Dermal Monitoring Decision Framework

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American® Chemistry Council

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Acronyms

ACC	American Chemistry Council
ACGIH	American Conference of Governmental Industrial Hygienists
AIHA	American Industrial Hygiene Association
ASTM	American Society for Testing and Materials
BEI	Biological Exposure Indices
CPC	Chemical Protective clothing
DNEL	Derived No-Effect Level
DRAM	Dermal Risk Assessment Model
EAWG	Exposure Assessment Working Group

ECHA	European Chemicals Agency
EPA	Environmental Protection Agency
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
HAZMAT	Hazardous Material
HTTK	High Throughput Toxicokinetics
IgE	Immunoglobulin E
IH	Industrial Hygiene
IUPAC	International Union of Pure and Applied Chemistry
LOD	Limit of Detection
LOQ	Limit of Quantification
LRI	Long Range Initiative
MOE	Margin of Exposure
MOS	Margin of Safety
NIOSH	National Institute of Occupational Safety and Health
NMP	n-Methylpyrrolidone
OEHS	Occupational Environmental Health and Safety
OEL	Occupational Exposure Limits
OES	Occupational Exposure Scenarios
OSHA	Occupational Safety Health Administration
POD	Point of Departure
PPE	Personal Protective Equipment
PVC	Polyvinyl Chloride
SDS	Safety Data Sheets
SEG	Similar Exposure Groups
TK	Toxicokinetics
TLV	Threshold Limit Values
TSCA	Toxic Substances Control Act
WEEL	Workplace Environmental Exposure Levels

Background

In 2021, EPA issued test orders for several existing chemical substances under Section 4 of the Toxic Substances Control Act (TSCA), including a request for workplace dermal monitoring data using a dermal sampling method. However, dermal sampling methods for many chemicals are not standardized and thus, conducting sampling can be challenging and approaches vary across research and regulatory institutions. Recent activities among chemical industry partners have highlighted the challenges of dermal exposure data collection.

This document was produced to assist ACC members in identifying or generating high-quality workplace dermal monitoring data. The framework is also intended to be useful in retrospectively evaluating the robustness of previously collected data for the dermal route. The overall utility of the framework is as a resource for conducting dermal risk assessments for occupational exposure scenarios (OES).

1 Introduction and Overview

1.1 Purpose and Objectives

The overarching purpose of the dermal exposure assessment framework is to assist the assessor to determine on whether collection of occupational dermal monitoring data is needed and to provide guidance to develop an appropriate dermal monitoring and data collection strategy. The framework is applicable to a variety of OES but draws most heavily from upstream manufacturing and processing and is intended to be especially pertinent for companies responding to TSCA Section 4 test orders. The predominant approach will draw from the exposure/risk assessment paradigm and is consistent with existing tiered approaches for occupational risk assessment. Other steps commonly used in the risk assessment process, such as risk characterization and risk management will be discussed briefly, but not in detail, to contextualize the relationships among exposure assessment and other aspects of the risk assessment process.

The framework draws from exposure assessment resources and methods from the following sources:

- Peer-reviewed literature,
- Agency and non-governmental organization guidance documents [from EPA, AIHA, the European Chemicals Agency (ECHA), among others],
- Other resources from regulatory agencies and programs, and
- Previous ACC project work and relevant documents provided by the ACC Exposure Assessment Working Group (ACC-EAWG) and associated stakeholders.

Specifically, the framework provides guidance on the following:

1.) gathering and assessing existing qualitative and quantitative information and data on dermal hazards and exposure,

2.) assessing the need to estimate or evaluate dermal exposure, including modeled data or empirical data,

3.) selecting appropriate models, and

4.) collecting empirical dermal exposure data.

Some steps within this framework are iterative and may need to be performed on a routine basis, especially if new information or approaches become available, or when OES change. Because the framework is presented in a general fashion to be widely applicable, additional resources are provided to facilitate chemical- and scenario-specific decision making. Furthermore, there are additional resources provided to guide other phases of the dermal risk assessment process that are not covered in detail in this document, such as how to develop dermal occupational exposure limits surface limits. More information regarding the utility of occupational exposure limits is provided in Section 4.1.4.

