# Review of TSCA Section 6 Risk Evaluation of the Conditions of Use of NMP in the Semiconductor Industry

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# Executive Summary

A comprehensive review of the U.S. EPA final risk evaluation for the conditions of use of n-methylpyrrolidone (NMP) in the semiconductor industry has been completed by human health risk assessors at Cardno ChemRisk. Our review considered the information reasonably available to the Agency, and applied the scientific standards of "best available science," and "weight of the scientific evidence" approach required under Section 26 of the Toxic Substances Control Act (TSCA)[1]. This review affirmed the conclusion of the Cardno ChemRisk assessment completed in January 2020, which substantiated that NMP is being used responsibly and safely in the U.S. semiconductor industry as indicated by calculated margins of exposure (MOEs) greater than the U.S. EPA benchmark MOE of 30. Based on the available data, our review leads us to conclude that none of the conditions of use of NMP in the U.S. semiconductor industry present an unreasonable risk to the health of workers.

Two notable themes were identified in critically reviewing the Agency's final NMP risk evaluation, including:

- U.S. EPA erred in not using, in the final risk evaluation, the "high quality" data and information SIA provided describing the industry's use of NMP. SIA represents 98% of the U.S. semiconductor industry by revenue and nearly two-thirds of non-U.S. chip firms and the SIA submittals included extensively substantiated information prepared by industry subject matter experts. Thus, U.S. EPA's failure to adopt the "high quality" information does not reflect use of the best available science, nor does it apply the required weight of the evidence standard.
- U.S. EPA's assertion that prolonged and up to full-hand dermal liquid contact occurs as a condition of use of NMP in the U.S. semiconductor industry is an incorrect and "beyond worst case" hypothetical assertion and is not substantiated by evidence.

When comparing the final December 2020 NMP risk evaluation to the October 2019 draft risk evaluation, Cardno ChemRisk found that the Agency made few changes to the physiologically based pharmacokinetic (PBPK) model input parameters ultimately used to estimate internal worker exposure to NMP in the U.S. semiconductor industry. Despite the comprehensive information and data provided by SIA and Cardno ChemRisk, the Agency maintained the use of generic, unsubstantiated assumptions regarding prolonged dermal-liquid contact times and exposures of appreciable hand surface areas (i.e., one or two hands immersed in concentrated or neat NMP for 30 or 60 hours per week), which were applied uniformly across various scenarios. The SIA data and information were timely and "reasonably available" to the Agency, and the U.S. EPA systematic review document rated the January 2020 SIA submission as "high quality" (U.S. EPA, 2020c). Thus, the omission of SIA submitted data reflecting the conditions of use of NMP in the U.S. semiconductor industry from the final conclusions in the NMP risk evaluation was unfounded. Thus, the final risk evaluation does not reflect the best available science and neglected to apply the required weight of the evidence standard.

[1] Weight of the scientific evidence is defined as "a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance." (US.EPA, 2017: p. 33733).

It is also worth noting that Agency prepared PBPK model estimates using input parameters more consistent with SIA-substantiated conditions of use resulted in predicted MOEs greater than 30 demonstrating no unreasonable risks for the conditions of use of NMP in the semiconductor industry. These modeling runs can be found in the public docket of the final NMP risk evaluation, but were not relied upon for reaching the final conclusions of the risk evaluation. A concise summary of the final U.S. EPA PBPK model input parameters and associated MOEs and the U.S. EPA supplemental modeling predictions using SIA data and associated MOEs is presented in Table ES-1. This table distills how the Agency's final risk evaluation, without reasonable scientific justification, failed to adopt industry-specific exposure factors based on SIA-submitted data in the portions of the final risk evaluation pertinent to the conclusions reached about the conditions of use in the semiconductor industry.

In conclusion, the U.S. EPA's final risk evaluation finding of unreasonable risk for certain conditions of NMP use within the U.S. semiconductor industry does not reflect use of the "best available science." Further, the incorporation of incorrect generic assumptions in the final risk evaluation, rather than incorporating industry-specific exposure factors based on SIA-submitted data, neglects to take a weight of evidence approach as mandated under Section 26 of TSCA. Using the data and information provided to the Agency by SIA for the input parameters of the PBPK modeling leads to a more appropriate science-based conclusion of no unreasonable risk as indicated by calculated acute and chronic MOEs greater than 30.

**Table ES-1**: Critical review of differences in the U.S. EPA and SIA PBPK modeling scenarios including U.S. EPA non-substantiated immersion (EPA) versus precautionary SIA-substantiated[a] condition of use (COU)[b]

| Consideration | Generic EPA PBPK input parameters used in the final risk evaluation and associated MOEs | Industry specific PBPK input parameters based on SIA-submitted data and associated MOEs[c] documented in the EPA supplemental model information |
|---|---|---|
| **Exposure Factors** | | |
| **Glove protection factor** | 10 | 20 (Industry workers handling chemicals received mandatory glove use training) |
| **Dermal loading[c]** | Equivalent to skin immersion | 0.7 to 2.1 mg/cm2 |
| **Surface area of liquid contact[c]** | One to two hands | Most work activities: 3 fingertips (central tendency) and 10 fingertips (high-end) |
| **Dermal contact time** | 360 to 720 minutes per shift or 240-480 minutes per shift depending on work activity | 20-60 minute per shift |
| **Shift duration** | 30 – 60 hours/week | 36 – 48 hours/week |
| **Fraction of skin exposed to dermal vapor** | 25% (Supplemental PBPK: 2%) | <2% (Conservative industry assumption based on typical skin coverage) |
| **Worker Risk Characterization [Acute and Chronic MOEs]** | | |
| **Container handing, small containers** | Unreasonable risk w/ immersion [A: 47-252; C: 2.1-18] | No unreasonable risk with actual COU [A: 4367-45377; 685-11011] |
| **Container handing, drums** | Unreasonable risk w/ immersion [A: 46-508; C: 2.0-36] | No unreasonable risk with actual COU [A: 4021-116379; C: 631-28648] |
| **Fab worker, container changeout** | No unreasonable risk w/ ≤5% NMP [A: 1925-9461; C: 85-667] | No unreasonable risk with actual COU [A: 71509-545017; C: 11189-127582] |
| **Fab worker, typical or non-exposed** | No unreasonable risk w/ inh. only [A: N/A; C: 1537-9014] | No unreasonable risk with actual COU [A: N/A; C: 1524-4485] |
| **Maintenance** | Unreasonable risk w/ immersion [A: 19-508; C: 0.85-36] | No unreasonable risk with actual COU [A: 455-10608; C: 71-2621] |
| **Virgin NMP unloading** | Unreasonable risk w/ immersion [A: 23-63; C: 1.3-5.8] | No unreasonable risk with actual COU [A:602-3436; C: 94-837] |
| **Waste truck unloading** | Unreasonable risk w/ immersion [A: 29-81; C: 1.7-7.4] | No unreasonable risk with actual COU [A: 785-4936; C: 123-1214] |
| **Critical Evaluation of U.S. EPA Final Risk Evaluation** | | |
| **Exposure Factors** | The U.S. EPA risk characterization analysis did not rely on the high-quality information consisting of exposure factors describing dermal contact time and skin surface are prepared by subject matter experts. | |
| **Conclusion** | NMP is used responsibly in the semiconductor industry with safe use substantiated by proper glove selection, limited surface area of direct contact and limited liquid contact time. | |

[a]"SIA-substantiated" COU denotes precautionary (conservative) and worst-case scenarios for the industry. Conditions of use at individual facilities may include more limited, less frequent or no liquid contact, such that contact area and time is appreciably lower than the SIA-substantiated level of exposure.

[b]NMP was not detected in a majority of personal air sampling, suggesting low potential for residual NMP-containing liquid to contact skin

[c]U.S. EPA systematic review evaluation rated SIA submissions overall "high quality" (including PBPK inputs).

# 1 Introduction

A comprehensive review of the U.S. EPA final risk evaluation for the conditions of use of n-methylpyrrolidone (NMP) in the semiconductor industry has been completed. Our review considered the information reasonably available to the Agency, and applied the scientific standards of "best available science," and "weight of the scientific evidence" approach required under Section 26 of the Toxic Substances Control Act (TSCA)[2]. Cardno ChemRisk reviewed the draft and final NMP risk evaluation dated October 2019 (U.S. EPA, 2019) and December 2020 (U.S. EPA, 2020a), respectively. The final December 2020 risk evaluation included several relevant supplementary documents, which have also been considered in this review, including:

- Summary of External Peer Review and Public Comments and Disposition for n-Methylpyrrolidone (NMP) (U.S. EPA, 2020b)
- Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data (U.S. EPA, 2020c)
- Supplemental Information on Occupational Exposure Assessment (U.S. EPA, 2020d)
- Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Excel File on Occupational Risk Calculations. Docket EPA-HQ-OPPT-2019-0236. (U.S. EPA, 2020e)

Our review includes a comparison between the data and information available to the U.S. EPA and the data and information used by the U.S. EPA to estimate exposure. These analyses collectively identified a number of shortcomings in the final U.S. EPA assessment, including a failure to correctly represent any NMP occupational use scenarios known to SIA members. As part of this review, a number of instances where the Agency failed to consider readily available occupational exposure modeling approaches were identified. Notable shortcomings were also identified in the U.S. EPA response to the Science Advisory Committee on Chemicals (SACC).

Our report concludes with an evaluation of the potential occupational risk associated with the use of NMP based on current industry conditions, which demonstrates that current practices are consistent with the safe use of NMP. This review affirmed the conclusion of the Cardno ChemRisk assessment completed in January 2020, which substantiated that NMP is being used responsibly and safely in the U.S. semiconductor industry as indicated by calculated margins of exposure (MOEs) greater than the U.S. EPA benchmark MOE of 30. Based on the available data, our review leads us to conclude that none of the conditions of use of NMP in the U.S. semiconductor industry present an unreasonable risk to the health of workers.

[2] Weight of the scientific evidence is defined as "a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance." (US.EPA, 2017: p. 33733).

# 2 Concise Summary of U.S. EPA Exposure and Risk Characterization

The U.S. EPA is required under TSCA Section 6(b) to complete risk evaluations to determine "whether a chemical substance presents unreasonable risk of injury to health or the environment, under the conditions of use, without consideration of costs or other non-risk factors, including an unreasonable risk to potentially exposed or susceptible subpopulations, identified as relevant to the risk evaluation" (U.S. EPA, 2020a). This report focuses on a comparison of the TSCA Section 6 Risk Evaluation of the conditions of use of NMP in the semiconductor industry published in December 2020 to the evaluation submitted by Cardno ChemRisk on behalf of SIA in January 2020.

## 2.1 Point of Departure and Benchmark MOE

The U.S. EPA adopted the chronic point of departure (POD) of 183 hr mg/L and benchmark MOE of 30 from the draft evolution. A reanalysis of the acute POD resulted in a slight increase (less precautionary) point of departure from a draft $C_{max}$ of 216 mg/L to a final $C_{max}$ of 437 mg/L. This change resulted in an increase in the acute MOE when all other parameters are held constant between the draft and final evaluation. The change to the acute POD was not an appreciable factor in the Agency risk evaluation due to the overwhelming impact of the non-representative skin surface area with liquid contact and the duration of that contact.

## 2.2 Dermal Permeability Coefficient

The Agency increased the final dermal permeability coefficient when the NMP weight percent increased above 50%, resulting in some differences in MOE between the SIA 2020 submission and the final U.S. EPA model runs that do not affect the safe use conclusion reached in the prior Cardno ChemRisk report. Notably, Cardno ChemRisk previously commented on the Agency's use of a single permeability coefficient and had evaluated the impact of using a higher permeability coefficient in the sensitivity analysis (i.e. Section 6.2.3 of the January 2020 report), so this change was not unanticipated. Use of an enhanced permeability coefficient does not appear to be justified for the semiconductor industry because prolonged contact with neat NMP does not occur in the industry. Nonetheless, it is notable that when the enhanced permeability coefficient was applied when weight percent exceeded 50%, the Agency analysis of the SIA-substantiated exposure factors results in MOEs > 30 as documented in U.S. EPA 2020e.

## 2.3 Activities and Scenarios

The U.S. EPA prepared exposure estimates for at least one scenario covering several potential semiconductor occupational activities including:

- Container handling, small containers
- Container handling, drums
- Fab worker w/ NMP container changeout
- Fab worker-typical (described as occupational non-user in the U.S. EPA evaluation)
- Maintenance
- Virgin NMP Unloading
- Waste Truck Loading

For each activity, the U.S. EPA presents exposure estimates for six scenarios including:

- Central tendency (Glove PF=1, 5, 10, 20)
- High-end (Glove PF=1, 5, 10, 20)
- What-if (task-based duration) – central tendency (Glove PF=1, 5, 10, 20)
- What-if (task-based duration) – high end (Glove PF=1, 5, 10, 20)
- SIA-substantiated – central tendency (Glove PF = 20)
- SIA-substantiated – high end (Glove PF = 20)

PBPK exposure estimates for the "what-if" and SIA-substantiated (termed "industry proposed" in Agency evaluation) scenarios were added to the analysis after the review and public comment period for the draft report. However, the U.S. EPA risk evaluation relies only on the margin of exposure estimates for the first two scenarios with an assumed glove PF of 10. As discussed in Section 3, the U.S. EPA systematic review scored the SIA-substantiated scenarios as "high quality" evidence, and a notable shortcoming of the final evaluation is the absence of a risk characterization conclusion associated with the Agency's consideration of the "high quality" SIA-substantiated activity factors. Additionally, the MOEs > 30 (safe use) in the U.S. EPA PBPK modeling runs are not transparently discussed in the risk evaluation document (U.S. EPA, 2020a), and instead have been recorded only in the docket spreadsheet (U.S. EPA, 2020e).

