

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0165 and P-18-0166

Number: P-18-0165 and P-18-0166

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

Chemical Name:

Generic (P-18-0165): 2,5-Furandione, polymer with ethenylbenzene, 4-hydroxy-substituted butyl amide, sodium salts.

Generic: (P-18-0166): 2,5-Furandione, polymer with ethenylbenzene, 4-hydroxy- substituted butyl [3-[2-[1-[(2-methoxyphenyl)amino]carbonyl]-2-oxopropyl]diazenyl]phenyl]substituted, sodium salts.

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

Intended conditions of use (specific): Manufacture for use as a chemical intermediate, consistent with the manufacturing, processing, use, distribution, and disposal information described in the PMNs.

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 substances are 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. The new chemical substances are ionic compounds, or salts, that are comprised of both an anion and cation (sodium). Estimations of physical/chemical and fate properties are not applicable for the cation (sodium); the cation (sodium) is an element (alkali metal) and is unlikely to impact the

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.

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0165 and P-18-0166

overall persistence and bioaccumulation of the new chemical substance. Although EPA estimated that the anions could be very persistent, the substances have a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Based on EPA's TSCA New Chemicals Program Chemical Category for Polyanionic Polymers (& Monomers)² and test data on analogous chemical substances, EPA estimates that the chemical substances have moderate environmental hazard and potential for the following human health hazards: developmental toxicity, systemic effects, and irritation to eyes, lungs and mucous membranes. EPA concludes that the new chemical substances are 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 anions using data for analogue(s) (polyanionic polymers) and data submitted for the new chemical substances. The cation (sodium) is not expected to drive the human health and ecological hazard assessments. The cation (sodium) is also not expected to be a concern for food chain effects and was not evaluated for persistence and bioaccumulation. In wastewater treatment, the anions are expected to be removed with an efficiency of 0% to 90% due to sorption. Removal of the anions by biodegradation is negligible. Sorption of the anions to sludge is expected to be low to moderate and to soil and sediment is expected to be moderate to strong. Migration of the anions to groundwater is expected to be slow to moderate due to moderate to strong sorption to soil and sediment. Due to low estimated vapor pressure and Henry's law constant, the anions are expected to undergo negligible volatilization to air. Overall, these estimates indicate that the anions have low potential to volatilize to air and have low to moderate 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 anions using data for analogues (polyanionic polymers). EPA estimated that the anions' aerobic and anaerobic biodegradation half-lives are > 6 months. These estimates indicate that the anions may be very persistent in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment).

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 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)

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0165 and P-18-0166

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 anions to bioaccumulate using data for analogues (polyanionic polymers). EPA estimated that the anions have low bioaccumulation potential based on large predicted molecular volume, which limits bioavailability. Although EPA estimated that the anions could be very persistent, the substances have a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms.

Human Health Hazard⁵: 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 these chemical substances based on their estimated physical/chemical properties and by comparing them to structurally analogous chemical substances for which there is information on human health hazard. Absorption of new chemical substances is expected to be nil via all routes; the low molecular weight (LMW) fractions are expected to have moderate to poor absorption through the lungs and GI tract and nil absorption through the skin based on physical/chemical properties. For the new chemical substances, EPA identified developmental toxicity, systemic effects (altered blood clotting, muscle toxicity, bone-antiresorption), and irritation to eyes, lungs and mucous membranes as hazards based on the pH of [claimed CBI]. EPA identified a NOAEL of 400 mg/kg/day for developmental effects which was protective for all health effects with the exception of irritation and was used to derive exposure route- and population-specific points of departure. EPA qualitatively evaluated irritation hazards.

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, 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.

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0165 and P-18-0166

Environmental Hazard⁶: 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 these new chemical substances based on SAR predictions for anionic polymers (special class within ECOSAR v.2.0). These substances fall within the TSCA New Chemicals Category of Polyanionic Polymers (& Monomers). Acute toxicity values estimated for fish, aquatic invertebrates, and algae are > 100 mg/L, > 100 mg/L, and 9.5 mg/L, respectively. Chronic toxicity values estimated for fish, aquatic invertebrates, and algae are > 10 mg/L, > 10 mg/L, and 5 mg/L, respectively. These toxicity values indicate that the new chemical substances are expected to have moderate 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 2.375 mg/L (2,375 ppb) and 0.5 mg/L (500 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 substances under the intended conditions of use described in the PMNs 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.

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>).

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0165 and P-18-0166

For this assessment, EPA assessed worker exposure via dermal contact and inhalation exposure to workers is not expected. Releases to air were estimated. Exposure to the general population via inhalation was not assessed because releases to air were expected to be negligible (below modeling thresholds). Exposure to the general population via oral ingestion was not assessed because no releases to water were predicted. 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 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 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 route-specific effect levels (i.e., NOAEL) described above. Risks were not identified for workers for developmental toxicity via dermal exposure based on quantitative hazard data for an analogue of the LMW fraction ($MOE > 2,000,000$; Benchmark $MOE = 100$). Irritation hazards to workers via dermal contact were identified based on basic pH of the new chemical substances. Risks for this endpoint were not quantified due to a lack of dose-response for this hazard. However, exposures can be mitigated by the use of appropriate personal protective equipment (PPE), including impervious gloves and eye protection. 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 exposures are not expected.

Risks were not evaluated for the general population because oral exposures are not expected and inhalation exposures are expected to be negligible (below modeling thresholds). Risks to consumers were not evaluated because consumer uses were not identified as conditions of use.

Risks to the environment were not identified due to no releases to water.

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

TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0165 and P-18-0166

EPA has determined that the new chemical substances are not likely to present unreasonable risk to human health or the environment under the conditions of use.

11/07/2019
Date:

/s/
Tala R. Henry, Ph.D.
Deputy Director for Programs
Office of Pollution Prevention and Toxics