TSCA Section 5(a)(3) Determination for Significant New Use Notice (SNUN) SN-19-0006

Number: SN-19-0006
TSCA Section 5(a)(3) Determination: The significant new use is not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Specific: 2-Propen-1-one, 1-(4-morpholinyl)- (CASRN: 5117-12-4)

Significant New Use: Use other than as described in previous TSCA submission. The significant new use rule (SNUR) at 40 CFR 721.5185 and proposed SNUR modification for this chemical substance requires notification to EPA for any use without personal protective equipment (PPE), including dermal protection and a respirator with an assigned protection factor (APF) of at least 50 for use as a monomer in stereolithography; use involving an application that generates vapor, mist, aerosol, or dust unless in an enclosed process; use without hazard communication; domestic manufacture of the chemical substance; use that results in a release to water that exceeds 100 ppb; use other than as a monomer in ultraviolet ink jet applications or in stereolithography unless the chemical substance is processed or used in an enclosed process.

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic): Import for use as and use as a component for 3D printing formulations, consistent with the manufacturing, processing, use, distribution, and disposal information described in the SNUN.
Known conditions of use: Applying such factors as described in footnote 1, EPA evaluated whether there are known conditions of use and found, based on previous TSCA submissions: use as a curable resin (P-95-0169), contained use in energy production (SN-08-0007), use as a monomer in ultraviolet ink jet application (SN-14-0001), and use as a monomer in stereolithography (SN-17-0010). The previous TSCA submissions are subject to TSCA 5(e) consent orders that require the companies to: dispose of the PMN as RCRA hazardous waste, have workers wear dermal protection (i.e. impervious gloves)

[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.

and a respirator with an assigned protection factor (APF) of at least 50 for use as a monomer in stereolithography, not use the PMN substance involving an application that generates vapor, mist, aerosol, or dust unless in an enclosed process, implement a hazard communication program, maintain distribution requirements, and maintain certain records.

Reasonably foreseen conditions of use: Applying such factors as described in footnote 1, EPA evaluated whether there are reasonably foreseen conditions of use and identified use in UV or radiation cured formulations for other applications and as a monomer for adhesives, based on patents on the chemical substance and other TSCA submissions.

Summary: The significant new use 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 and the SNUR and consent orders issued previously for this chemical substance. Although EPA estimated that the chemical substance could be 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. Based on available data on the chemical substance and structurally analogous chemical substances, EPA estimates that the chemical substance has moderate environmental hazard and potential for the following human health hazards: acute toxicity, skin and eye irritation, skin sensitization, genotoxicity, carcinogenicity, and specific target organ toxicity. EPA concludes that the significant new use 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 significant new use of a chemical may present an unreasonable risk. EPA estimated physical/chemical and fate properties of the chemical substance using data for analogue(s) (morpholine and acrylamide), data submitted for the chemical substance, and EPI (Estimation Program Interface) Suite™ (http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface). In wastewater treatment, the chemical substance is expected to be removed with an efficiency of 0% to 50% due to biodegradation. Removal of the chemical substance by biodegradation is moderate. Sorption of the chemical substance to sludge, soil, and sediment is expected to be low. Migration of the chemical substance to groundwater is expected to be negligible due to biodegradation. Due to low estimated vapor pressure and Henry's law constant, the chemical substance is expected to undergo negligible volatilization to air. Overall, these estimates indicate that the chemical substance has low potential to volatilize to air or migrate to groundwater.

Persistence[2]: Persistence is relevant to whether a significant new use of a chemical substance is likely to present an unreasonable risk because chemicals that are not degraded in the

[2] 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

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 chemical substance using data for analogue(s) (morpholine and acrylamide), data submitted for the chemical substance, and EPI Suite™. EPA estimated that the aerobic and anaerobic biodegradation half-lives of the chemical substance range from < 2 months to 6 months. These estimates indicate that the chemical substance may be persistent in aerobic environments (e.g., surface water) and anaerobic environments (e.g., sediment).

Bioaccumulation[3]: Bioaccumulation is relevant to whether a significant new use of a 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 chemical substance to bioaccumulate using EPI Suite™ and physicochemical data submitted for the chemical substance. EPA estimated that the chemical substance has low bioaccumulation potential based on BCFBAF model result < 1,000 (bioconcentration factor = 3 [estimated by linear regression from log Kow] and bioaccumulation factor = 1 [estimated by the Arnot-Gobas method (2003)])[4]. Although EPA estimated that the chemical substance could be 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 Hazard[5]: Human health hazard is relevant to whether a significant new use of a

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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)

[3] 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)

[4] 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.

[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.