## 2.4 Summary of Key Differences between Scenarios

A number of meaningful differences were identified between the six scenarios corresponding to U.S. EPA PBPK exposure estimates (Table ES-1; Appendix A). For each of the scenarios summarized in Table A.1 and A.2, detailed comparisons of exposure factors and the basis of the factors is presented in Appendix B, and a concise summary of acute and chronic exposure and MOE estimates are presented in Tables A.3 and A.4, respectively. Four of the six scenarios (typical, high-end, and the two "what-if" scenarios) do not describe the conditions of use for SIA member companies and are inappropriate for use in characterization of risk at SIA member company facilities. The current conditions of use at SIA member companies are represented by the SIA-substantiated inputs, which were considered to be "high quality" in the Agency systematic review.

The U.S. EPA risk evaluation scenarios were based largely on generic assumptions except for airborne concentration. Two sets of "what-if" scenarios were modeled, including evaluating the adoption of a total task time for the liquid contact time (irrespective of if there was contact with the liquid for the total duration of the task), and a set of precautionary (worst case) simulations for the SIA conditions of use of NMP in the semiconductor industry. The precautionary (conservative) MOEs associated with the actual conditions of use of NMP in the semiconductor industry are found only in the docket in U.S. EPA (2020e).

The following conclusions can be reached when examining the differences between the scenarios:

- The U.S. EPA implementation of the SIA-substantiated exposure factors resulted in PBPK modeled internal exposures corresponding to MOEs > 30 and a conclusion of safe use of NMP in semiconductor manufacturing scenarios.
- When modeling the SIA-substantiated PBPK parameters, the Agency ignored the exposure frequencies proposed by SIA, which resulted in non-representative chronic exposure estimates particularly for the truck loading and unloading scenarios. Despite this oversight, the MOEs were > 30. As noted in Section 4, the Agency expressed an intent to not model chronic exposure for truck unloading, yet chronic exposure estimates and MOEs are presented in the final evaluation (e.g. Table 4-55).

- The first set of U.S. EPA "what-if" scenarios is non-informative because the liquid contact time is equal to task duration, but U.S. EPA did not refine surface area nor consider that liquid contact time is appreciably less than the task duration.
- The primary differences between the final risk evaluation and the SIA submission can be attributed to:
    - Duration of contact (shift duration up to 6 to 12 hours equivalent to full hand immersion in final risk evaluation versus no more than 20 or 60 minutes incidental contact based on task description and loading estimates in SIA submission);
    - Skin surface area of dermal liquid contact (1 or 2 hands versus inadvertent contact of no more than a fraction of the hand based on task description);
    - Glove protection factor (10 in risk evaluation and at least 20 in SIA submission based on training and strict conditions);
    - Exposure frequency for truck operations (5 days per week in final risk evaluation versus limited frequency in SIA submission); and
    - Dermal permeability coefficient (single value in the draft evaluation and SIA public comment versus enhanced permeability when NMP weight percent is greater than 50% in final evaluation).

When considering the differences between the Agency and SIA scenarios, it is notable that Kirman (2020) conducted an evaluation of published studies on the glove protection provided against NMP and concluded that NMP can be safely used with appropriate PPE in paint stripping applications. Similarly, for the semiconductor industry, the Cardno ChemRisk assessment substantiated that NMP is being used responsibly and safely in the U.S. semiconductor industry as indicated by calculated margins of exposure (MOEs) greater than the U.S. EPA benchmark MOE of 30. This substantiation is clearly shown in the Table ES-1 concise summary of the final U.S. EPA PBPK modeling predictions, which distills how the Agency's final risk evaluation, without reasonable scientific justification, failed to adopt industry-specific exposure factors based on SIA-submitted information and data.

## 2.5 U.S. EPA Risk Evaluation

The U.S. EPA concluded an unreasonable risk for specific use scenarios identified in Tables 4-24 and 4-25 of the final risk evaluation (U.S. EPA, 2020a). It is important to emphasize that the U.S. EPA prepared exposure estimates for six sets of parameter selections (termed "Scenarios"), yet considered only a subset of "beyond worst-case" scenarios in the risk evaluation (Table A.1). In particular, as described in Section 3, the U.S. EPA did not consider high-quality scenario information submitted by SIA. Thus, the Agency decision based solely upon "beyond worst-case" conditions of use that do not exist at SIA member companies. Thus, the U.S. EPA's final risk evaluation finding of unreasonable risk for certain conditions of NMP use within the U.S. semiconductor industry does not reflect use of the "best available science." The Agency's assertion that the "model is representative of activities in semiconductor manufacturing" is refuted by the comprehensive data, task descriptions and conditions of use of NMP in the semiconductor industry provided by SIA to the Agency in public comments. These considerations are addressed in more detail in Sections 3 and 4.

# 3 U.S. EPA Systematic Review Findings

The U.S. EPA approach to the risk evaluation of NMP was described in the final risk evaluation as using "reasonably available information (defined in 40 CFR 702.33 as "information that EPA possesses, or can reasonably generate, obtain, and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation")" (U.S. EPA, 2020a: p. 22). Notably, SIA provided a large volume of information to the Agency within the scope of reasonable availability of evidence, and this information was found to be of high overall quality for consideration in the exposure and risk characterization.

## 3.1 U.S. EPA Systematic Review Process

The U.S. EPA risk evaluation of NMP included a systemic review of the available literature. According to U.S. EPA recommendations, systematic review scores are interpreted as follows (U.S. EPA, 2018):

- *High: No notable deficiencies or concerns are identified in the domain metric that are likely to influence results [score of 1].*
- *Medium: Minor uncertainties or limitations are noted in the domain metric that are unlikely to have a substantial impact on results [score of 2].*
- *Low: Deficiencies or concerns are noted in the domain metric that are likely to have a substantial impact on results [score of 3].*
- *Unacceptable: Serious flaws are noted in the domain metric that consequently make the data/information source unusable. [score of 4]*

The Agency has indicated an intent to use qualitative and quantitative data of overall low, medium and high quality, and generally exclude unacceptable data unless justified on a case by case basis. The U.S. EPA systematic review of several documents relevant NMP occupational exposure is summarized in Appendix C.

## 3.2 U.S. EPA Systematic Review of SIA and Cardno ChemRisk Submissions

The U.S. EPA rated information provided by SIA or SIA member companies as having an overall quality determination of "high" (Appendix C), indicating that the U.S. EPA found the exposure scenario information to be appropriate for risk assessment with no notable deficiencies (U.S. EPA, 2020c). The overall quality of the PBPK exposure model inputs documented in the Cardno ChemRisk submission received an overall quality rating of high. Focusing on individual metrics, the U.S. EPA systemic review noted that:

- the "[i]nformation does not indicate flaws or quality issues"
- the "[a]ssessment or report clearly documents its data sources, assessment methods, results, and assumptions," and
- "[t]he assessment addresses variability and uncertainty in the results. Uncertainty is well characterized." (U.S.EPA, 2020c: p. 470-471)

Specifically, the PBPK input parameters describing the use of NMP in the semiconductor industry extracted from the "high-quality" SIA submission included:

- Air concentration (central and high-end)
- Dermal surface area (central and high-end)
- Dermal loading (central and high-end)

- Dermal exposure duration (central and high-end)
- Dermal exposure frequency (central and high-end)

Taken together, it is concluded that the U.S. EPA systematic review process judged the information submitted by SIA to be reliable. The PBPK input parameters describing the use of NMP in the semiconductor industry as presented by SIA were found to be reasonable estimates of occupational exposure factors for SIA member companies, which represent 98% of the U.S. semiconductor industry by revenue and nearly two-thirds of non-U.S. chip firms.

However, the Agency notes in the Final Risk Evaluation Systematic Review Data Quality Evaluation that it is "*[u]nclear if these inputs are representative of all semiconductor manufacturing sites."* (U.S. EPA, 2020c: p. 471), implying uncertainty exists with respect to non-SIA member companies. It is recommended that instead of disregarding the SIA data because of this uncertainty, that the Agency prioritize the SIA input in the final risk determination. It is also suggested that the U.S. EPA rely on the SIA 2017, 2019 and 2020 submissions in future TSCA Section 6(a) proposed risk management actions based on the considerations that:

- the U.S. EPA rated the SIA industry submissions as high quality; and
- these submissions substantiate safe occupational use of NMP.

Considering the Agency's favorable systematic review of SIA's public submissions, it will be necessary for the Agency, in implementing its risk management policy, to make a clear distinction between the hypothetical "beyond worst case" conditions of use of NMP assumed for the semiconductor industry, as compared to the high-quality evidence submitted by SIA demonstrating safe occupational use of NMP. It can be concluded that the U.S. EPA determination of "unreasonable risk of injury to health or the environment" does not apply to SIA member companies, but rather are hypothetical scenarios which do not represent the occupational conditions of use of NMP in the semiconductor industry.

## 3.3 Other U.S. EPA Considerations of Data Quality

The U.S. EPA provided some further details regarding data quality in the document titled "Supplemental Information on Occupational Exposure Assessment" (U.S. EPA, 2020d). The U.S. EPA summarizes exposure factors for:

- U.S. EPA default scenarios used for MOE estimate (U.S. EPA, 2020d, Table 2-54)
- U.S. EPA what-if scenarios (U.S. EPA, 2020d, Table 2-54)
- SIA-substantiated scenarios (U.S. EPA, 2020d, Table 2-55)

Despite the availability of high-quality information on task duration from SIA, the U.S. EPA concluded that it "found no reasonably available data on actual duration of dermal contact with liquids" (U.S. EPA, 2020d: p. 22). Rather than using the determined high-quality information for dermal contact time to estimate the MOEs, the Agency chose to prepare exposure estimates for "what-if" scenarios and SIA-substantiated scenarios that were not considered in the estimation of MOEs in the final risk evaluation. No reasonable basis for excluding the SIA-substantiated data and subsequent PBPK modeling based on that data could be found in the documentation provided in U.S. EPA 2020a, b, c and d. A thorough review of the U.S. EPA analysis is presented in Section 4.

# 4 Review of Agency Risk Evaluation and Response to Comments

The U.S. EPA referenced the SIA public comments but did not include SIA-substantiated conditions in the final risk evaluation report (U.S. EPA, 2020a, b, c, d and e). This section analyses the U.S. EPA response to comments and provides an analysis of the U.S. EPA responses and final assessment. In summary, the exposure information submitted by SIA substantiated the safe use of NMP in the semiconductor industry, and the U.S. EPA prepared PBPK modeling results using the SIA-substantiated inputs affirmed MOEs greater than 30. The calculation of MOEs > 30 for the SIA conditions of use are documented in the public docket in the following file:

> "U.S. EPA. (2020e). Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Excel File on Occupational Risk Calculations. (Docket EPA-HQ-OPPT-2019-0236)."

The U.S. EPA's failure to discuss the MOE estimates corresponding to SIA-substantiated conditions of use in the main evaluation report lacks the level of transparency customary in risk assessment.

## 4.1 Overview of U.S. EPA Response to Comments and Final Evaluation

An analysis of the U.S. EPA final evaluation and response to comments is presented in Section 4.2. An overarching theme of the Agency response was that it was necessary to assume 1) a half-shift or full-shift of prolonged dermal exposure and 2) the surface area of one to two hands of dermal contact due to the lack of reasonably available data or information. However, the Agency had completed a systematic review of the SIA PBPK parameters (U.S. EPA, 2020c), judged the submission to be "high quality", and applied the proposed precautionary (conservative) exposure factors in their model to derive SIA-substantiated exposure estimates. A significant shortcoming of the final evaluation, then, was the failure of the Agency to consider the precautionary, "high quality" conditions of use of NMP in the risk evaluation. Cardno ChemRisk's review of the U.S. EPA PBPK internal exposure results and docket shows that safe use was concluded with MOEs > 30 for acute and chronic exposure using input parameters consist with data provided by SIA.

## 4.2 Detailed Analysis of U.S. EPA Response to Comments and Final Evaluation

The U.S. EPA provided an extensive response to comments in a stand-alone document (U.S. EPA, 2020b). The most relevant of these comments have been extracted in Appendix D and critically reviewed for responsiveness and application of "best available science." A synthesis and summary of the detailed review is presented below. There were two themes identified in the review, as well as several additional points.

### 4.2.1 U.S. EPA erred in not using, in the final risk evaluation, the "high quality" data and information SIA provided describing the industry's use of NMP.

The Agency indicated that the "EPA revised and expanded PBPK runs for industry-specific work activities using industry-specific air concentration data sets provided in public comments for the

lithium ion battery manufacturing industry, for the semiconductor manufacturing industry, and from the OSHA data set for capacitor, resistor, coil, transformer, and other inductor manufacturing" (U.S. EPA, 2020b: p: 45). Consistent with this assertion, the systematic review found the SIA submission to be "high quality", and the U.S. EPA presented internal exposure estimates based on the SIA-substantiated exposure factors (except exposure frequency) in Table 2-73. However, the Agency failed to consider the corresponding MOE in the risk evaluation, which substantiated safe use for the conditions of NMP use described by SIA member companies (MOEs corresponding to industry-proposed scenario was > 30). The MOEs corresponding to the agencies modeling of the SIA-substantiated exposure factors are discussed in Section 2 of this report.