Because dermal exposure characterization is inherently linked to the broader occupational dermal risk assessment framework, the following section provides a brief overview of the overall process of dermal risk assessment.

1.2 Overview of Dermal Risk Assessment Process

The Conceptual Framework for Dermal Risk Assessment Decision-Making provides an overview of key steps needed to characterize the potential for dermal exposure and risk (Figure 1). It outlines key decisions and associated tasks (such as problem formulation, data gathering, exposure assessment,

and/or data collection strategies) needed to conclude whether dermal risk is acceptable or not, and potential follow-up decisions based on the outcome. The framework is primarily focused on strategies for exposure data collection and other aspects are covered briefly.

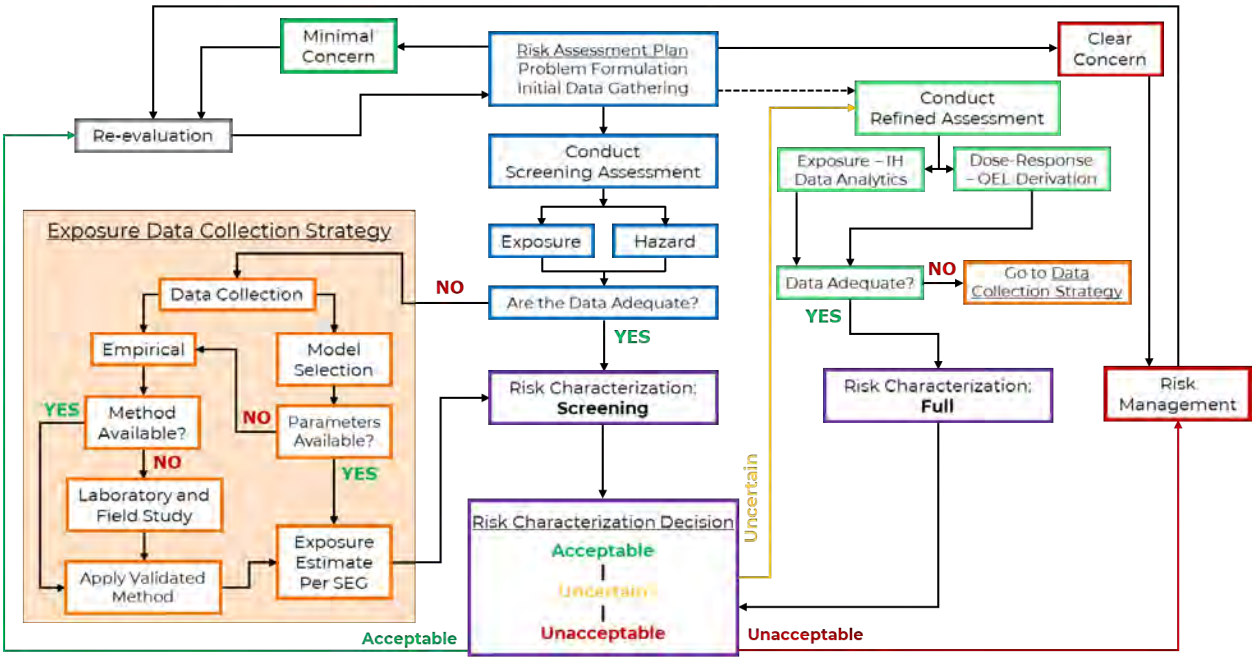


Figure 1. Conceptual Framework for Dermal Risk Assessment Decision-Making

This process is iterative, and certain outcomes may lead back to earlier steps in the process, especially when changes to the original scope are identified, including when:

1. A new chemical(s) is introduced into the manufacturing process;
2. A significant new use(s) is introduced for existing compounds, or the quantity of an existing compound is increased;
3. Additional worker populations are introduced to a facility;
4. Additional peer-reviewed data is published regarding new dermal hazards or increased potential for occupational dermal exposure;
5. Dermal sampling/monitoring data indicates that there is potential for dermal exposure, where previously none was expected or anticipated;
6. To confirm that personal protective equipment and/or engineering controls being used are sufficient for protection from dermal exposure potential;
7. Additional dermal sampling methods or modeling tools become available.