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 estimated physical/chemical properties, available data on the 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 the chemical substance is expected to be good through the skin, gastrointestinal (GI) tract, and lungs based on data on the chemical substance and analogues. For the chemical substance, EPA identified hazards for skin and eye irritation, skin sensitization, systemic effects, and genotoxicity based on data on the chemical substance, and carcinogenicity based on analogue data and the structural alert for acrylamide, a potential metabolite. Available data on the chemical substance indicate the following hazards: moderate eye irritation (Organisation for Economic Co-operation and Development (OECD) 405), slight skin irritation (Test Guideline Not Specified), positive skin sensitization (Magnusson and Kligman), negative in vivo genotoxicity (Test Guideline not specified), positive mutagenicity in an in vitro mammalian cell line (OECD 490), acute oral and inhalation toxicity (OECD 401 and Test Guideline Not Specified, respectively), low acute dermal toxicity (OECD 402), repeated-dose oral toxicity in a 28-day oral repeated-dose toxicity test (OECD 407) and 90-day oral repeated-dose toxicity test (OECD 408), and developmental/reproductive toxicity in an oral reproductive and developmental toxicity screening study (OECD 422). EPA identified a NOAEL of 20 mg/kg-bw/day based on systemic effects, which was protective of reproductive/developmental toxicity, an oral slope factor (OSF) of 4.5×10^{-1} $(mg/kg\text{-}bw/day)^{-1}$, and an inhalation unit risk (IUR) of 1×10^{-4} $(\mu g/m^3)^{-1}$ based on cancer. The OSF and IUR are protective of mutagenicity and carcinogenicity concerns. These values were used to derive exposure route- and population-specific points of departure. EPA qualitatively evaluated irritation and sensitization effects.

Environmental Hazard[6]: Environmental hazard is relevant to a significant new use of a 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 estimated environmental hazard of this chemical substance based on acute toxicity data submitted for the chemical substance. This substance falls within the TSCA New Chemicals Category of Acrylamides.[7] Acute toxicity values measured for fish, aquatic invertebrates, and algae are 222 mg/L, 120 mg/L, and >120 mg/L, respectively. Chronic toxicity values estimated and measured for fish, aquatic invertebrates, and algae are 8.54 mg/L

(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).

[7] 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.

(Acute-to-Chronic Ratio (ACR)26), 4.62 mg/L (ACR26), and >120 mg/L, respectively. These toxicity values indicate that the chemical substance is expected to have moderate environmental hazard. Application of assessment factors of 5 and 10 to acute and chronic toxicity values, respectively, results in acute and chronic concentrations of concern of 24 mg/L (24,000 ppb) and 0.462 mg/L (462 ppb), respectively.

Exposure: The exposure to a chemical substance is potentially relevant to whether a significant new use of a 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 chemical substance under the intended conditions of use described in the SNUN 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 exposures via the dermal and inhalation routes. Releases to air were estimated. No releases to surface water or landfill were expected. 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 significant new uses of chemicals. A benchmark (acceptable) margin of exposure 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 significant new use is not likely

to present an unreasonable risk. EPA assesses risks to workers considering engineering controls described in the SNUN 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 route-specific effect levels (i.e., NOAEL, OSF, and IUR) described above. Risks were not identified for workers for systemic effects via inhalation exposures based on quantitative hazard data for the new chemical substance (MOE > 70,000; Benchmark MOE = 100). Risks were identified for workers for systemic effects via dermal exposures based on quantitative hazard data for the new chemical substance (MOE = 1; Benchmark MOE = 100). Risks were identified for workers for cancer via inhalation exposures (Cancer risk = 1.0E-4; Target risk = 1.0E-4) and via dermal exposure (Cancer risk = 3.1E+0; Target risk = 1.0E-4) based on quantitative hazard data for acrylamide, a potential metabolite. Skin and eye irritation and skin sensitization hazards to workers were identified based on data for the new chemical. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards. However, risks 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.

Risks were not evaluated, including for cancer, for the general population via drinking water and fish ingestion because releases to surface water are not expected, via groundwater ingestion impacted by landfill leaching because releases to landfill are not expected, or via stack and fugitive air inhalation because exposures are expected to be negligible (below modeling threshold). Irritation and sensitization hazards to the general population are not expected via drinking water, fish ingestion, or groundwater ingestion impacted by landfill leaching because releases to surface water or landfill are not expected. Risks to consumer 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.

It is reasonably foreseen, based on previous TSCA submissions and patents, that this chemical could be used other than as described in the SNUN and previously submitted PMN. However, the existing SNUR for this chemical substance defines certain conditions of use as significant new uses. Conditions of use that fall under the restrictions of the SNUR are not likely to present unreasonable risk of injury to health or the environment because those conditions of use would be prohibited unless and until EPA makes an affirmative determination that the significant new use is not likely to present an unreasonable risk or takes appropriate action under section 5(e) or 5(f). EPA previously assessed the known conditions of use and identified unreasonable risk to human health or the environment. These risks were mitigated by issuing consent orders that restricted the conditions of use and by issuing a SNUR.

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 significant new use is not likely to present unreasonable risk to human health or the environment under the conditions of use.

06/30/2020
Date:

/s/
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