The Agency further remarked that "EPA cannot determine whether uncertainties in PBPK model inputs on exposure are reduced by using assumptions provided in semiconductor industry comments because EPA has no data to determine whether the proposed industry assumptions are more accurate than the assumptions applied by EPA" (U.S. EPA, 2020b: p: 127). Cardno ChemRisk disagrees with the characterization of the conditions of use that SIA provided as "assumptions". Information regarding the nature, duration, potential area of contact and other exposure factors as described in SIA submittals listed below were based on documented work conditions in operating semiconductor manufacturing facilities, and as such do not constitute "assumptions". The Agency's assertion regarding the SIA submission is concerning when compared to the conclusions of the Agency systematic review of the SIA submission (U.S. EPA, 2020c), which as described in Section 4 included:

- the "[i]nformation does not indicate flaws or quality issues"
- the "[a]ssessment or report clearly documents its data sources, assessment methods, results, and assumptions," and
- "[t]he assessment addresses variability and uncertainty in the results. Uncertainty is well characterized."

In particular, the Agency found uncertainty to be well characterized in the SIA PBPK exposure factor submission. In contrast, the Agency risk evaluation reflected policy choices dating back to the early 1990s. Reviewing the collection of documents associated with the final evaluation, no coherent basis could be identified for the Agency's failure to consider the SIA exposure factors in the risk evaluation.

It is important to note that the selection of exposure factors for dermal contact time and surface area were highly conservative in nature and informed by comprehensive task descriptions provided in the SIA submissions reflecting the collective subject matter expertise of the industry. The SIA provided detailed description of work tasks in the semiconductor industry in multiple submissions in addition to Cardno ChemRisk's prior comment letter, dated January 21, 2020, including:

- Comments of the Semiconductor Industry Association (SIA) on the draft Toxic Substances Control Act (TSCA) risk evaluation for n-methylpyrrolidone (NMP). (EPA-HQ-OPPT-2019-0236-0052). Washington, DC: U.S. Environmental Protection Agency. (SIA, 2020)
- Comments of the Semiconductor Industry Association (SIA) to the Science Advisory Committee on Chemicals (SACC) on the draft Toxic Substances Control Act (TSCA) risk evaluation for n-methylpyrrolidone (NMP). (EPA-HQ-OPPT-2019-0236-0031). Washington, DC: U.S. Environmental Protection Agency. (SIA, 2019)
- SIA Comments on the Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal N-Methylpyrrolidone (NMP), submitted March 15, 2017. (Isaacs, 2017a)

- SIA Comments to the EPA Docket on Methylene Chloride and N-Methylpyrrolidone (NMP). EPA Docket # EPA-HQ-OPPT-2016-0743, submitted September 18, 2017. (Isaacs, 2017b)
- Intel Comments to: Science Advisory Committee on Chemicals (SACC) On the Draft Toxic Substances Control Act (TSCA) Risk Evaluation for N-Methylpyrrolidone (NMP), submitted December 5, 2019. (Intel, 2019)
- Comments of Intel to the United States Environmental Protection Agency on the Draft Toxic Substances Control Act (TSCA) Risk Evaluation for N-Methylpyrrolidone (NMP); 84 Fed. Reg. 60,087 (Nov. 7, 2019) [EPA–HQ–OPPT–2019–0236; FRL–10001–87], submitted January 21, 2020. (Intel, 2020)
- U.S. EPA Meeting Minutes Re: Conference Call with Semiconductor Industry Association on n-Methylpyrrolidone, dated March 12, 2020. (U.S. EPA, 2020f)

The U.S. EPA adopted a glove PF of 10 in the Chapter 5 of the risk evaluation (5.2.1.15 and 5.2.1.18), which is inconsistent with the training and practices described in the SIA 2020 public comment, supporting a PF of 20. In practice, PFs much greater than 20 are likely as shown in a recent study by Kirman (2020), which illustrated the application of refined PBPK modeling to NMP paint stripping scenarios using a net permeability coefficient considering skin and glove permeability. The authors found acute and chronic protection factors averaging 510 and 720 when gloves with permeability coefficients offering “maximum protection” were modeled (Kirman, 2020). In addition, gloves are selected and glove use is managed at SIA member companies in consideration of breakthrough time and potential glove degradation in determining changeout schedules. Finally, exposure scenarios resulting in the complete coverage of the glove with NMP are not reasonably anticipated, further, increasing the likelihood that effect PFs exceed 20.

The adoption of beyond-worst case values for contact time and surface area when extensive subject matter expertise was made available to the Agency does not represent “best available science.” The information provided to the Agency was consistent with the AIHA tiered approach to skin exposure assessment presented in one of the key reference books for the discipline (Stefanik et al., 2011), consisting of 1) qualitative observation, 2) semi-qualitative indices (including use of models) and 3) application of the hierarchy of controls. These elements are all addressed in the Cardno ChemRisk and SIA submissions. Notably, the AIHA tiered approach does not recommend quantitative measurement unless the “semi-quantitative estimates cannot distinguish exposure estimates among exposure scenarios” (Stefanik et al., 2011: p. 550). In view of the high-quality information provided by SIA subject matter experts, a sufficient level of evidence was available to complete qualitative and semi-qualitative assessment and affirm that the hierarchy of controls is being appropriately applied in the semiconductor industry.

SIA represents 98% of the U.S. semiconductor industry by revenue and nearly two-thirds of non-U.S. chip firms and the SIA submittals included extensively substantiated information prepared by industry subject matter experts. Thus, U.S. EPA’s failure to adopt the “high quality” information does not reflect use of the best available science, nor does it apply the required weight of the evidence standard.

### 4.2.2 U.S. EPA's assertion that prolonged and up to full-hand dermal liquid contact occurs as a condition of use of NMP in the U.S. semiconductor industry is an incorrect and "beyond worst case" hypothetical assertion and is not substantiated by evidence.

The public comments and responses addressed many aspects of the prolonged dermal liquid contact assumption including a surface area up to 2 full hands and contact for up to 12 hours. The Agency stated “that the exposure duration assumptions of full-shifts for high-ends account for the possibility of repeated contact with NMP such that NMP does not fully volatilize from the skin before the next contact event, potentially resulting in prolonged exposure” (U.S. EPA, 2020b: p: 33). The SIA public comment substantiated definitively that conditions of use equating to immersion do not exist under the strictly controlled conditions present in the semiconductor industry. While the Agency suggests in the final evaluation that “EPA evaluated acute and chronic exposures to workers and occupational non-users and acute exposures to consumers by non-immersive dermal contact with liquid films” (U.S. EPA, 2020a: p. 72), the technical response to comments makes clear that conditions equivalent to immersion, were, in fact, assumed. Specifically, the Agency responded that the “use of the PBPK model under the assumption that the exposed skin is effectively immersed in NMP was considered the preferred option, making use of the best available science, despite its limitations” (U.S. EPA, 2020b: 39). The final evaluation main document (U.S. EPA, 2020a) is not transparent because it is not clearly stated that skin was assumed to be “effectively immersed in NMP” as described in the response to comments (U.S. EPA 2020b).

The Agency asserted that it “has not found reasonably available data on actual contact durations or contact surface area for workers in the semiconductor industry and most other OESs” (U.S. EPA, 2020b: p. 33). The U.S. EPA response mischaracterizes the SIA contact time as assumptions. The contact times were derived based on accepted occupational exposure assessment methodologies, including a consideration of liquid loading and the balance of absorption and evaporation (Sahmel et al., 2009). The SIA public comment also explained that the basis of the loading estimate originated from prior U.S. EPA research, which found a mean amount of liquid retained on the surface of hands after subjects wiped their hands with a cloth saturated with cooking oil (Cinalli et al., 1992). The comment further clarified that these data were reasonable for characterizing the semiconductor industry exposures due to the limited opportunity for contact. Notably, the U.S. EPA systematic review identified no specific concerns with the SIA exposure assessment approach.

It is important to note that regulatory modeling of dermal exposures using a more sophisticated approach than in the Agency NMP assessment reflects current “best available science”. For example, peer-reviewed studies concerning the estimation of dermal loads are readily available to the Agency to refine generic assumptions. Warren et al. (2003, 2006), published estimation methods for dermal liquid loading rates based on task descriptions with the 2006 publication specifically addressing use of the RISKOFDERM model in regulatory applications. The European Chemicals Agency (ECHA) specifically describes higher tier dermal modeling, including RISKOFDERM, in their occupational exposure guidelines, in Chapter R.14.6.4.3 (ECHA, 2016).

Taken together, the considerations above lead to the conclusion that a key shortcoming of the final risk evaluation is that the U.S. EPA final MOEs did not consider the loading estimate and contact time presented the SIA 2020 public comment. The SIA-substantiated exposure factors, which describe current industry conditions, should have been considered, because as explained in the SIA public comment, the Agency approach relies on generic assumptions used in Agency new chemical reviews dating back to at least 1991.The screening-level dermal liquid loading factors presented in Table 13.3 of Sahmel et al. (2009) are appropriate for describing the tasks with incidental NMP contact as documented by the SIA submissions. Some typical examples

provided in Table 13.3 of the reference include “maintenance” and “manual cleaning of equipment.” Considering the extensive task descriptions provided by SIA, selection of the loading corresponding to a single event is appropriate for exposure assessment, as explained comprehensively in the public comment and validated by the SIA member companies.

In addition to the above considerations, the dermal pathway is not expected to be a source of exposure to NMP in the semiconductor industry when considering the limited surface area, liquid contact time, and industrial hygiene programs at SIA member companies. As noted in the SIA comment, exposures consisting of prolonged dermal contact are expected to produce pervasive dermatitis, edema, redness, blister or cracking of skin (E.U. SCCS, 2011). The Agency failed to identify case reports or occupational compliance data substantiating pervasive skin damage associated with use of NMP in the semiconductor industry, and failed to identify evidence supporting that the dermal liquid contact route would contribute 99% or more of the dose.

The U.S. EPA presents the contribution of the dermal dose in Table 4-54. Across all industries, the contribution of the dermal routes is most frequently 99 or 100%, which is a direct outcome of the Agency’s assumption of up to 6 to 12 hours of prolonged contact with NMP over a surface area of 1 to 2 hands. The Poet et al. (2016) publication preceding the U.S. EPA analysis noted in the supplemental materials of their published model that “[h]man exposures to NMP will be primarily via the inhalation route with some contribution from the dermal route (vapors or liquid)” (Supplemental Materials, Section A.1.2, line 104-106). Considering the prior expectation that dermal is not the dominant pathway of worker exposure to NMP, an appreciable shortcoming of the Agency assessment is the lack of substantiation that prolonged contact with NMP over large (one or two hands) surface area of skin is occurring in the semiconductor industry. Notably, the SIA submissions substantiate that prolonged contact over large fractions of the glove or skin does not occur in the semiconductor industry. Thus, the U.S. EPA has not been responsive to public comment critiquing the dermal contact parameters used in the draft evaluation.

In conclusion, the SIA submittal was scored as “high quality” and the U.S. EPA prepared exposure estimates for the “industry-proposed” PBPK inputs in Table 2-73 of the industry document substantiating safe use (MOE>30). The SIA-substantiated factors were determined based on comprehensive task descriptions. Thus, the industry supplied PBPK model estimates should have been considered in the final risk evaluation. The task descriptions provided by SIA substantiate that repeated contacts are unlikely in the industry. Thus, the U.S. EPA assertion that it had “no reasonably available information on actual surface area of contact with liquid and that the assumed values represent adequate surrogates for most uses’ central tendency and high-end surface areas of contact with liquid” is incorrect with respect to the semiconductor industry, and represents an appreciable shortcoming of the final U.S. EPA analysis.

### 4.2.3 Other aspects of the analysis

Several other minor points were identified in reviewing the U.S.EPA final evaluation and response to comments.

#### *4.2.3.1 Inclusion of chronic MOEs for truck unloading*

The U.S EPA indicated that the Agency “removed the truck unloading from chronic estimates since this task is not performed 4 or 5 days per week” (U.S. EPA, 2020b: p. 37). However, in the final risk evaluation the U.S. EPA presents chronic MOEs for truck unloading, and in Section 5.2.1.18, concluded “[f]or workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end in virgin NMP truck unloading activities support an unreasonable risk

determination" (U.S. EPA, 2020a: p. 413). As discussed in detail in this report, the U.S. EPA truck loading and unloading scenarios are not representative of SIA member company conditions of use, and the Agency should have considered the exposure frequency information submitted by SIA.

#### *4.2.3.2 Inclusion of task duration "what-if" scenarios*

The U.S. EPA task duration or "what-if" analyses misrepresent that dermal contact occurs over a surface area up to 2 hands and that dermal liquid contact occurs for the entire task duration. It was unnecessary for the Agency to prepare these unrepresentative estimates because the Agency had separately modeled the SIA-substantiated exposure factors (excluding exposure frequency). As noted elsewhere in this report, the Agency judged the SIA 2020 submission and proposed PBPK model inputs as "high quality."

