TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-20-0008

Number: P-20-0008
TSCA Section 5(a)(3) Determination: The chemical substance is not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Generic: 7-Heteropolycyclicsulfonic acid, 2-[4-[2-[1-[[(2-methoxy-5-methyl-4-sulfophenyl)amino]carbonyl]-2-oxopropyl]diazenyl]phenyl]-6-methyl-, compd. with (alkylamino) alkanol and (hydroxyalkyl) amine

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (specific): Dye manufactured for use with paper, paper products, and nonwoven products produced from paper, 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 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. Based on EPA's TSCA New Chemicals

[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.

Program Chemical Categories for Acid Dyes and Amphoteric Dyes and Anilines[2], test data on analogous chemical substances and test data submitted on the new chemical substance, EPA estimates that the chemical substance has moderate environmental hazard and potential for the following human health hazards: systemic and developmental effects based on the cation components. 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 using data for analogue(s) (azo dyes) and data submitted for the new chemical substance, of the cation using data for analogue(s) (alkanolamines), and of the azo reduction degradants using EPI (Estimation Program Interface) Suite™ (http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface). In wastewater treatment, the anion and the azo reduction degradant are expected to be removed with an efficiency of 0% due to low biodegradability, low sorption, and low stripping and the cation is expected to be removed with an efficiency of 50% to 90% due to biodegradation. Removal of the anion and the azo reduction degradants by biodegradation is negligible, removal of the cation by biodegradation is moderate to high, and destruction (mineralization) of the cation by biodegradation is partial to complete. Sorption of the anion, the cation, and the azo reduction degradants to sludge, soil, and sediment is expected to be low. Migration of the anion to groundwater is expected to be moderate due to low sorption to soil and sediment, mitigated by anaerobic cleavage of the azo bond, migration of the cation to groundwater is expected to be slow due to low sorption to soil and sediment, mitigated by biodegradation, and migration of the azo reduction degradants to groundwater is expected to be rapid due to low sorption to soil and sediment. Due to low estimated vapor pressure and Henry's law constant, the anion, the cation, and the azo reduction degradant are expected to undergo negligible volatilization to air. Overall, these estimates indicate that the anion has low potential to volatilize to air and has moderate potential to migrate to groundwater, that the cation has low potential to volatilize to air or migrate to groundwater, and that the azo reduction degradants have 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 anion using data for analogues (azo dyes), of the cation

[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)

using data for analogue(s) (alkanolamines), and of the azo reduction degradants using EPI Suite™. EPA estimated that the anion's aerobic and anaerobic biodegradation half-lives are 2 to 6 months, that the cation's aerobic and anaerobic biodegradation half-lives are < 2 months, and that the azo reduction degradants' aerobic and anaerobic biodegradation half-lives are > 6 months. These estimates indicate that the anion may be persistent in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment). Further, these estimates indicate that the cation may have limited persistence in aerobic environments and anaerobic environments, and the azo reduction degradants may be very persistent in aerobic environments and anaerobic environments.

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 analogues (azo dyes), of the cation to bioaccumulate using data for analogue(s) (alkanolamines), and of the azo reduction degradants to bioaccumulate using EPI Suite™. EPA estimated that the anion has low bioaccumulation potential based on data for azo dyes and the cation has low bioaccumulation potential based on bioconcentration or bioaccumulation data reported for alkanolamines (anion parent compound bioconcentration factor = 250; cation bioconcentration factor = 1 [estimated]). Further, EPA estimated that the azo reduction degradants have low bioaccumulation potential based on BCFBAF model result < 1000. Although EPA estimated that the anion 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. Additionally, EPA estimated that the cation could have limited persistence and a low potential for bioaccumulation, such that repeated exposures are not expected to cause food-chain effects via accumulation in exposed organisms. Further, although EPA estimated that the azo reduction degradants could be very persistent, the substances have 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

[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

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 estimated physical/chemical properties, available data on the new chemical substance, and by comparing it to structurally analogous chemical substances for which there is information on human health hazard. Absorption is expected to be nil to poor through the skin when neat and poor when in solution based on physical/chemical properties; absorption is expected to be nil through the GI tract and good through lungs based on physical/chemical properties. EPA identified systemic and developmental effects as hazards based on the cation components. Submitted tests on the new chemical substance included an acute oral toxicity test in rats with a reported LD50 of > 2,000 mg/kg and < 5,000 mg/kg (OECD 423), negative in vitro skin irritation and in vitro eye irritation tests (OECD 439 and OECD 438, respectively), a negative local lymph node assay (LLNA) for dermal sensitization (OECD 429), and a negative Ames test in Salmonella and E. coli (OECD 471). EPA identified a NOAEC of 36.45 mg/m^3 based on maternal systemic toxicity and a NOAEL of 89 mg/kg-day based on developmental effects, which were protective for all health concerns and were used to derive exposure route- and population-specific points of departure.

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 and test data on an analogous chemical and using the Ecological Structure Activity Relationships (ECOSAR) Predictive Model (https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model); specifically the QSAR for Anilines. This substance falls within the TSCA New Chemicals Categories of Acid Dyes and Amphoteric Dyes and Anilines. Acute toxicity values measured for fish, aquatic invertebrates, and algae are > 100 mg/L (analogue test data), 85.25 mg/L (ECOSAR-degradation product), and 37.5 mg/L (new chemical test data), respectively. Chronic toxicity values measured for fish, aquatic invertebrates, and algae are > 10

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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).

mg/L (analogue test data with an ACR of 10), 8.525 mg/L (ECOSAR-degradation product with an ACR of 10), and 8.84 mg/L (new chemical test data), 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 9.375 mg/L (9,375 ppb) and 0.853 mg/L (853 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.

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 exposure via dermal exposure; inhalation exposure to workers is not expected. Releases to water were estimated. Exposure to the general population was assessed via drinking water and fish ingestion. 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 exposures are not expected under the 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 substance were evaluated using the route-specific effect levels (i.e., NOAEL, NOAEC) described above. Risks were not identified for workers for developmental effects via dermal exposure based on quantitative hazard data for a cation component of the new chemical substance (MOE=119; Benchmark MOE=100). Risks were not evaluated for workers for systemic effects via inhalation exposure since exposures were expected to be negligible.

Risks were not identified for the general population for developmental effects via drinking water or fish ingestion based on quantitative hazard data for the cation component ($MOE=747_{\text{Adult Drinking Water}}$, $MOE=178_{\text{Infant Drinking Water,}}$ $MOE=118_{\text{Fish Ingestion}}$; Benchmark MOE=100). This assessment is based on conservative exposure estimates of the anion; however, the cation is expected to be removed from wastewater 50-90% more efficiently than the anion and has a bioconcentration factor of 250 less than the anion. Additional refinements were not applied to estimate exposures and risks for the cation alone since risks were not identified using the conservative estimates. Risks were not evaluated for the general population for systemic effects via inhalation exposure since exposures were expected to be negligible. Risks to consumers were not evaluated because consumer exposures are not expected under the conditions of use.

Risks to the environment were evaluated by comparing estimated surface water concentrations with the acute and chronic concentrations of concern (COC). 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 due to the lack chronic releases to water for the new chemical substance.

Because risks to workers were not identified, 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.

2/28/2020
Date:

/s/
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