using data submitted on the PMN and other structural information. Absorption is likely poor through the skin, lung and GI tract based on physical/chemical properties. For the new chemical substance, EPA initially identified chelation, blood, liver, and developmental effects as hazards based on analogue data but dismissed these concerns in the risk assessment based on no effects observed in an OECD 422 study on the new chemical substance. Lung surfactancy was identified as a hazard based on structural properties (charged polar heads and hydrophobic tail). Sensitization was identified as a hazard based on submitted test data in an OECD 429 LLNA on the new chemical substance, however formulations containing approximately 5% of 2 close analogues were negative for sensitization in Guinea pigs (OECD 406). EPA quantitatively assessed this new chemical using submitted test data on the PMN and data on surfactant effects. A NOEL of 1000 mg/kg-bw/day was identified based on no effects observed at the highest tested dose in a repeated-dose study and reproductive/developmental toxicity screening test (OECD 422) on the new chemical substance. A LOAEC of 0.08 mg/m<sup>3</sup> was identified for surfactant effects in the lungs using didecyl dimethyl ammonium chloride in a 21-day inhalation toxicity study. The NOEL and LOAEC were used to derive exposure route- and population-specific points of departure for quantitative risk assessment, described below. Benchmark MOEs of 100 and 1000 were used for the NOEL and LOAEC, respectively.

**Environmental Hazard<sup>5</sup>:** Environmental hazard is relevant to whether a new chemical substance is likely to present unreasonable risk because the significance of the risk is dependent

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<sup>4</sup> 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.

<sup>5</sup> 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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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 predictions based on the negligible water solubility of the new chemical substance and submitted acute aquatic test data on an acceptable analogue. Acute and chronic toxicity values estimated for fish, aquatic invertebrates, and algae are all no effects at saturation. These toxicity values indicate that the new chemical substance is expected to have low environmental hazard. Because hazards are not expected up to the water solubility limit, acute and chronic concentrations of concern are not identified.

**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 assessment, EPA assessed worker exposure via dermal exposure but not inhalation exposures since they are expected to be negligible based on low vapor pressure ( $VP < 0.001$ ) and general population via drinking water and fish ingestion but not inhalation since exposures are expected to be negligible. Consumer exposures were assessed via dermal exposure but not inhalation since exposures are expected to be negligible.

**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

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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 substances were evaluated using the points of departure (i.e., NOEL) described above. Risks were not identified for workers based on no effects observed at the highest tested dose via dermal exposure based on quantitative hazard data for the new chemical (MOE = 622; benchmark MOE = 100). Sensitization hazards to workers via dermal contact were identified based on test data on the new chemical substance. 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. EPA expects that employers will require and that workers will use appropriate PPE consistent with the Safety Data Sheet prepared by the new chemical submitter, in a manner adequate to protect them. Risks were not evaluated for workers via inhalation because inhalation exposures were determined to be negligible.

Risks were not identified for the general population based on no effects observed at the highest tested dose via drinking water exposure or fish ingestion (All MOEs = >2,500; benchmark MOE = 100). Risks were not identified for the general population for sensitization via drinking water or fish ingestion since these concerns are expected to be mitigated by dilution in the media. Risks were not evaluated for the general population via stack air or fugitive air inhalation because inhalation exposures were below modeling thresholds.

Risks were not identified for the consumers (Adult ADR used) based on no effects observed at the highest tested dose via dermal exposure based on quantitative hazard data for the new chemical (MOEs >3 million; benchmark MOE = 100). Risks were not identified for sensitization effects via dermal exposure based on test data for close analogues in a formulation similar to the intended consumer product. Risks for this hazard endpoint were not quantified due to lack of dose-response information. However, based on negative results from submitted test data using similar formulations to the consumer product with close analogues, risks for sensitization were unlikely for consumers.

Risks to the environment from acute and chronic exposure are not expected at any concentration of the new chemical substance soluble in the water (i.e., no effects at saturation).

Because worker exposures can be controlled by PPE and no unreasonable risks to the general population, consumers, or environment were identified, 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.

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