#### *4.2.3.3 Vapor through skin exposure*

The U.S. EPA remarked that "the potential for associated direct skin contact with clothing saturated with NMP vapor are not included in quantifying exposures. The discussion further notes that these uncertainties could potentially result in underestimates of exposures" (U.S. EPA, 2020b: p. 44). It is important to clarify that the sensitivity analysis previously submitted in the SIA 2020 comments indicated that the vapor-through-skin pathway is not an appreciable determinant of internal exposure. Thus, it is unlikely that dose has been underestimated due to saturated clothing.

# 5 Conclusion of Safe Use of NMP at SIA Member Companies

A comprehensive review of the U.S. EPA final risk evaluation for the conditions of use of n-methylpyrrolidone (NMP) in the semiconductor industry has been completed by human health risk assessors at Cardno ChemRisk. Our review considered the information reasonably available to the Agency, and applied the scientific standards of “best available science,” and “weight of the scientific evidence” approach required under Section 26 of the Toxic Substances Control Act (TSCA).

Despite the comprehensive “high quality” information and data provided by SIA and Cardno ChemRisk, the Agency relied on generic and unsubstantiated assumptions regarding prolonged dermal-liquid contact times and exposures of appreciable hand surface areas (i.e., one or two hands immersed in concentrated or neat NMP for 30 or 60 hours per week). The assumptions were applied uniformly across various scenarios (notably, across many industries). The SIA data and information were timely and “reasonably available” to the Agency, and the U.S. EPA systematic review document rated the January 2020 SIA submission as “high quality” (U.S. EPA, 2020c). Thus, the omission of SIA submitted data reflecting the conditions of use of NMP in the U.S. semiconductor industry from the final conclusions in the NMP risk evaluation was unfounded. It is notable that the Agency prepared PBPK model estimates using input parameters more consistent with SIA conditions of use resulted in predicted MOEs greater than 30 demonstrating no unreasonable risks for the conditions of use of NMP in the semiconductor industry. These modeling runs can be found in the public docket of the final NMP risk evaluation but were not relied upon for reaching the final conclusions of the risk evaluation.

This review affirmed the conclusion of the Cardno ChemRisk assessment completed in January 2020, which substantiated that NMP is being used responsibly and safely in the U.S. semiconductor industry as indicated by calculated margins of exposure (MOEs) greater than the U.S. EPA benchmark MOE of 30. Based on the available data, our review leads us to conclude that none of the conditions of use of NMP in the U.S. semiconductor industry present an unreasonable risk to the health of workers.

# 6 References

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# Appendix A: Summary of Scenarios

**Table A.1:** Analysis of changes to MOE in draft and final evaluation, and substantiation of safe use at SIA companies in final docket. Cells highlighted in green indicate MOE > 30 (safe use). The generic exposure factors adopted by the U.S. EPA do not apply to SIA member companies and are inconsistent with the high quality data provided by SIA. Safe occupational use of NMP is substantiated in the final docket (See: U.S. EPA. (2020e. Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidinone, 1 Methyl-) (NMP), Supplemental Excel File on Occupational Risk Calculations. Docket EPA-HQ-OPPT-2019-0236). See Table ES-2 for a detailed summary of exposure factors.

| | | U.S. EPA October 2019 Draft Risk Evaluation | U.S. EPA December 2020 Risk Evaluation | U.S. EPA December 2020 SIA Evaluation | U.S. EPA October 2019 Draft Risk Evaluation | U.S. EPA December 2020 Risk Evaluation | U.S. EPA December 2020 SIA Proposed | Safe Use for SIA-substantiated Exposure Factors Documented in Final Docket | Primary reason for changes in EPA MOE in risk evaluation between 2019 draft and 2020 final evaluation (in addition to change in acute POD) |
|---|---|---|---|---|---|---|---|---|---|
| | | Acute POD, Glove PF, and Permeability | | | Chronic POD, Glove PF and Permeability | | | | |
| Point of Departure | | 216 mg/L | 437 mg/L | 437 mg/L | 183 hr mg/L | 183 hr mg/L | 183 hr mg/L | | |
| Glove PF. | | 10 | 10 | 20 | 10 | 10 | 20 | | |
| Permeability | | 4.78E-04 cm/h | 4.78E-4 to 2.05E-3 cm/h by wt. % linearly from 50 to 100% | | 4.78E-04 cm/h | 4.78E-4 to 2.05E-3 cm/h by wt. % linearly from 50 to 100% | | | |
| | | Acute Margin of Exposure | | | Chronic Margin of Exposure | | | | |
| Container handing, small containers | Central | 204 | 252 | 45377 | 29 | 18 | 11011 | Yes | Permeability increased |
| | High end | 65 | 47 | 4367 | 6 | 2.1 | 685 | Yes | Permeability increased |
| Container handling, drums | Central | 251 | 508 | 116379 | 36 | 36 | 28648 | Yes | None |
| | High end | 64 | 46 | 4021 | 6 | 2.0 | 631 | Yes | Permeability increased |
| Fab worker, container changeout | Central | 820 | 9461 | 545017 | 117 | 667 | 127582 | Yes | Wt. percent decreased |
| | High end | 48 | 1925 | 71509 | 4 | 85 | 11189 | Yes | Wt. percent decreased |
| Fab worker, typical or non-exposed | Central | N/A | N/A | N/A | 4502 | 9014 | 4485 | Yes | Wt. % dec. artifact |
| | High end | N/A | N/A | N/A | 1137 | 1537 | 1524 | Yes | Wt. % dec. artifact |
| Maintenance | Central | 228 | 508 | 10608 | 32 | 36 | 2616 | Yes | Wt. % decreased |
| | High end | 48 | 19 | 455 | 4 | 0.85 | 71 | Yes | Permeability increased |
| Virgin NMP unloading | Central | 125 | 63 | 3436 | 23 | 5.8 | 837 | Yes | Permeability increased |
| | High end | 52 | 23 | 602 | 6 | 1.3 | 94 | Yes | Permeability increased |
| Waste truck unloading | Central | 151 | 81 | 4936 | 28 | 7.4 | 1214 | Yes | Permeability increased |
| | High end | 59 | 29 | 785 | 7 | 1.7 | 123 | Yes | Permeability increased |

**Table A.2**: General overview of selected differences in the U.S. EPA PBPK modeling scenarios. The parameters contributing most appreciably to differences in the SIA and U.S. EPA risk evaluation are highlighted in yellow. Scenarios where all MOEs were greater than the benchmark MOE of 30 (safe use) are highlighted in green in the title and MOE rows.

| Parameter or Consideration | Typical/high end used in U.S. EPA risk evaluation | "What-if" typical and high-end | SIA-substantiated ("Industry Proposed") SIA, 2020[b] | SIA Public Comment |
|---|---|---|---|---|
| PBPK Model Run | U.S. EPA | U.S. EPA | U.S. EPA | Cardno / SIA |
| Exposure factors representative of SIA member company facilities | No | No | Yes except for truck exposure frequency | Yes |
| Peak acute blood concentration calculated | Yes | Yes | Yes | Yes |
| Chronic area under the curve calculated | Yes | Yes | Yes | Yes |
| MOE calculated | Report and docket | Docket only | Docket only | Yes |
| Exposure scenario considered in unreasonable risk determination | Yes, glove PF = 10 only | No | No | No |
| Breathing zone air concentration ($mg/m^3$) | Measured data (SIA; 0.013 – 9.560) | Measured data (SIA; 0.013 – 19) | Measured data; (SIA; 0.013 – 4.8) | Measured data (SIA; 0.013 – 4.8) |
| NMP Weight Fraction | (SIA; 0.05 – 1) | (SIA; 0.05 – 1) | (SIA; 0.05 – 1) | (SIA; 0.05 – 1) |
| Duration of contact with liquid (hours) | Shift or ½ shift time (Generic; 4 to 12)[a] | Total task time (SIA; 0.03 to 11) | Evaporation time and estimate of loading (SIA; 0.33 to 1 hour) | Evaporation time and estimate of loading (SIA; 0.33 to 1 hour) |
| Glove protection factor (PF) | 1, 5, 10, 20 based on ECETOC TRA; 10 used for MOE | 1, 5, 10, 20 based on ECETOC TRA; 10 used for MOE | 20 (SIA; strict work rules and ECETOC TRA) | 20 (SIA; strict work rules and ECETOC TRA) |
| Skin surface area exposed ($cm^2$) | 1 or 2 hands (Generic; 445 to 535 $cm^2$)[a] | 1 or 2 hands (Generic; 445 to 1075 $cm^2$)[a] | Fraction of hand based on task description (SIA; 20 to 375 $cm^2$) | Fraction of hand based on task description (SIA; 20 to 375 $cm^2$) |
| Exposure Frequency | 5 days/week | 5 days/week | 5 days/week | Task-specific frequency (3 to 4 shifts/week, except for truck unloading of 1 per year and truck loading 1 per month or 1 per 3 weeks) |
| Body Weight (kg) | 74 female; 88 male | 74 female; 88 male | 74 female; 88 male | 74 female; 88 male |

[a]Despite receiving extensive information from SIA, the U.S. EPA represented that there was "no reasonably available data on actual duration of dermal contact, thus relied on "standard model assumptions for the occupational dermal exposure modeling" developed for TSCA in 1991 in situations where there is an absence of high-quality data.

[b]"SIA-substantiated" denotes precautionary (conservative) and worst-case scenarios for the industry. Conditions of use at individual facilities may include more limited, less frequent or no liquid contact, such that contact area and time is appreciably lower than the SIA-substantiated level of exposure.

**Table A.3**: Overview of chronic exposure estimates and MOEs. Scenarios where the MOEs were greater than benchmark MOE of 30 (safe use) are highlighted in green.

| Scenario | Central Tendency | | | | High-End | | | |
|---|---|---|---|---|---|---|---|---|
| | U.S. EPA Risk Determination | U.S. EPA What-if Task Duration | U.S. EPA PBPK Model of SIA 2020 Parameters | Cardno PBPK Model as Submitted | U.S. EPA Risk Determination | U.S. EPA What-if Task Duration | U.S. EPA PBPK Model of SIA 2020 Parameters | Cardno PBPK Model as Submitted |
| | Chronic Area Under the Curve (hr mg/L) | | | | | | | |
| Container handling, small containers | 10 | 0.14 | 0.017 | 0.091 | 89 | 6.8 | 0.27 | 0.21 |
| Container handling, drums | 5.1 | 0.028 | 0.0064 | 0.0058 | 89 | 2.3 | 0.29 | 0.43 |
| Fab worker w/ NMP container changeout | 0.27 | 0.48 | 0.0014 | 0.024 | 2.2 | 1.9 | 0.016 | 0.097 |
| Fab worker-typical or non-exposed | 0.020 | 0.036 | 0.041 | 0.024 | 0.12 | 0.104 | 0.12 | 0.092 |
| Maintenance | 5.1 | 0.098 | 0.070 | 0.044 | 216 | 196 | 2.57 | 0.61 |
| Virgin NMP Truck Unloading | 32 | 16 | 0.22 | 0.004 | 139 | 32 | 1.9 | 0.0053 |
| Waste Truck Loading | 25 | 12 | 0.15 | 0.0083 | 108 | 25 | 1.5 | 0.035 |
| | Chronic Margin of Exposure (POD = 183 hr mg/L) | | | | | | | |
| Container handling, small containers | 18 | 1301 | 11011 | 2018 | 2.1 | 27 | 685 | 864 |
| Container handling, drums | 36 | 6566 | 28648 | 31345 | 2.0 | 81 | 631 | 430 |
| Fab worker w/ NMP container changeout | 667 | 381 | 127582 | 7717 | 85 | 97 | 11189 | 1883 |
| Fab worker-typical or non-exposed | 9014 | 5151 | 4485 | 7777 | 1537 | 1756 | 1524 | 1983 |
| Maintenance | 36 | 1859 | 2616 | 4151 | 0.85 | 0.93 | 71 | 298 |
| Virgin NMP Truck Unloading | 5.8 | 11 | 837 | 48186 | 1.3 | 5.7 | 94 | 34727 |
| Waste Truck Loading | 7.4 | 15 | 1214 | 22160 | 1.7 | 7.4 | 123 | 5179 |

**Table A.4**: Overview of acute exposure estimates (Cmax) and MOEs. Scenarios where the MOEs were greater than benchmark MOE of 30 (safe use) are highlighted in green. The Cardno PBPK model MOEs have been updated with the final point of departure.

| Scenario | Central Tendency | | | | High-End | | | |
|---|---|---|---|---|---|---|---|---|
| | U.S. EPA Risk Determination | U.S. EPA What-if Task Duration | U.S. EPA PBPK Model of SIA 2020 Parameters | Cardno PBPK Model as Submitted | U.S. EPA Risk Determination | U.S. EPA What-if Task Duration | U.S. EPA PBPK Model of SIA 2020 Parameters | Cardno PBPK Model as Submitted |
| | Peak Blood Concentration (mg/L), Cmax | | | | | | | |
| Container handling, small containers | 1.733987068 | 0.16 | 0.010 | 0.0165 | 9.390314507 | 2.54 | 0.10 | 0.042 |
| Container handling, drums | 0.859408686 | 0.042 | 0.0038 | 0.0036 | 9.427039113 | 1.32 | 0.11 | 0.052 |
| Fab worker w/ NMP container changeout | 0.046187503 | 0.056 | 0.0008 | 0.0045 | 0.226996824 | 0.22 | 0.01 | 0.013 |
| Fab worker-typical | - | - | - | 0.0045 | - | - | - | 0.013 |
| Maintenance | 0.859589852 | 0.10 | 0.04 | 0.0393 | 22.73602362 | 22 | 0.96 | 0.230 |
| Virgin NMP Truck Unloading | 6.9 | 4.65 | 0.13 | 0.1407 | 19.33845806 | 9.13 | 0.73 | 0.203 |
| Waste Truck Loading | 5.373397878 | 3.52 | 0.09 | 0.0246 | 15.07442066 | 7.11 | 0.56 | 0.152 |
| | Acute Margin of Exposure (POD = 437 mg/L). Note, Cardno ChemRisk estimate reflects revised acute point of departure. | | | | | | | |
| Container handling, small containers | 252 | 2715 | 45377 | 26517 | 47 | 172 | 4367 | 10395 |
| Container handling, drums | 508 | 10406 | 116379 | 121571 | 46 | 331 | 4021 | 8437 |
| Fab worker w/ NMP container changeout | 9461 | 7759 | 545017 | 98017 | 1925 | 1976 | 71509 | 33116 |
| Fab worker-typical | -- | -- | -- | 98115 | -- | -- | -- | 33355 |
| Maintenance | 508 | 4470 | 10608 | 11125 | 19 | 20 | 455 | 1903 |
| Virgin NMP Truck Unloading | 63 | 94 | 3436 | 3107 | 23 | 48 | 602 | 2158 |
| Waste Truck Loading | 81 | 124 | 4936 | 17766 | 29 | 61 | 785 | 2868 |

# Appendix B: Detailed Comparison of Scenarios

Note: The acute MOEs shown in this appendix for the SIA submission reflect the MOEs as submitted in the comment letter. The U.S. made changes to permeability coefficient and acute point of departure, which do not affect the conclusion of the SIA 202 public comment.