1.2.1 Risk Assessment Plan (Problem Formulation & Scoping)

Problem formulation refers to the process of defining the scope of an assessment (i.e., what is to be evaluated), and a high-level plan for how the assessment will be done (OHAT, 2019). Regardless of the occupational exposure scenario, the user will always begin with the problem formulation and data gathering. In some situations, it may be clear from qualitative information (e.g., a well-established hazardous substance and high dermal exposure potential for the scenario of interest) that a scenario is of

concern for human health, and one would move straight to managing risk. On the other hand, if problem formulation and initial data gathering reveals very low potential for exposure and health effects, the user may conclude there is minimal concern and will pause further detailed assessment unless conditions change. In many cases a clear initial decision cannot be made without more detailed data review either in the context of a screening assessment or refined assessment methodology. More information regarding developing a risk assessment plan is described in Section 2.

1.2.2 Dermal Hazard Assessment

The second step of a dermal risk assessment is hazard identification. The hazard identification process includes an evaluation of the innate potential of a chemical to cause adverse health effects. A chemical may be hazardous, but only under certain conditions of use. The outcome of the hazard identification is typically qualitative in nature – yielding categories of concerns, hazard bands, or classifications. For screening assessments such qualitative or categorical approaches are often sufficient to support decision making. However, in some cases a chemical may be hazardous, but only at a certain concentration or under specific conditions of use. Thus, in some cases it may be warranted to develop potency metrics or health-based benchmarks for the dermal exposure route (e.g., ACGIH threshold limit values-surface limits [TLV-SLs], dermal derived no-effect level [DNELs] in the European Union) for the adverse effects identified in the hazard assessment. Such dose-response analyses are more common for conduct of a refined risk assessment approach. Evaluating hazard is critical because an understanding of the toxicological potency will determine if an exposure assessment is necessary, and if so whether a screening or refined exposure assessment is needed. Thus, at a minimum, any assessment, even if only planning to conduct exposure estimation, should include a hazard identification exercise. As an example, and as outlined in the Appendix C – Dermal Occupational Hazard and Exposure Checklist, high hazard and high exposure potential would necessitate a more refined approach. For the purposes of this framework, a separate hazard assessment section is not provided because hazard assessment, rather key considerations are embedded in the problem formulation section.

1.2.3 Dermal Exposure Assessment

The dermal exposure assessment is intended to be tiered. A screening-level exposure assessment can be conducted to assess whether there are sufficient data to perform a risk characterization. However, a the final determination that the risk is unacceptable should leads to development of risk management options. If exposure data available at the beginning of the process are inadequate to make a screening assessment decision with confidence, developing a data collection strategy is recommended. Developing the data collection strategy should include consideration of the pros and cons of utilizing empirical data, exposure models, or both approaches. For empirical data, key considerations relate to the availability of validated sampling methods, or development of such methods, followed by their implementation for field data collection. Once annotated data are collated, statistical analysis can be used to validate existing process-based definitions of similarly exposed workers (i.e., similar exposure groups [SEGs]). Summary exposure estimates (e.g., mean, median, 95th percentile) are then generated for each of the identified SEGs (see Appendix G for an overview of Industrial Hygiene (IH) data analytics strategies). A complementary exposure assessment approach is applying dermal exposure models. Confidence in the modeling approach relies upon the quality of input parameters. Such model estimates can often support or add to the weight of evidence for an exposure assessment, and in some cases be the primary basis for an assessment (especially for screening assessments); however, models have limitations, and these are discussed below in Section 3.4.1. The resulting exposure estimates can be validated in the field and applied to develop exposure assessments for SEGs.

