TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-16-0483 & P-16-0484

Number: P-16-0483 & P-16-0484
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-16-0483): Inorganic acids, metal salts, compds. with modified heteroaromatics
Generic (P-16-0484): Inorganic acid, metal salt, compd. with substituted aromatic heterocycle

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (generic, P-16-0483): Manufacture for use as and use as a plastic additive, consistent with manufacturing, processing, use, distribution, and disposal information described in the PMN.
Intended conditions of use (generic, P-16-0484): Manufacture for use as and use as a chemical intermediate, consistent with 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 has identified, based on changes made to the conditions of use in the initial PMN, the following reasonably foreseen uses: manufacture, processing, or use in a manner that results in releases to water; or without the protective measures to limit exposure to dust as described in the PMN.

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 and

[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.

the terms of the proposed Significant New Use Rule (SNUR) signed by EPA.[2] Although EPA estimates that the new chemical substances could be very persistent, the chemical substances have low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative. EPA estimates that the new chemical substances have moderate environmental hazard with potential for aquatic toxicity at surface water concentrations exceeding 34 parts per billion (ppb). Based on data on P-16-0483 and on analogous chemical substances, EPA estimates that these new chemical substances have potential for the following human health hazards: irritation, sensitization, and systemic and reproductive toxicity. EPA estimates that identified risks to workers will be prevented by the use of engineering controls as described in Part II/Section A of the PMNs claimed confidential and personal protective equipment. EPA expects that workers will use appropriate personal protective equipment (i.e., respiratory protection) in a manner adequate to protect them. The PMNs describe conditions of use that mitigate both ecological and human health risks. Therefore, EPA concludes that the new chemical is not likely to present unreasonable risk to human health or the environment under the intended conditions of use.

As set forth below, the information available to EPA is sufficient to permit the Agency to conduct a reasoned evaluation of the health and environmental effects of the chemical substances under the conditions of use that are not subject to the proposed SNUR, in order to determine that the chemical substances are not likely to present an unreasonable risk under those conditions of use. As such, EPA does not need to impose test requirements to conduct this evaluation. Whether testing is needed to evaluate the effects of the intended, known, or reasonably foreseen conditions of use of a chemical substance subject to a PMN is determined on a case-by-case basis. To the extent that testing may be necessary to conduct a reasoned evaluation of the health or environmental effects of the reasonably foreseen conditions of use that are subject to the proposed SNUR, EPA will make the appropriate determination if a SNUN is submitted following finalization of the SNUR.

EPA found no known conditions of use, assessed the intended conditions of use, and addressed reasonably foreseen conditions of use by proposing a SNUR. Therefore, EPA determines the new chemical substance is not likely to present an unreasonable risk to human health or the environment.

[2] Reasonably foreseen conditions of use subject to a proposed SNUR are not likely to present an unreasonable risk of injury to health or the environment. Based on EPA's experience, it is the Agency's judgment that a new use would not commence during the pendency of a proposed SNUR because web posting of a proposed SNUR serves as the cut-off date for a significant new use. Therefore, manufacturers and processors would not commence a prohibited new use that would be legally required to cease upon the finalization of the SNUR. Once a SNUR is final and effective, no manufacturer or processor – including the PMN submitter – may undertake the conditions of use identified as a significant new use of the PMN substance in the SNUR. EPA must first evaluate the new use in accordance with the requirements of TSCA Section 5 and (a) either conclude that the new use is not likely to present an unreasonable risk under the conditions of use; or (b) take appropriate action under section 5(e) or 5(f). If EPA were not to finalize the proposed SNUR, then that decision would be based on information and data provided to the Agency during the comment period demonstrating that the reasonably foreseen conditions of use subject to the proposed SNUR are not likely to present an unreasonable risk. Under either scenario, the reasonably foreseen condition of use is not likely present an unreasonable risk.