**Table B.1a**: Container handling, small containers exposure factors

| Work Activity | Parameter or Estimate | Unit | Central Tendency | | | | High-End | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment |
| Container handling, small containers | **PBPK Model Parameters** | | | | | | | | | |
| | Duration-Based NMP Air Concentration | $mg/m^3$ | 0.507 | 0.507 | 0.511 | 0.511 | 0.608 | 0.608 | 0.613 | 0.613 |
| | NMP Weight Fraction | Unitless | 0.6 | 0.6 | 0.6 | 0.6 | 0.75 | 0.75 | 0.75 | 0.75 |
| | Glove Protection Factor | Unitless | 10 | 10 | 20 | 20 | 10 | 10 | 20 | 20 |
| | Dermal Contact Time | h | 6 | 0.0833 | 0.33 | 0.33 | 12 | 1 | 1 | 1 |
| | Skin Surface Area Exposed | $cm^2$ | 445 (f)<br>535 (m) | 445 (f)<br>535 (m) | 20.03 (f)<br>24.08 (m) | 20.03 (f)<br>24.08 (m) | 890 (f)<br>1070 (m) | 890 (f)<br>1070 (m) | 66.75 (f)<br>80.25 (m) | 66.75 (f)<br>80.25 (m) |
| | Exposure Frequency | -- | 5 days/week | 5 days/week | 5 days/week | 3 shifts/week | 5 days/week | 5 days/week | 5 days/week | 4 shifts/week |
| | Body Weight | kg | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) |
| | **Predictions** | | | | | | | | | |
| | Peak Blood Concentration - Acute | mg/L | 1.7 | 0.16 | 0.0096 | 0.02 | 9.4 | 2.5 | 0.10 | 0.04 |
| | MOE - Acute | - | 252 | 2715 | 45377 | 13107 | 47 | 172 | 4367 | 5169 |
| | AUC - Chronic | hr mg/L | 10 | 0.14 | 0.017 | 0.09 | 89 | 6.8 | 0.27 | 0.21 |
| | MOE - Chronic | - | 18 | 1301 | 11011 | 2018 | 2.1 | 26.7 | 685 | 864 |

**Table B.1b**: Container handling, small containers exposure basis

| Work Activity | Parameter or Estimate | Central Tendency | | | High-End | | |
|---|---|---|---|---|---|---|---|
| | | EPA Risk Determination | EPA What-If | SIA Submission | EPA Default | EPA What-If | SIA Submission |
| Container handling, small containers | Full-Shift NMP Air Concentration | Central Tendency (50th percentile) of 12-hr TWA | Central Tendency (50th percentile) | Central tendency (50th percentile) of 12-hr TWA | High-end (95th percentile) of 12-hr TWA | High-end (95th percentile) | High-end (95th percentile) of 12-hr TWA |
| | NMP Weight Fraction | Central Tendency | Central Tendency | Central tendency (50th percentile) | High-end | High-end | High-end (95th percentile) |
| | Shift Duration | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift |
| | Exposure Frequency | 5 days/week | 5 days/week | Once per shift, three shifts per week, 50 weeks per year | 5 days/week | 5 days/week | Once per shift, four shifts per week, 50 weeks per year |
| | Dermal Contact Time | Mid-point of shift duration (6 hours) | Task-based duration | With a dermal loading of 0.7 mg/cm2, the evaporation time of NMP is approximately 20 minutes. | High-end of shift duration (12 hours) | Task-based duration | With a dermal loading of 2.1 mg/cm2, the evaporation time of NMP is approximately 60 minutes. |
| | Skin Surface Area Exposed | 1-hand | 1-hand | 3 fingertips | 2-hands | 2-hands | 10 fingertips |

## **Table B.2a**: Container handling, drums exposure factors

| Work Activity | Parameter or Estimate | Unit | Central Tendency | | | | High-End | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment |
| Container handling, drums | **PBPK Model Parameters** | | | | | | | | | |
| | Duration-Based NMP Air Concentration | $mg/m^3$ | 0.013 | 0.013 | 0.013 | 0.013 | 1.54 | 1.54 | 1.557 | 1.557 |
| | NMP Weight Fraction | Unitless | 0.5 | 0.5 | 0.6 | 0.5 | 0.75 | 0.75 | 0.75 | 0.75 |
| | Glove Protection Factor | Unitless | 10 | 10 | 20 | 20 | 10 | 10 | 20 | 20 |
| | Dermal Contact Time | h | 6 | 0.033 | 0.33 | 0.33 | 12 | 0.33 | 1 | 1 |
| | Skin Surface Area Exposed | $cm^2$ | 445 (f)<br>535 (m) | 445 (f)<br>535 (m) | 20.03 (f)<br>24.08 (m) | 20.03 (f)<br>24.08 (m) | 890 (f)<br>1070 (m) | 890 (f)<br>1070 (m) | 66.75 (f)<br>80.25 (m) | 66.75 (f)<br>80.25 (m) |
| | Exposure Frequency | -- | 5 days/week | 5 days/week | 5 days/week | 3 shifts/week | 5 days/week | 5 days/week | 5 days/week | 4 shifts/week |
| | Body Weight | kg | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) |
| | **Predictions** | | | | | | | | | |
| | Peak Blood Concentration - Acute | mg/L | 0.86 | 0.042 | 0.0038 | 0.004 | 9.4 | 1.32 | 0.11 | 0.05 |
| | MOE - Acute | - | 508 | 10406 | 116379 | 60090 | 46 | 331 | 4021 | 4223 |
| | AUC - Chronic | hr mg/L | 5.1 | 0.028 | 0.0064 | 0.0058 | 89 | 2.26 | 0.29 | 0.43 |
| | MOE - Chronic | - | 36 | 6566 | 28648 | 31345 | 2.0 | 81 | 631 | 430 |

## **Table B.2b**: Container handling, drums exposure basis

| Work Activity | Parameter or Estimate | Central Tendency | | | High-End | | |
|---|---|---|---|---|---|---|---|
| | | EPA Default | EPA What-If | SIA Submission | EPA Default | EPA What-If | SIA Submission |
| Container handling, drums | Duration-Based NMP Air Concentration | Central Tendency (50th percentile) of 12-hr TWA | Central Tendency (50th percentile) | Central tendency (50th percentile) of 12-hr TWA | High-end (95th percentile) of 12-hr TWA | High-end (95th percentile) | High-end (95th percentile) of 12-hr TWA |
| | NMP Weight Fraction | Central Tendency | Central Tendency | Central tendency (50th percentile) | High-end | High-end | High-end (95th percentile) |
| | Shift Duration | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift |
| | Exposure Frequency | 5 days/week | 5 days/week | Once per shift, three shifts per week, 50 weeks per year | 5 days/week | 5 days/week | Once per shift, four shifts per week, 50 weeks per year |
| | Dermal Contact Time | Mid-point of shift duration (6 hours) | Task-based duration | With a dermal loading of 0.7 mg/cm2, the evaporation time of NMP is approximately 20 minutes. | High-end of shift duration (12 hours) | Task-based duration | With a dermal loading of 2.1 mg/cm2, the evaporation time of NMP is approximately 60 minutes. |
| | Skin Surface Area Exposed | 1-hand | 1-hand | 3 fingertips | 2-hands | 2-hands | 10 fingertips |

**Table B.3a**: Fab worker w/ NMP container changeout exposure factors

| Work Activity | Parameter or Estimate | Unit | Central Tendency | | | | High-End | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment |
| Fab worker w/ NMP container changeout | **PBPK Model Parameters** | | | | | | | | | |
| | Duration-Based NMP Air Concentration | $mg/m^3$ | 0.138 | 0.138 | 0.139 | 0.139 | 0.405 | 0.405 | 0.409 | 0.409 |
| | NMP Weight Fraction | Unitless | 0.025 | 0.025 | 0.025 | 0.025 | 0.05 | 0.05 | 1 | 0.05 |
| | Glove Protection Factor | Unitless | 10 | 10 | 20 | 20 | 10 | 10 | 20 | 20 |
| | Dermal Contact Time | h | 6 | 10.50 | 0.33 | 0.33 | 12 | 10.5 | 1 | 1 |
| | Skin Surface Area Exposed | $cm^2$ | 445 (f)<br>535 (m) | 445 (f)<br>535 (m) | 20.03 (f)<br>24.08 (m) | 20.03 (f)<br>24.08 (m) | 890 (f)<br>1070 (m) | 890 (f)<br>1070 (m) | 66.75 (f)<br>80.25 (m) | 66.75 (f)<br>80.25 (m) |
| | Exposure Frequency | -- | 5 days/week | 5 days/week | 5 days/week | 3 shifts/week | 5 days/week | 5 days/week | 5 days/week | 4 shifts/week |
| | Body Weight | kg | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) |
| | **Predictions** | | | | | | | | | |
| | Peak Blood Concentration - Acute | mg/L | 0.046 | 0.056 | 0.00080 | 0.0045 | 0.23 | 0.2 | 0.0061 | 0.013 |
| | MOE - Acute | - | 9461 | 7759 | 545017 | 48448 | 1925 | 1976 | 71509 | 16749 |
| | AUC - Chronic | hr mg/L | 0.27 | 0.5 | 0.0014 | 0.0237 | 2.2 | 1.9 | 0.02 | 0.1 |
| | MOE - Chronic | - | 667 | 381 | 127582 | 7717 | 85 | 97 | 11189 | 1883 |

**Table B.3b**: Fab worker w/ NMP container changeout exposure factors basis

| Work Activity | Parameter or Estimate | Central Tendency | | | High-End | | |
|---|---|---|---|---|---|---|---|
| | | EPA Default | EPA What-If | SIA Submission | EPA Default | EPA What-If | SIA Submission |
| Fab worker w/ NMP container changeout | Duration-Based NMP Air Concentration | Central Tendency (50th percentile) of 12-hr TWA | Central Tendency (50th percentile) | Central tendency (50th percentile) of 12-hr TWA | High-end (95th percentile) of 12-hr TWA | High-end (95th percentile) | High-end (95th percentile) of 12-hr TWA |
| | NMP Weight Fraction | Central Tendency | Central Tendency | Central tendency (50th percentile) | High-end | High-end | High-end (95th percentile) |
| | Shift Duration | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift |
| | Exposure Frequency | 5 days/week | 5 days/week | Once per shift, three shifts per week, 50 weeks per year | 5 days/week | 5 days/week | Once per shift, four shifts per week, 50 weeks per year |
| | Dermal Contact Time | Mid-point of shift duration (6 hours) | Task-based duration | With a dermal loading of 0.7 mg/cm2, the evaporation time of NMP is approximately 20 minutes. | High-end of shift duration (12 hours) | Task-based duration | With a dermal loading of 2.1 mg/cm2, the evaporation time of NMP is approximately 60 minutes. |
| | Skin Surface Area Exposed | 1-hand | 1-hand | 3 fingertips | 2-hands | 2-hands | 10 fingertips |