1.2.4 Dermal Risk Characterization and Management

Risk characterization reflects a comparison of the exposure potential to the health hazard benchmark to inform the need for various actions to mitigate health risks. The framework in this document includes a

risk characterization option at several process steps: problem formulation, screening assessment, and refined assessment. These steps rely on increasing levels of information evaluation that are intended as fit for purpose to support risk informed decisions. At the initial data gathering step, it may be possible to identify scenarios with minimal concern because the scenario involves very little if any exposure or only nonhazardous materials are present. In contrast, some scenarios may be deemed of clear concern because of observable and apparent significant potential for exposure to chemicals that present health hazards by the dermal route. For many scenarios however, a screening or refined risk assessment and risk characterization will be needed.

When exposure estimates (from empirical or modeled data) are paired with the hazard assessment and SEG-based exposure data are used to arrive at any one of three risk characterization conclusions: dermal risk is either a) acceptable, b) uncertain, or c) not acceptable. As previously mentioned, unacceptable risk will immediately lead to development of risk management options per the hierarchy of controls. If the risk is uncertain, a refined assessment is often conducted. A refined assessment may include conducting additional analyses, assessing dose-response relationships, developing health-based benchmarks, and modeled or empirical data. Even if risk is determined to be acceptable for the chemical and use scenario of interest, the process may require re-evaluation for management of changing conditions.

In all of these cases, clear criteria for defining risk metrics and resulting risk informed decisions are needed. Either categorical or quantitative estimates of both exposure and chemical toxicity (or hazard) are typically developed. The toxicity metrics provide a benchmark to determine if exposures may pose potential human health risks. For qualitative assessments categorical risk matrices are often employed as the input to make risk informed decisions. For refined assessments quantitative approaches are more typical and metrics such as margin of exposure, hazard index/ratio, or risk specific dose based on a potency factor (common for cancer endpoints). The resulting risk category or risk metric then drives the basis for decisions regarding the need for and extent of risk management. For this framework, the process is flexible and provides general descriptions of acceptability categories (not acceptable, uncertain acceptability, acceptable). This reflects that there is no single consensus cut point or definition for acceptable risk in all dermal risk assessment contexts. The risk metric cut points will vary by risk assessment context as well as risk policies relative to the organization applying the methods. It is important that the risk metrics be defined and communicated in the overall risk characterization process.

Risk management refers to the assessment and implementation of strategies to reduce chemical health risks. These strategies are implemented when potential health risk is identified in screening or refined exposure assessments. Risk management strategies are fit-for-purpose and vary depending on the scenario of interest, but generally follow the principles of the hierarchy of controls. The risk management strategy should outline steps required or suggested to minimize the potential dermal exposures and risks to the occupational cohort of interest. Later sections in this framework provide additional considerations and resources related to risk management options -- in particular, additional considerations regarding hierarchy of controls and personal protective equipment selection (see Section 4.2.5).

2 Risk Assessment Plan (Problem Formulation and Scoping)

As highlighted in Section 1.2.1, problem formulation is a very important step in any environmental health assessment. It can be applied to the risk assessment process as a whole, or individually to any phase of the assessment. For example, if starting with an exposure assessment, one can develop a problem formulation exercise strictly for exposure assessment. In general, data gathering for problem formulation could include collecting safety data sheets (SDS), process diagrams and descriptions, existing job hazard analyses, and incident reports. Further, problem formulation involves answering key questions, including:

1. What is the scope of the issue?
2. What question are we trying to answer?
3. What information is needed to answer the question?
4. Do we have sufficient information to make initial risk-informed decisions?
5. How do you decide if an exposure assessment is needed?
6. What type of exposure assessment is appropriate for the OES of interest (i.e., screening vs. refined)?

