5. UNREASONABLE RISK DETERMINATION

TSCA section 6(b)(4) requires EPA to conduct a risk evaluation to determine whether a chemical substance presents 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 by EPA as relevant to this Risk Evaluation, under the conditions of use.

EPA has determined that n-methylpyrrolidone (NMP) presents an unreasonable risk of injury to health under the conditions of use. This determination is based on the information in previous sections of this Risk Evaluation, the appendices and supporting documents of NMP, in accordance with TSCA section 6(b), as well as TSCA's best available science (TSCA section 26(h)) and weight of scientific evidence standards (TSCA section 26(i)), and relevant implementing regulations in 40 CFR part 702.

The full list of conditions of use evaluated for NMP are listed in Table 1-6 of this Risk Evaluation (Ref. 1). EPA's unreasonable risk determination for NMP is driven by risks associated with the following conditions of use, considered singularly or in combination with other exposures:

- Domestic manufacture
- Manufacture: import
- Processing: as a reactant or intermediate in plastic material and resin manufacturing and other non-incorporative processing
- Processing: incorporation into a formulation, mixture or reaction product in multiple industrial sectors
- Processing: incorporation into articles in lubricants and lubricant additives in machinery manufacturing
- Processing: incorporation into articles in paint additives and coating additives not described by other codes in transportation equipment manufacturing
- Processing: incorporation into articles as a solvent (which becomes part of product formulation or mixture), including in textiles, apparel and leather manufacturing
- Processing: incorporation into articles in other sectors, including in plastic product manufacturing
- Processing: repackaging in wholesale and retail trade
- Processing: recycling
- Industrial and commercial use in paints, coatings, and, adhesive removers
- Industrial and commercial use in paints and coatings in lacquers, stains, varnishes, primers and floor finishes, and powder coatings, surface preparation
- Industrial and commercial use in paint additives and coating additives not described by other codes in computer and electronic product manufacturing in electronic parts manufacturing
- Industrial and commercial use in paint additives and coating additives not described by other codes in computer and electronic product manufacturing for use in semiconductor manufacturing

- Industrial and commercial use in in paint additives and coating additives not described by other codes in several manufacturing sectors
- Industrial and commercial use as a solvent (for cleaning or degreasing) use in electrical equipment, appliance and component manufacturing
- Industrial and commercial use as a solvent (for cleaning or degreasing) in electrical equipment, appliance and component manufacturing for use in semiconductor manufacturing
- Industrial and commercial use in ink, toner, and colorant products in printer ink and inks in writing equipment
- Industrial and commercial use in processing aids, specific to petroleum production in petrochemical manufacturing, in other uses in oil and gas drilling, extraction and support activities, and in functional fluids (closed systems)
- Industrial and commercial use in adhesives and sealants including binding agents, single component glues and adhesives, including lubricant adhesives, and two-component glues and adhesives including some resins
- Industrial and commercial use in other uses in soldering materials
- Industrial and commercial use in other uses in anti-freeze and de-icing products, automotive care products, and lubricants and greases
- Industrial and commercial use in other uses in metal products not covered elsewhere, and lubricant and lubricant additives including hydrophilic coatings
- Industrial and commercial use in other uses in laboratory chemicals
- Industrial and commercial uses in other uses in lithium ion battery manufacturing
- Industrial and commercial use in other uses in cleaning and furniture care products, including wood cleaners and gasket removers
- Industrial and commercial use in other uses in fertilizer and other agricultural chemical manufacturing, processing aids and solvents
- Consumer use in adhesives and sealants in glues and adhesives, including lubricant adhesives and sealants
- Disposal

The following conditions of use do not drive EPA's unreasonable risk determination for NMP:

- Distribution in commerce
- Consumer use in paint and coating removers
- Consumer use in adhesive removers
- Consumer use in paints and coatings in lacquers, stains, varnishes, primers and floor finishes
- Consumer use in paint additives and coating additives not described by other codes in paints and arts and crafts paints
- Consumer use in other uses in automotive car products
- Consumer use in other uses in cleaning and furniture care products, including wood cleaners and gasket removers
- Consumer use in other uses in lubricant and lubricant additives, including hydrophilic coatings

EPA is not making condition of use-specific risk determinations for these conditions of use, is not issuing a final order under TSCA section 6(i)(1) for the conditions of use that do not drive the unreasonable risk, and does not consider the revised risk determination for NMP to constitute a final agency action at this point in time.

Consistent with the statutory requirements of TSCA section 6(a), EPA will propose a risk management regulatory action to the extent necessary so that NMP no longer presents an unreasonable risk. EPA expects to focus its risk management action on the conditions of use that drive the unreasonable risk. However, it should be noted that, under TSCA section 6(a), EPA is not limited to regulating the specific activities found to drive unreasonable risk and may select from among a suite of risk management requirements in section 6(a) related to manufacture (including import), processing, distribution in commerce, commercial use, and disposal as part of its regulatory options to address the unreasonable risk. As a general example, EPA may regulate upstream activities (e.g., processing, distribution in commerce) to address downstream activities (e.g., consumer uses) driving unreasonable risk, even if the upstream activities do not drive the unreasonable risk.

5.1 Background

5.1.1 Background on Policy Changes Relating to the Whole Chemical Risk Determination and Assumption of PPE Use by Workers

From June 2020 to January 2021, EPA published risk evaluations on the first ten chemical substances, including for NMP in December 2020. The risk evaluations included individual unreasonable risk determinations for each condition of use evaluated. The determinations that particular conditions of use did not present an unreasonable risk were issued by order under TSCA section 6(i)(1).