## **Table B.4a**: Fab worker – typical exposure factors

| Work Activity | Parameter or Estimate | Unit | Central Tendency | | | | High-End | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment |
| Fab worker-typical | **PBPK Model Parameters** | | | | | | | | | |
| | Duration-Based NMP Air Concentration | $mg/m^3$ | 0.138 | 0.138 | 0.139 | 0.139 | 0.405 | 0.405 | 0.409 | 0.409 |
| | NMP Weight Fraction | Unitless | 0 | 0 | 0 | N/A | 0 | 0 | 0 | N/A |
| | Glove Protection Factor | Unitless | 1 | 1 | 20 | 20 | 1 | 1 | 20 | 20 |
| | Dermal Contact Time | h | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Skin Surface Area Exposed | $cm^2$ | 0.1 | 0.1 | 0.1 | 0.00 | 0.1 | 0.1 | 0.1 | 0.00 |
| | Exposure Frequency | -- | 5 days/week | 5 days/week | 5 days/week | 3 shifts/week | 5 days/week | 5 days/week | 5 days/week | 4 shifts/week |
| | Body Weight | kg | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) |
| | **Predictions** | | | | | | | | | |
| | Peak Blood Concentration - Acute | mg/L | - | - | - | 0.0045 | - | - | - | 0.0 |
| | MOE - Acute | - | - | - | - | 48496 | - | - | - | 16931 |
| | AUC - Chronic | hr mg/L | 0.020 | 0.036 | 0.041 | 0.024 | 0.12 | 0.104 | 0.120 | 0.092 |
| | MOE - Chronic | - | 9014 | 5151 | 4485 | 7777 | 1537 | 1756 | 1524 | 1983 |

## **Table B.4b**: Fab worker – typical exposure factors basis

| Work Activity | Parameter or Estimate | Central Tendency | | | High-End | | |
|---|---|---|---|---|---|---|---|
| | | EPA Default | EPA What-If | SIA Submission | EPA Default | EPA What-If | SIA Submission |
| Fab worker-typical | Duration-Based NMP Air Concentration | Central Tendency (50th percentile) of 12-hr TWA | Central Tendency (50th percentile) | N/A | High-end (95th percentile) of 12-hr TWA | High-end (95th percentile) | N/A |
| | NMP Weight Fraction | N/A | N/A | Central tendency (50th percentile) | N/A | N/A | High-end (95th percentile) |
| | Shift Duration | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift |
| | Exposure Frequency | 5 days/week | 5 days/week | Once per shift, three shifts per week, 50 weeks per year | 5 days/week | 5 days/week | Once per shift, four shifts per week, 50 weeks per year |
| | Dermal Contact Time | N/A | N/A | No dermal expoure to NMP | N/A | N/A | No dermal expoure to NMP |
| | Skin Surface Area Exposed | N/A | N/A | No dermal expoure to NMP | N/A | N/A | No dermal expoure to NMP |

## **Table B.5a**: Maintenance exposure factors

| Work Activity | Parameter or Estimate | Unit | Central Tendency | | | | High-End | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment |
| Maintenance | **PBPK Model Parameters** | | | | | | | | | |
| | Duration-Based NMP Air Concentration | $mg/m^3$ | 0.020 | 0.020 | 0.02 | 0.020 | 0.690 | 0.690 | 0.696 | 0.696 |
| | NMP Weight Fraction | Unitless | 0.5 | 0.5 | 0.5 | 0.5 | 1 | 1 | 1 | 1 |
| | Glove Protection Factor | Unitless | 10 | 10 | 20 | 20 | 10 | 10 | 20 | 20 |
| | Dermal Contact Time | h | 6 | 0.117 | 0.33 | 0.33 | 12 | 11 | 1 | 1 |
| | Skin Surface Area Exposed | $cm^2$ | 445 (f)<br>535 (m) | 445 (f)<br>535 (m) | 222.5 (f)<br>267.5 (m) | 222.5 (f)<br>267.5 (m) | 890 (f)<br>1070 (m) | 890 (f)<br>1070 (m) | 311.5 (f)<br>374.5 (m) | 311.5 (f)<br>374.5 (m) |
| | Exposure Frequency | -- | 5 days/week | 5 days/week | 5 days/week | 3 shifts/week | 5 days/week | 5 days/week | 5 days/week | 4 shifts/week |
| | Body Weight | kg | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) |
| | **Predictions** | | | | | | | | | |
| | Peak Blood Concentration - Acute | mg/L | 0.9 | 0.1 | 0.041 | 0.0 | 23 | 22 | 1.0 | 0.2 |
| | MOE - Acute | - | 508 | 4470 | 10608 | 5499 | 19 | 20 | 455 | 942 |
| | AUC - Chronic | hr mg/L | 5.1 | 0.098 | 0.070 | 0.044 | 216 | 196 | 2.6 | 0.61 |
| | MOE - Chronic | - | 36 | 1859 | 2616 | 4151 | 0.85 | 0.93 | 71 | 298 |

## **Table B.5b**: Maintenance exposure factors basis

| Work Activity | Parameter or Estimate | Central Tendency | | | High-End | | |
|---|---|---|---|---|---|---|---|
| | | EPA Default | EPA What-If | SIA Submission | EPA Default | EPA What-If | SIA Submission |
| Maintenance | Duration-Based NMP Air Concentration | Central Tendency (50th percentile) of 12-hr TWA | Central Tendency (50th percentile) | Central tendency (50th percentile) of 12-hr TWA | High-end (95th percentile) of 12-hr TWA | High-end (95th percentile) | High-end (95th percentile) of 12-hr TWA |
| | NMP Weight Fraction | Central Tendency | Central Tendency | Central tendency (50th percentile) | High-end | High-end | High-end (95th percentile) |
| | Shift Duration | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift | 12 hour shift |
| | Exposure Frequency | 5 days/week | 5 days/week | Once per shift, three shifts per week, 50 weeks per year | 5 days/week | 5 days/week | Once per shift, four shifts per week, 50 weeks per year |
| | Dermal Contact Time | Mid-point of shift duration (6 hours) | Task-based duration | With a dermal loading of 0.7 mg/cm2, the evaporation time of NMP is approximately 20 minutes. | High-end of shift duration (12 hours) | Task-based duration | With a dermal loading of 2.1 mg/cm2, the evaporation time of NMP is approximately 60 minutes. |
| | Skin Surface Area Exposed | 1-hand | 1-hand | 50% of the palm side of each hand | 2-hands | 2-hands | 70% of the palm side of each hand |

## **Table B.6a**: Virgin NMP truck unloading exposure factors

| Work Activity | Parameter or Estimate | Unit | Central Tendency | | | | High-End | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment |
| Virgin NMP Truck Unloading | **PBPK Model Parameters** | | | | | | | | | |
| | Duration-Based NMP Air Concentration | $mg/m^3$ | 9.56 | 19.12 | 4.822 | 4.822 | 4.78 | 19.12 | 4.822 | 4.822 |
| | NMP Weight Fraction | Unitless | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | Glove Protection Factor | Unitless | 10 | 10 | 20 | 20 | 10 | 10 | 20 | 20 |
| | Dermal Contact Time | h | 4 | 2 | 0.33 | 0.33 | 8 | 2 | 1 | 1 |
| | Skin Surface Area Exposed | $cm^2$ | 445 (f)<br>535 (m) | 445 (f)<br>535 (m) | 66.75 (f)<br>80.25 (m) | 66.75 (f)<br>80.25 (m) | 890 (f)<br>1070 (m) | 890 (f)<br>1070 (m) | 222.5 (f)<br>267.5 (m) | 222.5 (f)<br>267.5 (m) |
| | Exposure Frequency | -- | 5 days/week | 5 days/week | 5 days/week | Once per year | 5 days/week | 5 days/week | 5 days/week | Once per year |
| | Body Weight | kg | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) |
| | **Predictions** | | | | | | | | | |
| | Peak Blood Concentration - Acute | mg/L | 6.9 | 4.6 | 0.13 | 0.14 | 19 | 9.1 | 0.73 | 0.20 |
| | MOE - Acute | - | 63 | 94 | 3436 | 1536 | 23 | 48 | 602 | 1067 |
| | AUC - Chronic | hr mg/L | 32 | 16 | 0.22 | 0.0038 | 139 | 32 | 1.9 | 0.0053 |
| | MOE - Chronic | - | 5.8 | 11 | 837 | 48186 | 1.3 | 5.7 | 94 | 34727 |

## **Table B.6b**: Virgin NMP truck unloading exposure factors basis

| Work Activity | Parameter or Estimate | Central Tendency | | | High-End | | |
|---|---|---|---|---|---|---|---|
| | | EPA Default | EPA What-If | SIA Submission | EPA Default | EPA What-If | SIA Submission |
| Virgin NMP Truck Unloading | Duration-Based NMP Air Concentration | Central Tendency (50th percentile) of 12-hr TWA | Central Tendency (50th percentile) | Central tendency (50th percentile) of 12-hr TWA | High-end (95th percentile) of 8-hr TWA | High-end (95th percentile) | High-end (95th percentile) of 12-hr TWA |
| | NMP Weight Fraction | Central Tendency | Central Tendency | Central tendency (50th percentile) | High-end | High-end | High-end (95th percentile) |
| | Shift Duration | 8 hour shift | 8 hour shift | 8 hour shift | 8 hour shift | 8 hour shift | 8 hour shift |
| | Exposure Frequency | 5 days/week | 5 days/week | Once per year | 5 days/week | 5 days/week | Once per year |
| | Dermal Contact Time | Mid-point of shift duration (4 hours) | Task-based duration | With a dermal loading of 0.7 mg/cm2, the evaporation time of NMP is approximately 20 minutes. | High-end of shift duration (8 hours) | Task-based duration | With a dermal loading of 2.1 mg/cm2, the evaporation time of NMP is approximately 60 minutes. |
| | Skin Surface Area Exposed | 1-hand | 1-hand | 10 fingertips | 2-hands | 2-hands | 50% of the palm side of each hand |

## **Table B.7a**: Waste truck loading exposure factors

| Work Activity | Parameter or Estimate | Unit | Central Tendency | | | | High-End | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment | Typical/high end used in U.S. EPA risk determination | What-if typical and high-end | Industry proposed typical and high end referencing SIA, 2020 | SIA Public Comment |
| Waste Truck Loading | **PBPK Model Parameters** | | | | | | | | | |
| | Duration-Based NMP Air Concentration | $mg/m^3$ | 0.709 | 0.709 | 0.715 | 0.715 | 0.709 | 0.709 | 0.715 | 0.715 |
| | NMP Weight Fraction | Unitless | 0.92 | 0.92 | 0.92 | 0.92 | 0.92 | 0.92 | 0.92 | 0.92 |
| | Glove Protection Factor | Unitless | 10 | 10 | 20 | 20 | 10 | 10 | 20 | 20 |
| | Dermal Contact Time | h | 4 | 2 | 0.33 | 0.33 | 8 | 2 | 1 | 1 |
| | Skin Surface Area Exposed | $cm^2$ | 445 (f)<br>535 (m) | 445 (f)<br>535 (m) | 66.75 (f)<br>80.25 (m) | 66.75 (f)<br>80.25 (m) | 890 (f)<br>1070 (m) | 890 (f)<br>1070 (m) | 222.5 (f)<br>267.5 (m) | 222.5 (f)<br>267.5 (m) |
| | Exposure Frequency | -- | 5 days/week | 5 days/week | 5 days/week | Once per month | 5 days/week | 5 days/week | 5 days/week | Once every three weeks |
| | Body Weight | kg | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) | 74 (f)<br>88 (m) |
| | **Predictions** | | | | | | | | | |
| | Peak Blood Concentration - Acute | mg/L | 5.4 | 3.5 | 0.089 | 0.025 | 15 | 7.1 | 0.56 | 0.15 |
| | MOE - Acute | - | 81 | 124 | 4936 | 8781 | 29 | 61 | 785 | 1417 |
| | AUC - Chronic | hr mg/L | 25 | 12 | 0.15 | 0.0083 | 108 | 25 | 1.5 | 0.035 |
| | MOE - Chronic | - | 7.4 | 15 | 1214 | 22160 | 1.7 | 7.4 | 123 | 5179 |

## **Table B.7b**: Waste truck loading exposure factors basis

| Work Activity | Parameter or Estimate | Central Tendency | | | High-End | | |
|---|---|---|---|---|---|---|---|
| | | EPA Default | EPA What-If | SIA Submission | EPA Default | EPA What-If | SIA Submission |
| Waste Truck Loading | Duration-Based NMP Air Concentration | Central Tendency (50th percentile) of 12-hr TWA | Central Tendency (50th percentile) | Central tendency (50th percentile) of 12-hr TWA | High-end (95th percentile) of 8-hr TWA | High-end (95th percentile) | High-end (95th percentile) of 12-hr TWA |
| | NMP Weight Fraction | Central Tendency | Central Tendency | Central tendency (50th percentile) | High-end | High-end | High-end (95th percentile) |
| | Shift Duration | 8 hour shift | 8 hour shift | 8 hour shift | 8 hour shift | 8 hour shift | 8 hour shift |
| | Exposure Frequency | 5 days/week | 5 days/week | Once per month | 5 days/week | 5 days/week | Once every three weeks |
| | Dermal Contact Time | Mid-point of shift duration (4 hours) | Task-based duration | With a dermal loading of 0.7 mg/cm2, the evaporation time of NMP is approximately 20 minutes. | High-end of shift duration (8 hours) | Task-based duration | With a dermal loading of 2.1 mg/cm2, the evaporation time of NMP is approximately 60 minutes. |
| | Skin Surface Area Exposed | 1-hand | 1-hand | 10 fingertips | 2-hands | 2-hands | 50% of the palm side of each hand |