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 new chemical substance is likely to present an unreasonable risk. EPA estimated physical/chemical and fate properties of these new chemical substances using EPI (Estimation Programs Interface) Suite™, a suite of physical/chemical property and environmental fate estimation programs (http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface) and data for analogous chemicals. The chemical substances are estimated to be removed with an efficiency of 25-50% during wastewater treatment due to moderate sorption to sludge. The chemical substances are estimated to have moderate sorption to soil and sediment, resulting in moderate migration to groundwater. Volatilization to air is estimated to be negligible because the substances have low vapor pressures and low Henry's Law constants. Overall, these estimates are indicative of low potential for these chemical substances to volatilize into the air and a moderate potential for these chemicals to migrate into 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 biodegradation half-lives of these new chemical substances using EPI (Estimation Programs Interface) Suite™, a suite of physical/chemical property and environmental fate estimation programs (http://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface) and data for analogous chemicals. EPA estimates the aerobic biodegradation half-lives to be greater than six months, which indicates that the chemical substances may be very persistent in aerobic environments (e.g., surface water). The anaerobic biodegradation half-lives are estimated to be greater than six months, which indicates that the chemical substances may be very persistent in 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 substances to bioaccumulate using EPI Suite™. These estimates indicate that the chemical substances have low bioaccumulation potential (P-16-0483: bioconcentration factor = 3.16; bioaccumulation factor =

[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)

[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)

0.938. P-16-0484: bioconcentration factor = 3.16; bioaccumulation factor = 0.894). Although EPA estimates that the new chemical substances could be very persistent, the chemical 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 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 new chemical substances based on their estimated physical/chemical properties, data on the chemical substance described in P-16-0483 (irritation, sensitization, irritation, sensitization and subchronic toxicity), and analogue data for the chemical substance described in P-16-0484 (EPA identified [claimed CBI] as an analogue). For these new chemical substances, absorption is estimated to be nil through the skin and poor to moderate through the lung and GI tract based on physical/chemical properties.

For the chemical substance described in P-16-0483, EPA identified systemic toxicity as potential hazards based on submitted test data and lung irritation based on information in the SDS provided by the submitter. Test data on the PMN substance were negative for skin sensitization. Potential for blood clotting effects and lung toxicity were identified based on an analogue, [claimed CBI]. EPA quantitatively assessed the chemical substance described in P-16-0483 using submitted test data on the PMN. A LOAEL of 111 mg/kg-bw/day was identified for increased lymph node size in a 28-day oral repeated-dose toxicity study (OECD 407). This LOAEL was used to derive exposure route- and population-specific points of departure for quantitative risk assessment of the chemical substance described in P-16-0483. A benchmark MOE of 300 was used due to the limited severity of effects.

For the chemical substance described in P-16-0484, EPA considered potential hazards posed by [claimed CBI] (counterion in the new chemical substance). However, the counterion is an essential element. Therefore, EPA selected to use another analogue that is the primary organic component of the new chemical [claimed CBI] with a benchmark MOE of 100 to conduct the

[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.

health risk assessment. EPA identified the following hazards associated with this analogue: effects on kidneys, spleen lymphocytes, and reproductive/developmental toxicity. EPA quantitatively assessed the chemical substance described in P-16-0484 using data for the analogue [claimed CBI]. A NOAEL of 2 mg/kg-bw/day for histopathological effects on sperm cells and seminiferous tubules was identified based on a 14-day repeated-dose oral toxicity test in mice (OECD SIDS abstracts/PubChem profile for [claimed CBI]). Because humans are considered more sensitive to effects on sperm (especially sperm count) than rodents (U.S. EPA, 1996, Guidelines for Reproductive Toxicity Risk Assessment. Risk Assessment Forum), this NOAEL is appropriate given that humans might exhibit functional reproductive effects at doses lower than doses at which rodents exhibit decreased fertility. This NOAEL was used to derive exposure route- and population-specific points of departure for quantitative risk assessment of the chemical substance described in P-16-0484. A benchmark MOE of 100 was used.

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 environmental hazard of this new chemical substance based on acute toxicity data submitted on the chemical substance described in P-16-0483 and using SAR predictions for [claimed CBI] with molecular weight adjustments based on the percentage of [claimed CBI] present. Acute ecotoxicity values measured for fish, aquatic invertebrates and algae are > 43, > 42 and 2.4 mg/L, respectively. Chronic ecotoxicity values estimated for fish, aquatic invertebrates and measured for algae are 1.1, 0.34 and 1.2 mg/L, respectively. These toxicity values indicate 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 results in estimated acute and chronic concentrations of concern (COCs) of 600 ppb and 34 ppb, respectively, for both chemical substances.

Exposure and Risk Characterization: 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 releases of the 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-

[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).

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 these assessments, EPA also used area and personal air monitoring data provided in the PMN submission to assess occupational inhalation exposures. For P-16-0483, one manufacturing, one processing and one use exposure scenarios were assessed. For P-16-0484, one manufacturing and one use exposure scenarios were assessed. For exposures to the general population, inhalation exposures were below modeling thresholds for the intended conditions of use and therefore exposures were not assessed. While water releases were initially estimated for P-16-0483, the company provided new information indicating no releases to water. Consumer exposures were not assessed because consumer uses were not identified as conditions of use.