In accordance with Executive Order 13990 ("Protecting Public Health and the Environment and Restoring Science to Tackle the Climate Crisis") and other Administration priorities (Refs. 2, 3, 4, and 5), EPA reviewed the risk evaluations for the first ten chemical substances to ensure that they meet the requirements of TSCA, including conducting decision-making in a manner that is consistent with the best available science and weight of the scientific evidence.

As a result of this review, EPA announced plans to revise specific aspects of certain of the first ten risk evaluations in order to ensure that the risk evaluations appropriately identify unreasonable risks and thereby can help ensure the protection of health and the environment (Ref. 6). To that end, EPA has reconsidered two key aspects of the risk determinations for NMP published in December 2020. First, EPA has determined that the appropriate approach to these determinations is to make an unreasonable risk determination for NMP as a whole chemical substance, rather than making unreasonable risk determinations separately on each individual condition of use evaluated in the risk evaluation. Second, EPA has determined that the risk determination explicitly state that it does not rely on assumptions regarding the use of personal protective equipment (PPE) in making the unreasonable risk determination under TSCA section 6; rather, the use of PPE will be considered during risk management. Making unreasonable risk

determinations based on the baseline scenario without assuming PPE should not be viewed as an indication that EPA believes there are no occupational safety protections in place at any location or that there is widespread noncompliance with applicable OSHA standards. EPA understands that there could be occupational safety protections in place at workplace locations; however, not assuming use of PPE reflects EPA's recognition that unreasonable risk may exist for subpopulations of workers that may be highly exposed because they are not covered by OSHA standards, or their employers are out of compliance with OSHA standards, or because many of OSHA's chemical-specific permissible exposure limits largely adopted in the 1970's are described by OSHA as being "outdated and inadequate for ensuring protection of worker health,"[1] or because OSHA has not issued a chemical-specific permissible exposure limit (PEL) (as is the case for NMP), or because EPA finds unreasonable risk for purposes of TSCA notwithstanding existing OSHA requirements.

Separately, EPA is conducting a screening approach to assess risks from the air and water pathways for several of the first 10 chemicals, including this chemical. For NMP the exposure pathways that were or could be regulated under another EPA-administered statute were not fully assessed as part of the final risk evaluation (see Section 1.4.2 of the December 2020 NMP Risk Evaluation). For NMP, some exposure pathways received only a screening-level analysis. During problem formulation, EPA conducted a first-tier screening analysis for the ambient air pathway to near field populations downwind from industrial and commercial facilities releasing NMP which indicated low risk. In the December 2020 NMP Risk Evaluation EPA conducted a first-tier analysis to estimate NMP surface water concentrations and did not identify risks from incidental ingestion or dermal contact during swimming. This resulted in the ambient air and drinking water pathways for NMP not being fully assessed in the risk evaluation published in December 2020. The goal of the recently-developed screening approach is to remedy this exclusion and to determine if there may be risks that were unaccounted for in the NMP risk evaluation. The screening-level approach has gone through public comment and independent external peer review through the SACC. The Agency received the final peer review report on May 18, 2022, and has reviewed public comments and SACC comments. EPA expects to describe its findings regarding the chemical-specific application of this screening-level approach in the forthcoming proposed rule under TSCA section 6(a) for NMP.

Further discussion of the rationale for the whole chemical approach is found in the Federal Register Notice in the docket accompanying this revised NMP unreasonable risk determination and further discussion of the decision to not rely on assumptions regarding the use of PPE is provided in the Federal Register Notice and in Section 5.2.4 below. With respect to the NMP risk evaluation, EPA did not amend, nor does a whole chemical approach or change in assumptions regarding PPE require amending, the underlying scientific analysis of the risk evaluation in the risk characterization section of the risk evaluation.

[1] As noted on OSHA's Annotated Table of Permissible Exposure Limits: "OSHA recognizes that many of its permissible exposure limits (PELs) are outdated and inadequate for ensuring protection of worker health. Most of OSHA's PELs were issued shortly after adoption of the Occupational Safety and Health (OSH) Act in 1970, and have not been updated since that time" (Ref. 7).

With regard to the specific circumstances of NMP, as further explained below, EPA has determined that a whole chemical approach is appropriate in order to protect health and the environment. The whole chemical approach is appropriate for NMP because there are benchmark exceedances for multiple of conditions of use (spanning across most aspects of the chemical lifecycle– from manufacturing (including import), processing, commercial and consumer use, and disposal) for human health and risk of the health effects associated with NMP exposures are irreversible. Because these chemical-specific properties cut across the conditions of use within the scope of the risk evaluation, and a substantial amount of the conditions of use drive the unreasonable risk, it is therefore appropriate for the Agency to make a determination that the whole chemical presents an unreasonable risk. In addition, as discussed below in Section 5.2.4, in making this risk determination, EPA believes it is appropriate to evaluate the levels of risk present in baseline scenarios where PPE is not assumed to be used by workers. EPA is revising the assumption for NMP that workers always and properly use PPE, although it does not question the public comments received regarding the occupational safety practices often followed by industry respondents. PPE use will be considered during risk management.