# Appendix C: Systematic Review of SIA Submissions

T**able C.1**: U.S. EPA systematic review of semiconductor industry documents

| Parameters(s) | Document | Page No. | Overall Quality |
|---|---|---|---|
| Engineering controls | Isaacs 2017a | 208 | High |
| Container handling, activity description and PPE | SIA 2019 | 392-406 | High |
| Maintenance air concentration, activity description/PPE | SIA 2019 | 408 | High |
| Fab operator air concentration, activity description/PPE | SIA 2019 | 410 | High |
| Fab area air concentration, activity description/PPE | SIA 2019 | 412 | High |
| Waste truck loading activity, air concentration/PPE | SIA 2019 | 414 | High |
| Virgin NMP off-loading air concentration/activity PPE | SIA 2019 | 416 | High |
| Exposure control, PPE, air measurements | Isaacs 2017a | 464 | High |
| Work activity and PPE | Intel 2019 | 466 | High |
| Engineering controls and PPE | Intel 2020 | 468 | High |
| Container handling, small containers scenario | SIA 2020 | 470 | High |
| Container handling, drums scenario | SIA 2020 | 472 | High |
| Typical fab worker scenario | SIA 2020 | 474 | High |
| Fab worker with NMP container changeout scenario | SIA 2020 | 476 | High |
| Maintenance scenario | SIA 2020 | 478 | High |
| Virgin NMP scenario | SIA 2020 | 480 | High |
| Waste truck loading scenario | SIA 2020 | 482 | High |
| Process description, weight % | Isaacs 2017a | 635 | High |
| Process description, weight %, container handling | SIA 2019 | 679 | High |
| Process description, #6 of sites, days and weight % | Isaacs 2017a | 681 | High |
| Process description, weight % | SIA 2020 | 684 | High |
| Environmental emission factor | Isaacs 2017a | 63 | High |
| Environmental emission factor | Intel 2020 | 65 | High |

# Appendix D: Detailed Review of Response to Comments

**Table D.1**: Review of response to comments

| Index | Page | Comment Topic | Agency Response | Cardno ChemRisk Analysis |
|---|---|---|---|---|
| 1 | 33 | Prolonged dermal contact | EPA has improved and clarified dermal input parameter assumptions in Section 2.4.1.1. EPA clarified in Section 2.4.1.1 that the exposure duration assumptions of full-shifts for high-ends account for the possibility of repeated contact with NMP such that NMP does not fully volatilize from the skin before the next contact event, potentially resulting in prolonged exposure. | The U.S. EPA final risk evaluation did not consider the loading estimate and contact time presented the SIA 2020 public comment. The SIA submittal was scored as "high quality" and the U.S. EPA prepared exposure estimates for the "industry-proposed" PBPK inputs in Table 2-73 of the industry document substantiating safe use (MOE>30). Thus, the industry supplied PBPK model estimates should have been considered in the final risk evaluation. The task descriptions provided by SIA substantiate that repeated contacts are unlikely in the industry. |
| 2 | 33 | Prolonged dermal contact | EPA clarified in Section 2.4.1.1 that EPA has no reasonably available information on actual surface area of contact with liquid and that the assumed values represent adequate surrogates for most uses' central tendency and high-end surface areas of contact with liquid that may sometimes include exposures to much of the hands and also beyond the hands, such as wrists, forearms, neck, or other parts of the body. | The U.S. EPA systematic review scored the SIA 2020 submission concerning dermal contact exposure factors as "high quality." These factors were determined based on comprehensive task descriptions, and validated by the member companies. Thus, the U.S. EPA assertion that it had "no reasonably available information on actual surface area of contact with liquid and that the assumed values represent adequate surrogates for most uses' central tendency and high-end surface areas of contact with liquid" is incorrect with respect to the semiconductor industry, and represents an appreciable shortcoming of the final U.S. EPA analysis. |
| 3 | 33 | Prolonged dermal contact | EPA clarified in Section 2.4 that non-immersive dermal contact with liquid films is evaluated. | The U.S. EPA final risk evaluation assumes a contact time of 6 to 12 hours where repeated contacts occurred before evaporation could occur. This assumption produces an exposure equivalent to assuming 6 to 12 hours of prolonged and immersive contact. As discussed in the SIA 2020 submittal, prolonged contact with NMP is associated with dermatitis, edema, redness, blister or cracking, which indicates that assumptions corresponding to prolonged contact are implausible when evaluated in consideration of operational conditions in the semiconductor industry. |
| 3 | 33 | Prolonged dermal contact | In the Electronics Manufacturing OES, EPA includes 6 worker activities within semiconductor manufacturing. EPA added several PBPK model runs using semiconductor industry-proposed input values and data including assumed contact durations. EPA has not found reasonably available data on actual contact durations or contact surface area for workers in the semiconductor industry and most other OESs. | The U.S. EPA response mischaracterizes the SIA contact time as assumptions, and should have used the contact times included in the high quality information submitted in the final risk evaluation. The contact times were derived based on accepted occupational exposure assessment methodologies, including a consideration of liquid loading and the balance of absorption and evaporation (Sahmel et al.2009). The U.S. EPA systematic review identified no specific concerns with the SIA exposure assessment approach. |

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| 4 | 34 | Prolonged dermal contact | EPA added discussion in Section 2.4.1.1 regarding the relative contributions of each exposure pathway to total exposures, which vary according to parameter values for NMP weight fraction in the liquid product contacted, skin surface areas in contact with the liquid product and with vapor, durations of dermal contact with liquid product and with vapor, air concentration for inhalation and vapor-through-skin exposure, body weight of the exposed person, and glove protection factor and respirator assigned protection factor (if applicable). In scenarios where the three parameters involving dermal contact with liquid product (NMP weight fraction in the liquid product contacted, skin surface areas in contact with the liquid product and with vapor, durations of dermal contact with liquid product) have relatively high values, this route can be the dominant route for worker exposures. | The U.S. EPA presents the contribution of the dermal dose in Table 4-54. Across all industries, the contribution of the dermal routes is most frequently 99 or 100%, which is a direct outcome of the Agency's assumption of up to 6 to 12 hours of prolonged contact with NMP over a surface area of 1 to 2 hands. As discussed in the prior SIA submission, there has been a consensus (e.g. Poet et al., 2016) that the fraction of exposure attributable to the dermal pathway is minor as compared to the inhalation pathway. The Agency has provided no substation or evidence that prolonged contact with NMP over large (one or two hands) surface area of skin is occurring in the semiconductor industry. Thus, it is important to note that the U.S. EPA has not been responsive to public comment critiquing the dermal contact parameters used in the draft evaluation. |
| 5 | 35 | Prolonged dermal contact | EPA believes that engineering controls would not impact contact duration with liquids but would generally reduce air concentrations. Such reductions would be reflected in air monitoring data. EPA considers chemical handling practices by reflecting different worker activities in each OES to the extent that these activities are known. | As noted in the SIA 2020 comment, airborne concentration is an indicator of the presence of dispersive or non-dispersive uses, as well as a determinate of evaporation rate. The Agency assertion regarding the lack of correlation between dermal exposure and airborne concentration does not justify the Agency conclusion that across many industries the final risk evaluation concluded an unexpectedly high contribution of the dermal pathway, frequently equaling 99 or 100% of the dose. |
| 6 | 36 | Prolonged dermal contact | EPA does not have reasonably available data or information to inform specific durations of contact and associated concentrations and formulations that would be implausible or cause toleration issues. | As noted in the SIA 2020 comment, the dermal pathway is not expected to be the major pathway of exposure, and pervasive dermal exposure is expected to produce pervasive dermatitis, edema, redness, blister or cracking of skin. The Agency has failed to identify case reports or occupational compliance data substantiating pervasive skin damage associated with use of NMP in the semiconductor industry. |
| 7 | 36 | Prolonged dermal contact | EPA does not have reasonably available data or information that shows assumed exposure durations for dermal contact with liquids to be incorrect for any tasks. EPA added several PBPK model runs using semiconductor industry-proposed input values and data including their assumed contact durations. EPA has not found reasonably available data on actual contact durations or methods for measuring these durations for workers in any industry, including the semiconductor industry. | See Index Analysis #2. |

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| 8 | 37 | Prolonged dermal contact | EPA clarified in Section 2.4.1.1 that the contact duration assumptions of full-shifts for high-ends account for the possibility of repeated contact with NMP such that NMP does not fully volatilize from the skin before the next contact event, potentially resulting in prolonged exposure. In this section EPA also clarified that where available, EPA utilized exposure durations from the available task-based inhalation monitoring data for generating what-if type exposure scenarios assuming that the workers were contacting NMP-containing liquids over only the monitoring duration (i.e., the entire task duration). Task-based duration estimates do not account for either liquid remaining on the skin after the task is completed or for workers performing a task multiple times during their shift. EPA expanded PBPK runs using both shift-based and task-based duration estimates for many OESs. | See Index Analysis #4. The U.S. EPA "what-if" task duration analyses do not properly represent exposures in the semiconductor industry because dermal contact does not occur for the entire duration of the task. |
| 8 | 37 | Prolonged dermal contact | EPA did not assume that truck unloading at semiconductor sites is a 4- or 8-hour/day task but assumed shift-based durations for central tendency and high-end estimates and task-based durations for what-if estimates. EPA removed the truck unloading from chronic estimates since this task is not performed 4 or 5 days per week. | In contrast to the representation in the response to comments, the U.S. EPA presents chronic MOEs for truck unloading, and in Section 5.2.1.18, concluding "For workers, when assuming the use of respirators with APF of 10 and gloves with PF of 10, the risk estimates of non-cancer effects from acute inhalation and dermal exposures at the high-end, and from chronic inhalation and dermal exposures at the central tendency and high-end in virgin NMP truck unloading activities support an unreasonable risk determination." As discussed in detail in this report, the U.S. EPA estimates used for truck loading and unloading are not representative of SIA member company exposure scenarios. As discussed in Index Analysis #3, the shift-based approach to setting liquid dermal contact duration is not scientifically reliable. |
| 9 | 37 | Prolonged dermal contact | EPA used the most recent industry-provided task duration estimates in some PBPK runs for the lithium ion battery industry and for the semiconductor applications, including fab facilities. | The U.S. EPA task duration, or "what-if" analyses misrepresent that dermal contact occurs over a surface area up to 2 hands and that dermal liquid contact occurs for the entire task duration. It was unnecessary for the Agency to prepare these unrepresentative estimates because the Agency had separately modeled the SIA-substantiated (termed "proposed" in E.P.A. report) exposure factors (excluding exposure frequency). As noted elsewhere in this report, the Agency judged the SIA 2020 submission and proposed PBPK model inputs as "high quality." |

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| 10 | 38 | Prolonged dermal contact | EPA's current dermal liquid contact exposure assumptions are based on the "best available science" approach and have considered detailed information supplied by the assessed industry, including industry-proposed parameter values as well as additional parameter values that consider more factors, such as repeated contact with liquids during the workers' shifts and time for NMP-containing liquids to evaporate. EPA's approach is consistent with the dermal exposure chapter of the American Industrial Hygiene Association (AIHA) reference by using scenario-specific surface area and contact time that are determined based on the conditions of use.<br><br>The liquid loading aspect covered in AIHA's dermal chapter and in AIHA's IH SkinPerm model is handled differently because PBPK modeling for internal dose does not use a liquid loading parameter as do the more simplistic potential dose models covered by the AIHA reference. EPA clarified in Section 2.4 that non-immersive dermal contact with liquid films is evaluated. EPA does not have reasonably available data to indicate dissimilarity of industries grouped into OESs. EPA did not group paint, coatings, adhesives, and semiconductor manufacturing into an OES. | As noted in the Index Response #1, the "EPA clarified in Section 2.4.1.1 that the exposure duration assumptions of full-shifts for high-ends account for the possibility of repeated contact with NMP such that NMP does not fully volatilize from the skin before the next contact event, potentially resulting in prolonged exposure." Thus, the Agency has effectively assumed conditions equivalent to immersion where pervasive repeated contacts sustain a liquid film on the skin for up to the duration of a shift. These conditions of use equating to immersion do not exist in the semiconductor industry. The SIA 2020 comment advised the Agency to consider the AIHA methodologies because they provide a scientific basis to extract exposure factors from comprehensive task descriptions, such as the ones provided in SIA public comment. As such, the Agency response misrepresents that consideration of liquid loading on the skin and mass-balance methodologies are less sophisticated than the approach used by the Agency. |
| 11 | 38 | Prolonged dermal contact | Regarding AIHA's IH SkinPerm model contact time (h) based on a consideration of evaporation, this model's treatment does not account for repeated contacts during a worker's shift, task duration, nor worker activities for particular NMP OESs and COUs. Therefore, the evaporation-based contact times estimated by this AIHA model are less useful for EPA's risk evaluation. | The screening-level dermal liquid loading factors presented in Table 13.3 of Sahmel et al., 2009 are appropriate for describing the tasks with incidental NMP contact as documented by the SIA submissions. Some typical examples provided in Table 13.3 of the reference include "maintenance" and "manual cleaning of equipment." Considering the extensive task descriptions provided by SIA selection of the loading corresponding to single event is appropriate for exposure assessment. |
| 11 | 38 | Prolonged dermal contact | EPA considers evaporation of volatile or semi-volatile chemicals from the skin as a determinant of dermal exposure potential by using contact duration. This evaporation is only one of many determinants toward contact duration. | The U.S. EPA effectively eliminated consideration of evaporation in the risk evaluation by assuming prolonged contact equal to the entirety or ½ of the shift time. |
| 12 | 39 | Prolonged dermal contact | Scenario-specific factors available for dermal liquid exposure assessment in the IH SkinPerm model are not specific enough to specifically determine surface area of contact, the number of repeated contacts during a worker's shift, task duration, or worker activities for particular NMP OESs and COUs. Therefore, parameters estimated by this AIHA model are less useful for EPA's risk evaluation. | The exposure factors presented in the Cardno ChemRIsk analysis were based on comprehensive task descriptions supported numerous SIA submissions with detailed descriptions of work task in the semiconductor industry in multiple submission. |

