TSCA Section 5(a)(3) Determination for Premanufacture Notice (PMN) P-18-0077

Number: P-18-0077
TSCA Section 5(a)(3) Determination: The chemical substance is not likely to present an unreasonable risk (5(a)(3)(C))

Chemical Name:
Specific: Urea, reaction products with N-butylphosphorothioic triamide and formaldehyde (CASRN: 2093385-47-6)

Conditions of Use (intended, known, or reasonably foreseen)[1]:
Intended conditions of use (specific): Manufacture for use as an additive for urea-containing fertilizer, 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 one of the hydrolysis products of the new chemical substance could be very persistent, this hydrolysis product has low potential for bioaccumulation, such that repeated exposures are not expected to be cumulative. Based on test data on the chemical substance and analogous chemical substances, EPA estimates that the chemical substance has moderate environmental hazard and potential for the following human health hazards: neurotoxicity, reproductive, blood, and kidney toxicity, sensitization, and irritation. EPA concludes that the new chemical substance is not likely to present an unreasonable risk under the

[1] Under TSCA § 3(4), the term "conditions of use" means "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." In general, EPA considers the intended conditions of use of a new chemical substance to be those identified in the section 5(a) notification. Known conditions of use include activities within the United States that result from manufacture that is exempt from PMN submission requirements. Reasonably foreseen conditions of use are future circumstances, distinct from known or intended conditions of use, under which the Administrator expects the chemical substance to be manufactured, processed, distributed, used, or disposed of. The identification of "reasonably foreseen" conditions of use will necessarily be a case-by-case determination and will be highly fact-specific. Reasonably foreseen conditions of use will not be based on hypotheticals or conjecture. EPA's identification of conditions of use includes the expectation of compliance with federal and state laws, such as worker protection standards or disposal restrictions, unless case-specific facts indicate otherwise. Accordingly, EPA will apply its professional judgment, experience, and discretion when considering such factors as evidence of current use of the new chemical substance outside the United States, evidence that the PMN substance is sufficiently likely to be used for the same purposes as existing chemical substances that are structurally analogous to the new chemical substance, and conditions of use identified in an initial PMN submission that the submitter omits in a revised PMN. The sources EPA uses to identify reasonably foreseen conditions of use include searches of internal confidential EPA PMN databases (containing use information on analogue chemicals), other U.S. government public sources, the National Library of Medicine's Hazardous Substances Data Bank (HSDB), the Chemical Abstract Service STN Platform, REACH Dossiers, technical encyclopedias (e.g., Kirk-Othmer and Ullmann), and Internet searches.

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 this new chemical substance and its hydrolysis products (N-butylphosphorothioic triamide and urea-formaldehyde oligomers) using data on the new chemical substance and 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). The new chemical substance is estimated to be removed during wastewater treatment with an efficiency of 90% due to rapid hydrolysis. Based on test data on the new chemical substance, the hydrolysis half-life is hours to days. The hydrolysis product N-butylphosphorothioic triamide is estimated to be removed during wastewater treatment with an efficiency of 0-10% based on low biodegradability, low sorption and low stripping. Sorption to sludge, soil, and sediment is estimated to be low. Volatilization to air is expected to be negligible because the hydrolysis product is estimated to have low vapor pressure and a low Henry's Law constant. Migration to groundwater is estimated to be rapid. The urea-formaldehyde oligomers produced via hydrolysis are estimated to be removed during wastewater treatment with an efficiency of 75-90% via biodegradation and further hydrolysis. Sorption to sludge, soil, and sediment is estimated to be low. Volatilization to air is expected to be negligible because the hydrolysis products are estimated to have low vapor pressure and a low Henry's Law constant. Removal by biodegradation in wastewater treatment is estimated to be moderate. Migration to groundwater is estimated to be slow.

Persistence[2]: 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. Based on EPI Suite™ and test data on analogous chemical substances and the chemical substance, EPA estimated hydrolysis and/or biodegradation half-lives for the new chemical substance and its hydrolysis products. Based on test data on the new chemical substance, the hydrolysis half-life is hours to days. EPA estimated the aerobic and anaerobic biodegradation half-lives for the hydrolysis product N-butylphosphorothioic triamide to be greater than six months. The urea-formaldehyde oligomers produced by hydrolysis are expected to undergo further hydrolysis, with an estimated hydrolysis half-life of days based on analogous chemicals. These estimates indicate that the new chemical substance and the urea-formaldehyde oligomers produced by hydrolysis are not likely to be persistent in aerobic environments (e.g., surface water) or in anaerobic

[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 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)

environments (e.g., sediment), but that the hydrolysis product N-butylphosphorothioic triamide may be very persistent in aerobic and anaerobic environments.

Bioaccumulation[3]: 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. The new chemical substance has low bioaccumulation potential based on its hydrolysis half-life. EPA estimated the potential for the hydrolysis products N-butylphosphorothioic triamide and urea-formaldehyde oligomers to bioaccumulate using EPI Suite™. These estimates indicate that both hydrolysis products have low bioaccumulation potential (bioconcentration factor = 3; bioaccumulation factor = 1 for each hydrolysis product). Although EPA estimated that one of the hydrolysis products (N-butylphosphorothioic triamide) of the new chemical substance could be very persistent, the chemical substance and its hydrolysis products 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[4]: 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 this chemical substance based on data on the new chemical substance and on analogues. For the new chemical substance, absorption is estimated to be good through the lungs and GI tract based on physical/chemical properties. Absorption of the neat material is estimated to be nil through the skin and absorption is estimated to be poor through the skin when in solution based on physical/chemical properties. An acute oral toxicity test (OECD 423) indicates the new chemical has low acute oral toxicity (LD_{50} >

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[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] 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.