As explained in the Federal Register Notice, the revisions to the unreasonable risk determination (Section 5 of this Risk Evaluation) follow the issuance of a draft revision to the TSCA NMP unreasonable risk determination (87 FR 39511, July 1, 2022) (Ref. 8) and the receipt of public comment. A response to comments document is also being issued with this final revised unreasonable risk determination for NMP (Ref. 9). As noted in the Federal Register Notice, the revisions to the unreasonable risk determination are based on the existing risk characterization section of this Risk Evaluation (Section 4), and do not involve additional technical or scientific analysis. The discussion of the issues in this revision to the risk determination supersedes any conflicting statements in the prior NMP risk evaluation (December 2020) and the response to comments document (*Summary of External Peer Review and Public Comments and Disposition for n-Methylpyrrolidone (NMP), December 2020*). EPA also views the peer reviewed hazard and exposure assessments and associated risk characterization as robust and upholding the standards of best available science and weight of the scientific evidence, per TSCA sections 26(h) and (i).

5.1.2 Background on Unreasonable Risk Determination

In each risk evaluation under TSCA section 6(b), EPA determines whether a chemical substance presents an unreasonable risk of injury to health or the environment, under the conditions of use. The unreasonable risk determination does not consider costs or other nonrisk factors. In making the unreasonable risk determination, EPA considers relevant risk-related factors, including, but not limited to: the effects of the chemical substance on health and human exposure to such substance under the conditions of use (including cancer and non-cancer risks); the effects of the chemical substance on the environment and environmental exposure under the conditions of use; the population exposed (including any potentially exposed or susceptible subpopulations (PESS)); the severity of hazard (including the nature of the hazard, the irreversibility of the hazard); and uncertainties. EPA also takes into consideration the Agency's confidence in the data used in the risk estimate. This includes an evaluation of the strengths, limitations, and uncertainties associated with the information used to inform the risk estimate and the risk

characterization. This approach is in keeping with the Agency's final rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726, July 20, 2017).[2]

This section describes the revised unreasonable risk determination for NMP, under the conditions of use in the scope of the Risk Evaluation for NMP. This revised unreasonable risk determination is based on the risk estimates in the final Risk Evaluation, which may differ from the risk estimates in the draft Risk Evaluation due to peer review and public comments.

5.2 Unreasonable Risk to Human Health

5.2.1 Human Health

EPA's NMP risk evaluation identified risks for non-cancer adverse effects from acute (developmental) and chronic (reproductive) inhalation and dermal exposures to NMP. The health risk estimates for all conditions of use are in Tables 4-55 and 4-56 of Section 4.6 of this Risk Evaluation.

In developing the exposure assessment for NMP, EPA identified the following groups as Potentially Exposed or Susceptible Subpopulations (PESS): workers and occupational non-users (ONUs[3]), consumers and bystanders, males and females of reproductive age, pregnant women and the developing fetus, infants, children and adolescents, people with pre-existing conditions and people with lower metabolic capacity due to life stage, genetic variation, or impaired liver function (Section 4.4 and Tables 4-4 and 4-5 of this Risk Evaluation).

EPA evaluated exposures to workers, ONUs, consumer users, and bystanders using reasonably available monitoring and modeling data for inhalation and dermal exposures, as applicable. For example, EPA assumed that ONUs and bystanders do not have direct contact with NMP; therefore, non-cancer effects from dermal exposures to NMP are not expected and were not evaluated. Additionally, EPA did not evaluate chronic exposures for consumer users and bystanders because daily use intervals are not reasonably expected to occur for all consumer uses. The description of the data used for human health exposure is in Section 4.2 of the Risk Evaluation. Uncertainties in the analysis are discussed in Section 4.3. of this Risk Evaluation and are considered in the unreasonable risk determination.

5.2.2 Non-Cancer Risk Estimates

The risk estimates of non-cancer effects (expressed as margins of exposure or MOEs) refer to adverse health effects associated with health endpoints other than cancer, including to the body's organ systems, such as reproductive and developmental effects. The MOE is the point of departure (POD) (an approximation of the no-observed adverse effect level (NOAEL) or benchmark dose level (BMDL)) for a specific health endpoint divided by the exposure

[2] This risk determination is being issued under TSCA section 6(b) and the terms used, such as unreasonable risk, and the considerations discussed are specific to TSCA. Other EPA programs have different statutory authorities and mandates and may involve risk considerations other than those discussed here.

[3] ONUs are workers who do not directly handle NMP but perform work in an area where NMP is present. (Executive Summary of this Risk Evaluation).

concentration for the specific scenario of concern. Section 3.2.5 of this Risk Evaluation presents the PODs for acute and chronic non-cancer effects for NMP and Section 4.2 of this Risk Evaluation presents the MOEs for acute and chronic non-cancer effects.

The MOEs are compared to a benchmark MOE. The benchmark MOE accounts for the total uncertainty in a POD, including, as appropriate: (1) the variation in sensitivity among the members of the human population (i.e., intrahuman/intraspecies variability); (2) the uncertainty in extrapolating animal data to humans (i.e., interspecies variability); (3) the uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure to lifetime exposure (i.e., extrapolating from subchronic to chronic exposure); and (4) the uncertainty in extrapolating from a lowest observed adverse effect level (LOAEL) rather than from a NOAEL. A lower benchmark MOE (e.g., 30) indicates greater certainty in the data (because fewer of the default uncertainty factors (UFs) relevant to a given POD as described above were applied). A higher benchmark MOE (e.g., 1000) would indicate more uncertainty for specific endpoints and scenarios. However, these are often not the only uncertainties in a risk evaluation. The benchmark MOE for acute and chronic non-cancer risks for NMP is 30 (accounting for intraspecies and interspecies variability). Additional information regarding the non-cancer hazard identification is in Section 3.2.3.1 and the benchmark MOE is in Section 4.2.1. of this Risk Evaluation.

