TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-19-0130

Number: P-19-0130
TSCA Section 5(a)(3) Determination: The chemical substances are not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Generic: Aminohydroxy naphthalenesulfonic acid, coupled with diazotized[(aminophenyl) sulfonyl]ethyl hydrogen sulfate and diazotized amino[[(sulfooxy)ethyl]sulfonyl]benzenesulfonic acid, salts.

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic): Import for processing and use as a dye, 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 identified a known use as a dye based on another TSCA submission.
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 and its hydrolysis product could be persistent, the substance and its hydrolysis product 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 Categories for

[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.

Acid Dyes and Amphoteric Dyes and Vinyl Sulfones[2] and test data on the new chemical substance and analogous chemical substances, EPA estimates that the chemical substance has moderate environmental hazard and potential for the following human health hazards: irreversible damage to eyes, irritation to eyes and mucous membranes, and kidney effects. 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 new chemical substance using data for analogue(s) (reactive azo dye) and data submitted for the new chemical substance and of the hydrolysis product using data for analogue(s) (azo dye) and data submitted for the new chemical substance. In wastewater treatment, the new chemical substance is expected to be removed with an efficiency of 0% to 90% due to variable hydrolysis (based on pH) and possible sorption (based on soil type) and the hydrolysis product is expected to be removed with an efficiency of 0% due to low biodegradability, low sorption, and low stripping. Removal of the new chemical substance by biodegradation is negligible and removal of the hydrolysis product by biodegradation is negligible. Sorption of the new chemical substance to sludge, soil, and sediment is expected to be low to strong and sorption of the hydrolysis product to sludge, soil, and sediment is expected to be low. Migration of the new chemical substance to groundwater is expected to be slow to rapid due to hydrolysis and migration of the hydrolysis product to groundwater is expected to be rapid due to low sorption to soil and sediment. Due to low estimated vapor pressure, the new chemical substance is expected to undergo negligible volatilization to air and the hydrolysis product is expected to undergo negligible volatilization due to low estimated vapor pressure and Henry's law constant. Overall, these estimates indicate that the new chemical substance has low potential to volatilize to air and has unknown potential to migrate to groundwater; and that the hydrolysis product has low potential to volatilize to air and has high potential to migrate to 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 degradation half-lives of the new chemical substance using data for analogue(s) (reactive azo dye) and data submitted for the new chemical substance and of the hydrolysis product using data submitted for the new chemical substance. EPA estimated that the new

[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)

chemical substance's aerobic and anaerobic biodegradation half-lives are 2 to 6 months and hydrolysis half-life is days; and that the hydrolysis product's aerobic and anaerobic biodegradation half-lives are 2 to 6 months and indirect photolysis is slow to moderate. These estimates indicate that the new chemical substance may be persistent in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediments), depending on the rate of hydrolysis. Further, these estimates indicate that the hydrolysis product may 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 new chemical substance to bioaccumulate using data for analogue(s) (reactive azo dye) and of the hydrolysis product to bioaccumulate using data for analogue(s) (azo dye). EPA estimated that the new chemical substance has low bioaccumulation potential based on hydrolysis and the hydrolysis product has low bioaccumulation potential based on data for azo dyes. Although EPA estimated that the new chemical substance could be 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. Although EPA estimated that the hydrolysis product could be 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.

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

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[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)), structure-activity relationships, and/or structural alerts to support characterizing human health hazards.

substance. EPA estimated the human health hazard of this chemical substance based on its estimated physical/chemical properties, available data on the new chemical substance, by comparing it to structurally analogous chemical substances for which there is information on human health hazard, and other structural information. Absorption of intact dye is expected to be nil through the skin and GI tract and good through the lungs based on physical/chemical properties. Following azo bond reduction, absorption of the reduction products is expected to be good through the GI tract based on analogue data. For the new chemical substance, EPA identified irreversible damage to eyes and irritation to mucous membranes as hazards based on test data for the new chemical substance, analogue data, and the reactivity of the new chemical substance. Available test data for the new chemical substance reported the test substance as non-irritating to the skin (OECD 404), not a dermal sensitizer (OECD 406), causing irreversible eye damage (OECD 405), and having low acute oral toxicity (OECD 402). Results of testing of the new chemical substance in a bacterial reverse mutation assay (OECD 471), mammalian cell gene mutation assay (OECD 476), and a mouse micronucleus assay (OECD 474) were all negative; however, positive results were observed in an in vitro chromosomal aberration assay (OECD 473). Kidney effects were observed in a 28-day oral toxicity study (OECD 407) and an oral reproduction/developmental toxicity screening study (OECD 421). EPA identified a NOAEL of 200 mg/kg/day based on increased kidney weights and histopathological changes in the kidneys of males, which was used to derive exposure route- and population-specific points of departure. EPA qualitatively evaluated eye damage and irritation 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 determined the environmental hazard for this new chemical substance based on acute toxicity data submitted for the new chemical substance. This substance falls within the TSCA New Chemicals Category of Acid Dyes and Amphoteric Dyes. Acute toxicity values measured for fish, aquatic invertebrates, and algae are >100 mg/L, >100 mg/L, and 18 mg/L, respectively. Chronic toxicity values measured for fish, aquatic invertebrates, and algae are >10 mg/L (data on the new chemical substance with an ACR 10), >10 mg/L (data on the new chemical substance with an ACR 10), and 6.8 mg/L, respectively. These toxicity values indicate that the new chemical substance is 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 4.5 mg/L (4,500 ppb) and 0.68 mg/L (680 ppb), respectively.

[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).

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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.

For this assessment, EPA assessed worker exposure via the inhalation and dermal routes. Releases to water, air, and landfill were estimated. Exposure to the general population was assessed via ingestion of drinking water, groundwater (via landfill leaching), and fish. Exposure to the general population via inhalation was not assessed because releases to air 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 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 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 substances were evaluated using the route-specific effect levels (i.e., NOAEL) described above. Risks were not identified for workers for kidney effects via inhalation or dermal exposure based on quantitative hazard data for the new chemical substance (Inhalation $MOE_{Respirable}$ = 2,909; Inhalation MOE_{Total} = 1,000; Dermal MOE = 47,059; benchmark MOE = 100). Eye and mucous membrane irritation to workers were identified based on the reactivity of the substance and test data. 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 PPE, including eye and respiratory 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 identified for the general population for kidney effects via ingestion of drinking water, fish, or groundwater (via landfill leachate) based on quantitative hazard data for the new chemical substance (drinking water MOE_{Adult} = 21,515; drinking water MOE_{Infant} = 5,123; fish ingestion MOE = 3,571; groundwater MOE > 4 million; benchmark MOE = 100). Irritation hazards to the general population are not expected via drinking water, groundwater, or fish ingestion due to dilution of the chemical substance in the media. Risks were not evaluated for the general population for inhalation because 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 evaluated by comparing estimated surface water concentrations with the acute and chronic concentrations of concern. Risks from acute exposure to the environment were not identified due to releases to water that did not exceed the acute COC. Risks from chronic exposure to the environment were not identified since the chronic COC is exceeded less than 20 days per year.[7]

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, 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.

9/20/19 /s/

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[7] 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.