2000 mg/kg-bw). EPA identified neurotoxicity, reproductive toxicity, kidney toxicity, irritation and sensitization as hazards based on data on an analogous chemical. EPA identified a LOAEL of 250 mg/kg-day for blood toxicity and neurotoxicity hazards based on a submitted 28-day oral repeated-dose toxicity test (OECD 407) conducted with the new chemical substance. EPA identified the potential for formaldehyde degradation products but expects that formaldehyde release would be slow, though it could be a greater concern under acidic conditions. EPA identified a NOAEL of 11 mg/kg/day based on decreased body weights in males and females and increased epididymal lesions and decreased sperm motility in a two-generation reproductive toxicity test on an analogous chemical. This NOAEL was used to derive exposure route- and population-specific points of departure for quantitative risk assessment, described below, because it was the most sensitive endpoint.

Environmental Hazard[5]: Environmental hazard is 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 estimated environmental hazard of this new chemical substance using data on an analogous chemical and 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 substituted ureas. Acute toxicity values estimated for fish, aquatic invertebrates, and algae are >100 mg/L, >100 mg/L, and 8.4 mg/L, respectively. Chronic toxicity values estimated for fish, aquatic invertebrates, and algae are >10 mg/L, >10 mg/L, and 2.8 mg/L, respectively. Based on these toxicity values, EPA expects the new chemical substance to have moderate environmental hazard. Application of assessment factors of 4 and 10 to acute and chronic toxicity values, respectively, results in acute and chronic concentrations of concern of 2.1 mg/L (2,100 ppb) and 0.280 mg/L (280 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-

[5] 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 this new chemical assessment, EPA assessed dermal exposure to workers, and inhalation exposure to workers is not expected. Releases to water and air 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). Exposure to consumers was not assessed because consumer uses were not identified as conditions of use. Exposures to aquatic organisms were assessed by estimating maximum surface water concentrations.

Risk Characterization: EPA applies a margin of exposure approach to calculate potential human health risks of new chemicals. A benchmark (acceptable) margin of exposure is derived by applying uncertainty factors for the following types of extrapolations: intra-species extrapolation (UF_H = 10 to account for variation in sensitivity among the human population), inter-species extrapolation (UF_A = 10 to account for extrapolating from experimental animals to humans) and LOAEL-to-NOAEL extrapolation (UF_L = 10 to account for using a LOAEL when a NOAEL is not available). Hence, in the New Chemicals Program, a benchmark MOE is typically 100 and 1000 when NOAELs and LOAELs, respectively, are used to identify hazard. When allometric scaling or pharmacokinetic modeling is used to derive an effect level, the UF_H may be reduced to 3, for a benchmark MOE of 30. The benchmark MOE is used to compare to the MOE calculated by comparing the toxicity NOAEL or LOAEL to the estimated exposure concentrations. When the calculated MOE is equal to or exceeds the benchmark MOE, the new chemical substance is not likely to present an unreasonable risk. EPA assesses risks to workers considering engineering controls described in the PMN but in the absence of personal protective equipment (PPE) such as gloves and respirators. If risks are preliminarily identified, EPA then considers whether the risks would be mitigated by the use of PPE (e.g., impervious gloves, respirator).

Risks to human health for the new chemical were evaluated using the points of departure (i.e., NOAEL) described above. Risks were identified for workers for reproductive toxicity via dermal exposure during manufacture and processing (MOE_{Liquid} = 7; MOE_{Solid} = 3,667; benchmark MOE = 100). Risks were not identified for workers for reproductive toxicity via dermal exposure during use (MOE = 3,667; benchmark MOE = 100). Irritation and sensitization hazards to workers are identified via dermal exposure during processing and use. Risks for these hazard endpoints cannot be quantified due to a lack of dose-response for these hazards. Risks for reproductive toxicity, irritation, and sensitization will be mitigated if exposures are controlled by the use of appropriate PPE, including impervious gloves and eye protection. EPA expects that

workers will use appropriate personal protective equipment (i.e., impervious gloves and eye protection), consistent with the Safety Data Sheet prepared by the PMN submitter, in a manner adequate to protect them. Therefore, EPA has not identified risks for the irritation and sensitization endpoints.

Risks were not identified for the general population for sensitization or irritation from oral exposure to drinking water or fish ingestion. The new chemical substance is unlikely to be present in the environment at concentrations that are sufficient to result in these hazards in the general population. Risks were not identified for the general population for reproductive toxicity via drinking water (MOE_{Adult} = 1,332; MOE_{Infant} = 319; benchmark MOE = 100) or fish ingestion (MOE = 14,360; benchmark MOE = 100). Risks were not evaluated for consumers because consumer uses were not identified as conditions of use.

Risks to the environment were evaluated by comparing estimated surface water concentrations with the estimated acute and chronic COCs. Risks to the environment were not identified because the estimated maximum surface water concentrations did not exceed the acute or chronic COCs.

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

12/03/2018
Date:

/s/
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