5.2.3 Cancer Risk Estimates

Usually, EPA determines cancer risk estimates to represent the incremental increase in probability of an individual in an exposed population developing cancer over a lifetime (excess lifetime cancer risk (ELCR)) following exposure to the chemical. EPA did not evaluate cancer risk from exposure to NMP because NMP is not mutagenic and is not considered carcinogenic so EPA did not conduct analysis of genotoxicity and cancer hazards during risk evaluation. (Section 3.2.3.2 of this Risk Evaluation).

5.2.4 Determining Unreasonable Risk of Injury to Health

Calculated risk estimates (MOEs or cancer risk estimates) can provide a risk profile of NMP by presenting a range of estimates for different health effects for different conditions of use. A calculated MOE that is less than the benchmark MOE supports a determination of unreasonable risk of injury to health, based on noncancer effects. Similarly, a calculated cancer risk estimate that is greater than the cancer benchmark supports a determination of unreasonable risk of injury to health from cancer. Whether EPA makes a determination of unreasonable risk for the chemical substance depends upon other risk-related factors, such as the endpoint under consideration, the reversibility of effect, exposure-related considerations (e.g., duration, magnitude, or frequency of exposure, or population exposed), and the confidence in the information used to inform the hazard and exposure values.

In the NMP risk characterization, the best representative endpoints for non-cancer effects were from acute (developmental toxicity) and chronic (reproductive toxicity) inhalation and dermal exposures for all conditions of use. Additional risks associated with other adverse effects (*e.g.*, liver toxicity, kidney toxicity, immunotoxicity, neurotoxicity, irritation and sensitization) were identified for acute and chronic inhalation and dermal exposures. The NMP unreasonable risk determination uses reproductive and developmental toxicity as driving endpoints. Addressing

unreasonable risk by using the developmental and reproductive endpoints will also address the risk from other endpoints resulting from acute or chronic inhalation and dermal exposures.

When making a determination of unreasonable risk for the chemical substance, the Agency has a higher degree of confidence where uncertainty is low. For example, EPA has high confidence in the hazard and exposure characterizations when the basis for characterizations is measured data or monitoring data or a robust model and the hazards identified for risk estimation are relevant for conditions of use. This Risk Evaluation discusses major assumptions and key uncertainties according to steps of the risk assessment process including around the representativeness of exposure monitoring data, activity pattern information, PPE use and efficacy, and incomplete information on some hazard endpoints and factors that may contribute to increased exposure and susceptibility to NMP. Important assumptions and key sources of uncertainty in the risk characterization are described in more detail in Section 4.3 of this Risk Evaluation.

When determining the unreasonable risk for a chemical substance, EPA considers the central tendency and high-end exposure levels in occupational settings, and low, moderate and high intensity of use for consumer uses. Risk estimates based on high-end exposure levels or high intensity use scenarios (e.g., 95th percentile) are generally intended to cover individuals or sub-populations with greater exposure (PESS) as well as to capture individuals with sentinel exposure, and risk estimates at the central tendency exposure are generally estimates of average or typical exposure (Section 4.4 of this Risk Evaluation).

As shown in Section 4 of this Risk Evaluation, when characterizing the risk to human health from occupational exposures during risk evaluation under TSCA, EPA believes it is appropriate to evaluate the levels of risk present in baseline scenarios where PPE is not assumed to be used by workers. It should be noted that, in some cases, baseline conditions may reflect certain mitigation measures, such as engineering controls, in instances where exposure estimates are based on monitoring data at facilities that have engineering controls in place. This approach of not assuming PPE use by workers considers the risk to potentially exposed or susceptible subpopulations (workers and ONUs) who may not be covered by Occupational Safety and Health Administration (OSHA) standards, such as self-employed individuals and public sector workers who are not covered by a State Plan. In addition, EPA risk evaluations may characterize the levels of risk present in scenarios considering applicable OSHA requirements (e.g., chemical-specific PELs and/or chemical-specific health standards with PELs and additional ancillary provisions), as well as scenarios considering industry or sector best practices for industrial hygiene that are clearly articulated to the Agency. EPA's evaluation of risk under scenarios that, for example, incorporate use of engineering or administrative controls, or personal protective equipment, serves to inform its risk management efforts. By characterizing risks using scenarios that reflect different levels of mitigation, EPA risk evaluations can help inform potential risk management actions by providing information that could be used to tailor risk mitigation appropriately to address worker exposures where the Agency has found unreasonable risk. In particular, EPA can use the information developed during its risk evaluation to determine whether alignment of EPA's risk management requirements with existing OSHA requirements or industry best practices will adequately address unreasonable risk as required by TSCA.

When undertaking unreasonable risk determinations as part of TSCA risk evaluations, EPA cannot assume as a general matter that an applicable OSHA requirement or industry practice is consistently and always properly applied. Mitigation scenarios included in the NMP risk evaluation (e.g., scenarios considering use of various personal protective equipment (PPE)) likely represent what is happening already in some facilities. However, the Agency cannot assume that all facilities will have adopted these practices for the purposes of making the TSCA risk determination.