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 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., NOAEL or LOAEL) described above. For the chemical substance described in P-16-0483, risks were not identified for workers for systemic toxicity via inhalation during manufacturing based on air monitoring data. MOEs calculated using area air monitoring data (MOE=16,755) and personal monitoring data (MOE = 897) exceeded the benchmark MOE of 300. Risks were not identified for workers for systemic toxicity via inhalation of fugitive emissions during processing and use based on exposure estimates from ChemSTEER. The MOEs calculated for fugitive emissions from processing and use activities (MOE = 404 for both processing and use) exceeded the benchmark MOE of 300. Risks were identified for workers for

systemic effects via inhalation when unloading raw materials during processing and use based on exposure estimates from ChemSTEER. The MOEs calculated for processing and use scenarios involving unloading of raw material (MOE = 59) were below the benchmark MOE of 300, indicating risk from these exposure scenarios (i.e., unloading raw material). Risks will be mitigated with use of appropriate PPE, including a respirator with an APF of 10. EPA expects that workers will use appropriate personal protective equipment (i.e., a respirator with an APF of 10), consistent with the Safety Data Sheet prepared by the PMN submitter, in a manner adequate to protect them.

For the chemical substance described in P-16-0484, risks were identified for workers for reproductive toxicity via inhalation using air monitoring data. The MOEs calculated using area air monitoring data for both manufacturing and use scenarios (MOE=302) exceeded the benchmark MOE of 100. However, the MOEs calculated using personal air monitoring data (MOE = 16) were less than the benchmark MOE of 100, indicating risk for both the manufacturing and use exposure scenarios. Risks will be mitigated with use of appropriate PPE, including a respirator with an APF of 10. EPA expects that workers will use appropriate personal protective equipment (i.e., a respirator with an APF of 10), consistent with the Safety Data Sheet prepared by the PMN submitter, in a manner adequate to protect them.

For the intended conditions of use of the chemical substances described in P-16-0483 & P-16-484, risks were not evaluated for the general population for reproductive or systemic toxicity via ingestion because there are no releases to water based on information provided by the submitter. Risks were also not evaluated for the general population for reproductive or systemic toxicity via inhalation because releases to air were below modeling thresholds. Consumer risks were not evaluated because consumer uses were not identified as conditions of use.

Risks to the environment are evaluated by comparing estimated surface water concentrations with the acute and chronic concentrations of concern. Risks to the environment were not evaluated for the new chemical substances because no releases to water are associated with the intended conditions of use.

Reasonably foreseen conditions of use could involve releases to water which may exceed the acute or chronic concentrations of concern and use without the protective measures (i.e., engineering controls) described in the PMN to limit exposure to dust. These conditions of use are reasonably foreseen because they were present in the initial PMN submission, which was subsequently amended to mitigate risks identified under the initial conditions of use. The SNUR that has been proposed for these chemical substances defines certain conditions of use as significant new uses. The proposed significant new uses include predictable or purposeful release of a manufacturing, processing, or use stream associated with any use of the substances into waters of the United States exceeding a surface water concentration of 34 ppb; and manufacture, processing, or use of the substances without the protective measures (i.e., engineering controls) to limit inhalation exposure described in Part II/Section A of the PMNs claimed confidential. To verify that maximum surface water concentrations based on the chronic concentrations of concern (34 ppb) would also prevent risk of injury to human health, a drinking water equivalent

level (DWEL)[7] was calculated for each new chemical substance for both adults and infants, and all DWELs exceeded the chronic COC of 34 ppb (P-16-0483: adult DWEL = 9,800 ppb; infant DWEL = 2,400 ppb. P-16-0484: adult DWEL = 530 ppb, infant DWEL = 130 ppb). Conditions of use that fall under the restrictions of the proposed SNUR are not likely to present unreasonable risk of injury to health or the environment because (1) those conditions of use are not likely to be commenced during the pendency of the proposed SNUR, and (2) upon finalization of the SNUR, 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).

10/9/18
Date:

/s/
Jeffery T. Morris, Director
Office of Pollution Prevention and Toxics

[7] Drinking Water Equivalent Level (DWEL): a DWEL is a drinking water lifetime exposure level, assuming 100% exposure from that medium, at which adverse, noncarcinogenic health effects would not be expected to occur. (Drinking Water Standards and Health Advisories, https://www.epa.gov/sites/production/files/2018-03/documents/dwtable2018.pdf)