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| 12 | 39 | Prolonged dermal contact | To address dynamic loading on the skin (*i.e.*, where deposition is defined by an amount/area/time deposited) or exposure to very thin films would require significant revision of the PBPK model. It is likely that for a film on exposed skin on the order of microns of thickness (1.02 mg/cm2 is equivalent to a layer 10 µm thick), evaporation will become a significant factor, with that evaporation being temperature dependent. A film on exposed skin will be simultaneously warmed by body heat and cooled by evaporation. The U.S. EPA is not aware of a PBPK model of dermal exposure that accounts for the complex interplay of these factors; *i.e.*, such a model is not in the realm of available science. On the other hand, if NMP penetrates under a protective glove, that film would not be subject to evaporation and EPA is not aware of science to indicate that absorption would vary as a function of the film thickness, as long as it was present. Therefore, EPA considered two options: making the best possible use of the Poet et al. PBPK model (with minor corrections) or performing the risk assessment without a PBPK model. The use of the PBPK model under the assumption that the exposed skin is effectively immersed in NMP was considered the preferred option, making use of the best available science, despite its limitations. | The U.S. EPA acknowledges that films of NMP would likely "become a significant factor", however, in earlier responses rejected consideration of scenario-specific liquid contact time and loading. Notably, the Agency explicitly opines that the "use of the PBPK model under the assumption that the exposed skin is effectively immersed in NMP was considered the preferred option, making use of the best available science, despite its limitations." Thus, the Agency has presented conflicting responses to public comment rejecting the use of higher tier exposure factors, yet acknowledging that industrial hygiene guidance for selection of these exposure factors based is available from professional societies, such as AIHA. |
| 13 | 40 | Prolonged dermal contact | Unlike EPA estimates of contact durations, the Cardno ChemRisk analysis equates evaporation time to contact durations, which does not account for extended, continued contact or repeated contacts over a shift. | The contact times estimated by Cardno ChemRisk were derived through a consideration of the comprehensive task descriptions provided by SIA member companies, and validated by member companies as representative of the current conditions of use. |
| 14 | 44 | Vapor-through-skin exposure | The PBPK model accounts for reduction in skin surface area for vapor-through-skin exposure based on PPE usage. EPA included additional PBPK runs for semiconductor fab workers assuming 98% skin coverage to supplement runs that assume 75% skin coverage. EPA has included discussion in Uncertainties Sections 2.4.1.4 and 4.3 that dermal exposures to NMP vapor that may penetrate clothing fabrics and the potential for associated direct skin contact with clothing saturated with NMP vapor are not included in quantifying exposures. The discussion further notes that these uncertainties could potentially result in underestimates of exposures. | The sensitivity analysis previously submitted in the SIA 2020 comments indicated that the vapor-through-skin pathway is not an appreciable determinant of internal exposure. Thus, it is unlikely that dose has been underestimated due to saturated clothing. |

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| 15 | 45-46 | Aggregate exposure | EPA revised the occupational exposure assessment in the risk evaluation to separately assess occupational exposure scenarios associated with three categories of electronic part manufacturing: lithium ion battery manufacturing (2.4.1.2.15); Other electronics manufacturing, including capacitor, resistor, coil, transformer, and other inductor manufacturing (2.4.1.2.9); and semiconductor manufacturing (2.4.1.2.10). In these separate OESs, EPA revised and expanded PBPK runs for industry-specific work activities using industry-specific air concentration data sets provided in public comments for the lithium ion battery manufacturing industry, for the semiconductor manufacturing industry, and from the OSHA data set for capacitor, resistor, coil, transformer, and other inductor manufacturing (LICM, 2020a; Semiconductor Industry Association, 2020, 2019b, c; OSHA, 2017). | The U.S. EPA presents internal exposure estimates for the SIA-substantiated exposure factors (except exposure frequency) in Table 2-73. PBPK Exposure Results for Central and High-End Worker and ONU Scenarios by Use. However, the Agency failed to consider the corresponding MOE in the risk evaluation, which substantiated safe use for the condition of use at SIA member companies (MOEs corresponding to industry-proposed scenario was > 30). |
| 16 | 56 | Conditions of use | EPA updated the process description and PPE information for semiconductor manufacturing in Section 2.10 (Semiconductor Manufacturing OES) of the Supplemental Information on Occupational Exposure Assessment document. To supplement shift-based contact duration estimates, EPA updated the what-if (task duration-based) work activities for semiconductor manufacturing based on the task duration estimates provided by SIA in public comments (Semiconductor Industry Association, 2020, 2019a).<br>EPA updated the central tendency and high-end NMP weight fractions for the semiconductor work activities using | See Index Analysis #15 |
| 17 | 56 | Conditions of use | EPA added several PBPK runs for semiconductor fab workers assuming 98% skin coverage to supplement runs that assume 75% skin coverage. These runs are available in the Supplemental Excel File on Occupational Risk Calculations. For any particular male Fab worker or Fab ONU activity, the differences in AUC internal concentrations obtained by varying only the assumed whole-body skin coverage between 75% and 98% but no other parameter variation was found to be less than 1% in EPA's anecdotal comparison. Therefore, the skin coverage assumption does not appear to significantly impact the AUC internal concentration estimates. | See Index Analysis #14 |

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| 18 | 59 | Conditions of use | EPA updated the air concentrations for semiconductor manufacturing work activities and did not adjust the duration-adjusted air concentrations to normalize to contact duration estimates due to the high number of non-detect values. The air concentration values used by EPA are very similar to those proposed by SIA in the public comment (Semiconductor Industry Association, 2020) with their proposed input values for PBPK runs. Frequency of truck unloading is accounted for in the analysis by modeling only acute and not chronic exposures for this work activity. | The inhalation pathway contributed minimally to internal exposure in the U.S. EPA analysis. See Index Analysis #8 for a discussion of truck unloading. |
| 19 | 61-62 | Conditions of use | EPA revised the occupational exposure assessment in the risk evaluation to separately assess occupational exposure scenarios associated with three categories of electronic part manufacturing: Lithium ion battery manufacturing (2.4.1.2.15); Other electronics manufacturing, including capacitor, resistor, coil, transformer, and other inductor manufacturing (2.4.1.2.9); and Semiconductor manufacturing (2.4.1.2.10). In these separate OESs and where feasible, EPA used some industry-specific PBPK input data and information provided in public comments for the lithium ion battery manufacturing industry (EaglePicher Technologies, 2020a, b; LICM, 2020a, b, c) and for the semiconductor manufacturing industry (Intel Corporation, 2020; Semiconductor Industry Association, 2020; Intel Corporation, 2019; Semiconductor Industry Association, 2019a, b, c).<br><br>EPA reviewed all information in the public comments provided by SIA and updated the PBPK inputs for the semiconductor manufacturing OES work activities, including NMP weight fractions, NMP air concentration, and task duration (for what-if, task duration-based work activities). | See Index Analysis #15. |
| 20 | 62 | Conditions of use | In Chapter 2, EPA has removed assignments/ assumptions of specific glove PFs to apply to each OES. Table 2-77 has been updated to include worker exposures for all glove PFs for all OESs. Table 2-77 in Section 2.4.1.3 has been updated to include worker exposures for all glove PFs for all OESs. | The U.S. EPA adopted a glove PF of 10 in Chapter 5 of the risk evaluation (5.2.1.15 and 5.2.1.18), which is inconsistent with the training and practices described in the SIA 2020 public comment. |

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| 21 | 62 | Conditions of use | EPA clarified in Section 2.4.1.1 that EPA has no reasonably available information on actual surface area of contact with liquid and that the assumed values represent adequate surrogates for most uses' central tendency and high-end surface areas of contact with liquid that may sometimes include exposures to much of the hands and also beyond the hands, such as wrists, forearms, neck, or other parts of the body. EPA accounts for distributed values using the central tendency and high-end assumptions for surface areas. EPA clarified in Section 2.4 that non-immersive dermal contact with liquid films is evaluated. | See Index Analysis #1, #2,.and #3 |
| 22 | 72 | Conditions of use | In these separate OESs and where feasible, EPA revised and expanded PBPK runs for industry-specific work activities using industry-specific PBPK input data and information provided in public comments for the lithium ion battery manufacturing industry (EaglePicher Technologies, 2020a, b; LICM, 2020a, b, c) and for the semiconductor manufacturing industry (Intel Corporation, 2020; Semiconductor Industry Association, 2020; Intel Corporation, 2019; Semiconductor Industry Association, 2019a, b, c). | See Index Analysis #15 |
| 23 | 73 | Conditions of use | EPA updated the air concentrations for work activities assessed for semiconductor manufacturing. EPA provided additional explanation of the analysis of SIA's air sampling results in the Supplemental Information on Occupational Exposure Assessment. | See Index Analysis #18 |
| 24 | 127 | PBPK Modeling | Regarding PBPK occupational inputs, EPA has included data and assumptions provided in semiconductor industry comments in many PBPK runs for occupational exposures. While weight fraction data provided in semiconductor industry comments reduce uncertainties, EPA cannot determine whether uncertainties in PBPK model inputs on exposure are reduced by using assumptions provided in semiconductor industry comments because EPA has no data to determine whether the proposed industry assumptions are more accurate than the assumptions applied by EPA. | The U.S. EPA systematic review classified the SIA 2020 submission as high quality, and thus should have been considered in the risk evaluation. As noted previously, the Agency provided exposure estimated corresponding to the SIA-actual parameters in Table 2-73. PBPK Exposure Results for Central and High-End Worker and ONU Scenarios by Use. However, the Agency failed to consider the corresponding MOE in the risk evaluation, which substantiated safe use for the condition of use at SIA member companies (MOEs corresponding to industry-proposed scenario was > 30). It is important to emphasize that the systemic review found the SIA submission to be well documented with a consideration of uncertainty. Furthermore, the submission reflected the subject matter expertise of SIA member companies and Cardno ChemRisk, and there is no apparent explanation for failure of the Agency to consider the information submitted in the public comments. |

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| 25 | 140 | MOE determination (Cardno ChemRisk) | EPA does not have reasonably available information and data to verify parameter assumptions in the Cardno ChemRisk analysis.<br>EPA also did not identify reasonably available information or data indicating that any of the assumptions EPA used in the analysis are incorrect. For the Semiconductor manufacturing OES (Section 2.4.1.2.10), EPA revised and expanded PBPK runs for industry-specific work activities using industry-specific sets provided in public comments<br>As demonstrated by various PBPK parameter sets, the EPA analysis indicates a differentiation on exposure potential between jobs as does the Cardno ChemRisk analysis. EPA's analysis uses ONUs to indicate functions having no opportunity for dermal direct contact. | See Index Analysis #24 |
| 26 | 143 | PPE Assumptions | In Section 2, EPA has removed assignments/ assumptions of specific glove PFs to apply to each OES. Table 2-77 has been updated to include worker exposures for all glove PFs for all OESs. EPA revised and expanded PBPK runs for industry-specific work activities using industry-specific data and information provided in public comments for the semiconductor manufacturing industry. To the extent that information is reasonably available on PPE use for specific occupational exposure scenarios, it is described in Section 2.<br>In Section 4, EPA presents risks for all occupational exposure scenarios both with and without glove use and with and without respirator use. Table 4-54 demonstrates the extent to which gloves and respirators influence risk estimates for each condition of use. | See Index Analysis #18 and #20 |
| 27 | 169 | Risk Conclusions | EPA worked with the semiconductor industry to incorporate documented assumptions and information into the Final Risk Evaluation. EPA revised the occupational exposure assessment in the risk evaluation to separately assess occupational exposure scenarios associated with three categories of electronic part manufacturing: Lithium ion battery manufacturing (2.4.1.2.15); Other electronics manufacturing, including capacitor, resistor, coil, transformer, and other inductor manufacturing (2.4.1.2.9); and Semiconductor manufacturing (2.4.1.2.10). In these separate OESs, EPA revised and expanded PBPK runs for industry-specific work activities using industry-specific air concentration data sets provided in public comments for the lithium ion battery manufacturing industry and for the semiconductor manufacturing industry, and from the OSHA data set for capacitor, resistor, coil, transformer, and other inductor manufacturing (SIA, 2019b, c; SIA, 2020; LICM, 2020b; OSHA, 2017). | See Index Analysis #15 |

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| 28 | 182 | Editorial - Accuracy | EPA replaced the statement “EPA did not find data on exposure duration” with “EPA did not find reasonably available data on actual duration of dermal contact with liquids." EPA also revised PBPK inputs for this OES to include “what-if” task duration-based durations for liquid contact, which use tasks durations provided from public comments, including from SIA public comments (Semiconductor Industry Association, 2020, 2019b, c).<br><br>While EPA revised the assessment to include “what-if” task duration-based PBPK inputs when available, EPA retains full-shift and half-shift shift-based duration PBPK inputs for all OESs due to uncertainty of task durations representing actual durations of contact with liquids. | See Index Analysis #1, #2, #3. #9, #13, #15 and #24, |

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