Therefore, EPA conducts baseline assessments of risk and makes its determination of unreasonable risk from a baseline scenario that is not based on an assumption of compliance with OSHA standards, including any applicable exposure limits or requirements for use of respiratory protection or other PPE. Making unreasonable risk determinations based on the baseline scenario should not be viewed as an indication that EPA believes there are no occupational safety protections in place at any location, or that there is widespread noncompliance with applicable OSHA standards. Rather, it reflects EPA's recognition that unreasonable risk may exist for subpopulations of workers that may be highly exposed because they are not covered by OSHA standards, such as self-employed individuals and public sector workers who are not covered by a State Plan, or because their employer is out of compliance with OSHA standards, or because many of OSHA's chemical-specific permissible exposure limits largely adopted in the 1970's are described by OSHA as being "outdated and inadequate for ensuring protection of worker health,"[4] or because OSHA has not issued a chemical-specific permissible exposure limit (PEL) (as is the case for NMP), or because EPA finds unreasonable risk for purposes of TSCA notwithstanding existing OSHA requirements.

The revised unreasonable risk determination for NMP is based on the peer reviewed risk characterization of the December 2020 Risk Evaluation, which was developed according to TSCA section 26(h) requirements to make science-driven decisions, consistent with best available science. Changing the risk determination to a whole chemical approach does not impact the underlying data and analysis presented in the risk characterization of the risk evaluation. Section 4.6.2 and Table 4-55 of this Risk Evaluation summarize the risk estimates with and without PPE, and informed the revised unreasonable risk determination.

[4] As noted on OSHA's Annotated Table of Permissible Exposure Limits: "OSHA recognizes that many of its permissible exposure limits (PELs) are outdated and inadequate for ensuring protection of worker health. Most of OSHA's PELs were issued shortly after adoption of the Occupational Safety and Health (OSH) Act in 1970, and have not been updated since that time" (Ref. 7).

5.3 Unreasonable Risk to the Environment

5.3.1 Environment

EPA calculated a risk quotient (RQ) to compare environmental concentrations against an effect level. The environmental concentration is determined based on the levels of the chemical released to the environment (e.g., surface water, sediment, soil, biota) under the conditions of use, based on the fate properties, release potential, and reasonably available environmental monitoring data. The effect level is calculated using concentrations of concern that represent hazard data for aquatic, sediment-dwelling, and terrestrial organisms. Section 4.1 of this Risk Evaluation provides more detail regarding the environmental risk characterization for NMP.

5.3.2 Determining Unreasonable Risk of Injury to the Environment

Calculated risk quotients (RQs) can provide a risk profile by presenting a range of estimates for different environmental hazard effects for different conditions of use. An RQ equal to 1 indicates that the exposures are the same as the concentration that causes effects. An RQ less than 1, when the exposure is less than the effect concentration, generally indicates that there is not risk of injury to the environment that would support a determination of unreasonable risk for the chemical substance. An RQ greater than 1, when the exposure is greater than the effect concentration, generally indicates that there is risk of injury to the environment that would support a determination of unreasonable risk for the chemical substance. Consistent with EPA's human health evaluations, the RQ is not treated as a bright line and other risk-based factors may be considered (*e.g.*, confidence in the hazard and exposure characterization, duration, magnitude, uncertainty) for purposes of making an unreasonable risk determination.

EPA considered the effects on aquatic, sediment-dwelling, and terrestrial organisms. NMP is not likely to accumulate in sediment based on its physical and chemical properties and is not expected to adsorb to sediment due to its water solubility and low partitioning to organic matter. For all conditions of use in ambient water, the RQ values in Section 4.1.1 of this Risk Evaluation do not support an unreasonable risk determination for acute and chronic exposures to NMP for amphibians, fish, and aquatic invertebrates. To characterize the exposure to NMP by aquatic organisms, modeled data were used to represent surface water concentrations near facilities actively releasing NMP to surface water, and modeled concentrations were used to represent ambient water concentrations of NMP. EPA considered the biological relevance of the species to determine the concentrations of concern (COCs) for the location of surface water concentration data to produce RQs, as well as frequency and duration of the exposure. NMP is not expected to partition to or accumulate in soil; rather, based on its physical and chemical properties, it is expected to volatilize to air or migrate through soil into groundwater. Therefore, risk to terrestrial organisms is not expected.

When making a determination of unreasonable risk, EPA has a higher degree of confidence where uncertainty is low. For example, EPA has high confidence in the hazard and exposure characterizations when the basis for the characterizations is measured or representative monitoring data or a robust model and the hazards identified for risk estimation are relevant for conditions of use. Where EPA has made assumptions in the scientific evaluation, the degree to which these assumptions are conservative (i.e., more protective) is also a consideration.

Additionally, EPA considers the central tendency and high-end scenarios when determining the unreasonable risk. High-end risk estimates (*e.g.*, 90th percentile) are generally intended to cover organisms or populations with greater exposure (those inhabiting ecosystems near industries) and central tendency risk estimates are generally estimates of average or typical exposure.

EPA considered several uncertainties in its evaluation of risk of injury to the environment for NMP. First, more acute duration toxicity data were reasonably available in the literature compared to chronic duration data. Therefore, EPA is less certain of chronic hazard values than the acute hazard values. Second, EPA used assessment factors to calculate the acute and chronic COCs for NMP. Assessment factors account for differences in inter- and intra-species variability, as well as laboratory-to-field variability and are routinely used within TSCA for assessing the hazard of new industrial chemicals (with very limited environmental test data). There is some uncertainty associated with the use of standardized assessment factors for hazard assessment. Additionally, in the NMP Problem Formulation (*Problem formulation of the risk evaluation for n-methylpyrrolidone*), EPA did not conduct any further analyses on pathways of exposure for terrestrial receptors, as described in Section 2.5.3.1 of the NMP Problem Formulation and further described in Section 2.2 and 2.3 of this Risk Evaluation. Assumptions and key sources of uncertainty in the risk characterization are detailed in Section 4.1.2. of this Risk Evaluation.

Therefore, based on this Risk Evaluation, EPA did not identify risk of injury to the environment that would drive the unreasonable risk determination for NMP.

5.4 Additional Information Regarding the Basis for the Unreasonable Risk Determination

Table 5-1 and Table 5-2 summarize the basis for the revised determination of unreasonable risk of injury to health presented by NMP. In these tables, a checkmark indicates the risk of the type of effect and the exposure route to the population evaluated for each condition of use that drive the unreasonable risk determination. As explained in Section 5.2, for the revised unreasonable risk determination, EPA considered the effects on the environment of exposure to NMP, and to human health at the central tendency and high-end (or low, moderate, and high intensity use), the exposures from the condition of use, the risk estimates, and the uncertainties in the analysis. See Sections 4.6.1 and 4.6.2 of this Risk Evaluation for a summary of risk estimates.

Table 5-1. Supporting Basis for the Revised Unreasonable Risk Determination for Human Health (Occupational Conditions of Use)[5]

Life Cycle Stage	Category [a]	Subcategory [b]	Population [c, d]	Exposure Route	Human Health Effects			
					Acute Non-cancer		Chronic Non-cancer	
					High End	Central Tendency	High End	Central Tendency
Manufacture	Domestic Manufacture	Domestic Manufacture	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			
Manufacture	Import	Import	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			
Processing	Processing as a reactant or intermediate	Intermediate in Plastic Material and Resin Manufacturing	Worker	Inhalation & Dermal	✓	✓	✓	✓
		Other Non-Incorporative Processing						
			ONU	Inhalation	--			
Processing	Incorporation into formulation, mixture or reaction products	Adhesives and sealant chemicals in Adhesive Manufacturing	Worker	Inhalation & Dermal	✓	✓	✓	✓
		Anti-adhesive agents in Printing and Related Support Activities						
		Paint additives and coating additives not described by other codes in Paint and Coating Manufacturing; and Print Ink Manufacturing						

[5] The checkmarks indicate the risk of the type of effect and the exposure route to the population evaluated for each condition of use that supports the revised unreasonable risk determination for NMP. This table is based on Table 4-55 of this Risk Evaluation.

Life Cycle Stage	Category [a]	Subcategory [b]	Population [c, d]	Exposure Route	Human Health Effects			
					Acute Non-cancer		Chronic Non-cancer	
					High End	Central Tendency	High End	Central Tendency
		Processing aids not otherwise listed in Plastic Material and Resin Manufacturing						
		Solvents (for cleaning or degreasing) in Non-Metallic Mineral Product Manufacturing; Machinery Manufacturing; Plastic Material and Resin Manufacturing; Primary Metal Manufacturing; Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Services; Wholesale and Retail Trade						
		Surface active agents in Soap, Cleaning Compound and Toilet Preparation Manufacturing						
		Plating agents and surface treating agents in Fabricated Metal Product Manufacturing						

Life Cycle Stage	Category [a]	Subcategory [b]	Population [c, d]	Exposure Route	Human Health Effects			
					Acute Non-cancer		Chronic Non-cancer	
					High End	Central Tendency	High End	Central Tendency
		Solvents (which become part of product formulation or mixture) in Electrical Equipment, Appliance and Component Manufacturing; Other Manufacturing; Paint and Coating Manufacturing; Print Ink Manufacturing; Soap, Cleaning Compound and Toilet Preparation Manufacturing; Transportation Equipment Manufacturing; All Other Chemical Product and Preparation Manufacturing; Printing and Related Support Activities; Wholesale and Retail Trade						
		Other uses in Oil and Gas Drilling, Extraction and Support Activities; Plastic Material and Resin Manufacturing; Services	ONU	Inhalation	--			
Processing	Incorporation into articles	Lubricants and lubricant additives in Machinery Manufacturing	Worker	Inhalation & Dermal	✓		✓	✓
			ONU	Inhalation	--			
Processing	Incorporation into articles	Paint additives and coating additives not described by other codes in Transportation Equipment Manufacturing	Worker	Inhalation & Dermal	✓		✓	
			ONU	Inhalation	--			
Processing	Incorporation into articles	Solvents (which become part of product formulation or mixture), including in Textiles, Apparel and Leather Manufacturing	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			

Life Cycle Stage	Category [a]	Subcategory [b]	Population [c, d]	Exposure Route	Human Health Effects			
					Acute Non-cancer		Chronic Non-cancer	
					High End	Central Tendency	High End	Central Tendency
Processing	Incorporation into articles	Other, including in Plastic Product Manufacturing	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			
Processing	Recycling	Recycling	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			
Processing	Repackaging	Wholesale and Retail Trade	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			
Industrial and Commercial use	Paints and coatings	Paint and coating removers	Worker	Inhalation & Dermal	✓		✓	✓
		Adhesive removers						
			ONU	Inhalation	--			
Industrial and Commercial use	Paints and coatings	Lacquers, stains, varnishes, primers and floor finishes	Worker	Inhalation & Dermal	✓		✓	
		Powder coatings (surface preparation)						
			ONU	Inhalation	--			
Industrial and Commercial use	Paint additives and coating additives not described by other codes	Use in Computer and Electronic Product Manufacturing in Electronic Parts Manufacturing	Worker	Inhalation & Dermal	✓		✓	✓
			ONU	Inhalation	--			
Industrial and Commercial use	Paint additives and coating additives not described by other codes	Use in Computer and Electronic Product Manufacturing in Semiconductor Manufacturing	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			

Life Cycle Stage	Category [a]	Subcategory [b]	Population [c, d]	Exposure Route	Human Health Effects			
					Acute Non-cancer		Chronic Non-cancer	
					High End	Central Tendency	High End	Central Tendency
Industrial and Commercial use	Paint additives and coating additives not described by other codes	Use in Construction, Fabricated Metal Product Manufacturing, Machinery Manufacturing, Other Manufacturing, Paint and Coating Manufacturing, Primary Metal Manufacturing, Transportation Equipment Manufacturing, Wholesale and Retail Trade	Worker	Inhalation & Dermal	✓		✓	
			ONU	Inhalation	--			
Industrial and Commercial use	Solvent (for cleaning or degreasing)	Use in Electrical Equipment, Appliance and Component Manufacturing	Worker	Inhalation & Dermal	✓		✓	✓
			ONU	Inhalation	--			
Industrial and Commercial use	Solvent (for cleaning or degreasing)	Use in Electrical Equipment Appliance and Component Manufacturing in Semiconductor Manufacturing	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			
Industrial and Commercial use	Ink, toner, and colorant products	Printer Ink	Worker	Inhalation & Dermal			✓	
		Inks in writing equipment						
			ONU	Inhalation	--			
Industrial and Commercial use	Processing aids, specific to petroleum production	Petrochemical Manufacturing	Worker	Inhalation & Dermal	✓	✓	✓	✓
	Other uses	Other uses in Oil and Gas Drilling, Extraction and Support Activities						
		Functional fluids (closed systems)						
			ONU	Inhalation	--			

Life Cycle Stage	Category [a]	Subcategory [b]	Population [c, d]	Exposure Route	Human Health Effects			
					Acute Non-cancer		Chronic Non-cancer	
					High End	Central Tendency	High End	Central Tendency
Industrial and Commercial use	Adhesives and sealants	Adhesives and sealant chemicals including binding agents	Worker	Inhalation & Dermal	✓		✓	
		Single component glues and adhesives, including lubricant adhesives						
		Two-component glues and adhesives, including some resins						
			ONU	Inhalation	--			
Industrial and Commercial use	Other uses	Soldering materials	Worker	Inhalation & Dermal			✓	
			ONU	Inhalation	--			
Industrial and Commercial use	Other uses	Anti-freeze and de-icing	Worker	Inhalation & Dermal			✓	
		Automotive care products						
		Lubricants and greases						
			ONU	Inhalation	--			
Industrial and Commercial use	Other uses	Metal products not covered elsewhere	Worker	Inhalation & Dermal	✓		✓	✓
		Lubricant and lubricant additives, including hydrophilic coatings						
			ONU	Inhalation	--			
Industrial and Commercial use	Other uses	Laboratory chemicals	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			
Industrial and Commercial use	Other uses	Lithium Ion battery manufacturing	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			
Industrial and Commercial use	Other uses	Cleaning and furniture care products, including wood cleaners, gasket removers	Worker	Inhalation & Dermal	✓	✓	✓	✓
			ONU	Inhalation	--			

Life Cycle Stage	Category [a]	Subcategory [b]	Population [c, d]	Exposure Route	Human Health Effects			
					Acute Non-cancer		Chronic Non-cancer	
					High End	Central Tendency	High End	Central Tendency
Industrial and Commercial use	Other uses	Fertilizer and other agricultural chemical manufacturing - processing aids and solvents	Worker	Inhalation & Dermal			✓	
			ONU	Inhalation	--			
Disposal	Disposal	Industrial pre-treatment	Worker	Inhalation & Dermal	✓	✓	✓	✓
		Industrial wastewater treatment						
		Publicly owned treatment works (POTW)						
		Underground injection						
		Landfill (municipal, hazardous or other land disposal)						
		Incinerators (municipal and hazardous waste)						
		Emissions to air						
			ONU	Inhalation	--			

[a] These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent additional information regarding all conditions of use of NMP.

[b] These subcategories reflect more specific information regarding the conditions of use of NMP.

[c] ONU risk from acute exposure are not expected to be below the benchmark MOE.

[d] Based on EPA's analysis, the data for worker and ONU inhalation exposures could not be distinguished; however, ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation and-vapor-through-skin exposures when determining ONUs' unreasonable risk. See further explanation in Section 2.4.3 of this Risk Evaluation.

"--" = ONU risk from acute exposures are not expected to be below the MOE; see further explanation in Section 4.2.3

Table 5-2. Supporting Basis for the Revised Unreasonable Risk Determination for Human Health (Consumer Conditions of Use)[6]

Life Cycle Stage	Category [a]	Subcategory [b]	Population [c]	Exposure Route	Human Health	
					Acute Non-cancer	
					High Intensity Use	Medium Intensity Use
Consumer use	Paints and coatings	Paint and coating removers	Consumer user	Inhalation & Dermal		
			Bystander user	Inhalation		N/A
Consumer use	Paints and coatings	Adhesive removers	Consumer user	Inhalation & Dermal		
			Bystander user	Inhalation	N/A	N/A
Consumer use	Paints and coatings	Lacquers, stains, varnishes, primers and floor finishes	Consumer user	Inhalation & Dermal		
			Bystander user	Inhalation	N/A	N/A
Consumer use	Paint additives and coating additives not described by other codes	Paints and Arts and Crafts Paints	Consumer user	Inhalation & Dermal		
			Bystander user	Inhalation	N/A	N/A
Consumer use	Adhesives and sealants	Glues and adhesives, including lubricant adhesives	Consumer user	Inhalation & Dermal	✓	
			Bystander user	Inhalation		N/A
Consumer use	Other uses	Automotive care products	Consumer user	Inhalation & Dermal		
			Bystander user	Inhalation	N/A	N/A
Consumer use	Other uses	Cleaning and furniture care products, including wood cleaners, gasket removers	Consumer use	Inhalation & Dermal		
			Bystander user	Inhalation		N/A

[6] The checkmarks indicate the risk of the type of effect and the exposure route to the population evaluated for each condition of use that support the revised unreasonable risk determination for NMP. This table is based on Table 4-56 of this Risk Evaluation.

Life Cycle Stage	Category [a]	Subcategory [b]	Population [c]	Exposure Route	Human Health	
					Acute Non-cancer	
					High Intensity Use	Medium Intensity Use
Consumer use	Other uses	Lubricant and lubricant additives, including hydrophilic coatings	Consumer user	Inhalation		
			Bystander user	Inhalation	N/A	N/A

[a] These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent additional information regarding all conditions of use of NMP.
[b] These subcategories reflect more specific information regarding the conditions of use of NMP.
[b] N/A = not assessed. Bystander exposure was evaluated for three high-end scenarios that indicated potential risk.

5.5 Order Withdrawing TSCA Section 6(i)(1) Order

The December 2020 risk evaluation for NMP included individual risk determinations for each condition of use evaluated. The determinations that particular conditions of use did not present unreasonable risk were issued by order under TSCA section 6(i)(1). Section 5.4.1 of the December 2020 Risk Evaluation stated: "This subsection of the final Risk Evaluation … constitutes the order required under TSCA section 6(i)(1), and the 'no unreasonable risk' determinations in this subsection are considered to be final agency action effective on the date of issuance of this order."

In this revised risk determination, EPA has determined that NMP as a whole chemical substance presents an unreasonable risk of injury to health under the conditions of use. This revised risk determination supersedes the no unreasonable risk determinations in the December 2020 Risk Evaluation that were premised on a condition of use-specific approach to determining unreasonable risk. This subsection of the revised risk determination also constitutes an order withdrawing the TSCA section 6(i)(1) order in the December 2020 Risk Evaluation. EPA has inherent authority to reconsider previous decisions and to revise, replace, or repeal a decision to the to the extent permitted by law and supported by reasoned explanation. *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 515 (2009); *see also Motor Vehicle Mfrs. Ass'n v. State Farm Mutual Auto. Ins. Co.*, 463 U.S. 29, 42 (1983). Further explanation and justification for this action can be found in the Federal Register Notice announcing the availability of the draft revised risk determination for NMP, 87 Fed. Reg. 39511 (July 1, 2022) (Ref. 8), and in the Federal Register Notice accompanying this revised risk determination.

5.6 References

1. EPA. Risk Evaluation for n-Methylpyrrolidone (NMP). December 2020. *https://www.regulations.gov/document/EPA-HQ-OPPT-2019-0236-0081*.

2. Executive Order 13985. Advancing Racial Equity and Support for Underserved Communities Through the Federal Government. *Federal Register* (86 FR 7009, January 25, 2021).

3. Executive Order 13990. Protecting Public Health and the Environment and Restoring Science to Tackle the Climate Crisis. *Federal Register* (86 FR 7037, January 25, 2021).

4. Executive Order 14008. Tackling the Climate Crisis at Home and Abroad. *Federal Register* (86 FR 7619, February 1, 2021).

5. Presidential Memorandum. Memorandum on Restoring Trust in Government Through Scientific Integrity and Evidence-Based Policymaking. *Federal Register* (86 FR 8845, February 10, 2021).

6. EPA Press Release. EPA Announces Path Forward for TSCA Chemical Risk Evaluations. June 30, 2021. *https://www.epa.gov/newsreleases/epa-announces-path-forward-tsca-chemical-risk-evaluations.*

7. Occupational Safety and Health Administration. Permissible Exposure Limits – Annotated Tables. Accessed June 13, 2022. *https://www.osha.gov/annotated-pels.*

8. Notice. n-Methylpyrrolidone (NMP); Draft Revision to Toxic Substances Control Act (TSCA) Risk Determination; Notice of Availability and Request for Comment. *Federal Register* (87 FR 39511, July 1, 2022).

9. EPA. Response to Public Comments to the Revised Unreasonable Risk Determination; n-Methylpyrrolidone (NMP). December 2022.