Problem formulation must be rooted in a key question or hypothesis and a goal for the assessment. For occupational dermal exposure or risk assessment, different issues that could instigate an assessment include, for example:

- Basic information gathering for conduct of a baseline assessment (e.g., not much is known about the exposure potential of the chemical, or use of the chemical).
- Regulatory requirement or request (e.g., TSCA Section 4 testing request from EPA or EU OSH Framework Directives).
- Incidences of health effects or specific concerns related to health effects (e.g., skin sensitization, systemic effects, reproductive toxicity) in workers potentially related to dermal exposures.
- Introduction of new chemicals into the workplace in which the dermal exposure risk is unknown or anticipated.
- Introduction of new use or process for handling an existing chemical in which the dermal exposure risk may change from the original use or handling.

Information gathering and questions developed in problem formulation can be divided into those pertaining to hazard and exposure potential, respectively. Examples of key questions that can guide problem formulation are discussed below. In the final section, overall assessment questions are provided.

2.1 Hazard Identification/Health Hazards

The following discussion outlines key information needed to perform a hazard identification for potential dermal hazards in occupational settings. The general goal is to determine if the chemical substance in the context of the occupational use scenario poses any potential adverse health effects following exposure via the dermal route. This section is intended to inform the process for problem formulation and initial screening level assessment. Discussion of qualitative and quantitative approaches for assessing adverse health effect risk from the dermal route are provided in the section risk characterization. At the end of this process, one should be able to identify a potential workplace dermal chemical hazard. Additional

categories and examples of key resources to the hazard assessment of chemicals following dermal exposure are outlined and discussed in detail in **Appendix A – Dermal Hazard Resources**.

Examples of key questions to ask regarding hazard potential during problem formulation:

1. What are the hazards associated with the chemical(s) of interest via dermal exposure?
    a. Is there existing information regarding whether the chemical(s) is a health hazard if in contact with the skin or dermally absorbed?
    b. Are there harmonized hazard codes or classifications pertinent to dermal exposure?
    c. Are there specific health endpoints and toxicity data associated with the chemical(s)?
    d. Has toxicity hazard potential *in silico* evaluations or other new approach methods been explored?
    e. Are there other chemicals in the workplace with similar hazards?
    f. Is there potential for synergistic effects?
    g. If no hazard data is available, are there structurally similar chemicals which may be evaluated for read-across potential?
2. Will dermal exposure/penetration of the chemical(s) lead to systemic or point of contact health effects?
    a. Is the chemical(s) assigned a skin notation?
    b. What is the anticipated dermal absorption? This could be based on peer reviewed literature (e.g., animal or human studies, in vitro studies), or a fixed percentage of the applied dose. See Kissel et al. 2011.
    c. Have absorption models or absorption predictions been evaluated? (Refer to Section 3.4.1, and Appendix F)
3. What are key exposure determinants (such as concentration, frequency, or route of exposure)? Is the chemical of interest handled neat or found in a mixture or matrix?
4. Is there an occupational exposure limit or other benchmark? Can one be derived from existing information? Are hazard data already available from internal or external sources to derive such a benchmark?

Appendix A: Dermal Hazard Assessment Resources provides an annotated list of numerous resources and a hazard information workflow to identify sources of hazard information, including the following main information resource categories:

- Health effects and toxicological data
- Hazard notations and classifications
- Health-based exposure limits

2.2 Exposure Potential

The following outlines examples of key information needed to perform a scoping assessment for exposure potential in occupational settings that guide the development of the problem formulation. Such information is often available from initial facility observation, document review, and interviews with individuals knowledgeable in the process and site operations.

Examples of key questions to ask regarding exposure potential during problem formulation:

1. What is the chemical or contaminant of concern?
    a. Are there physical or chemical properties that affect the potential for dermal exposure? (e.g., molecular weight, octanol/water coefficient, water solubility)
    b. Are there any properties that might reduce or limit the potential for dermal exposure? (e.g., is the chemical corrosive or pungent?)
    c. Is the chemical used in combination or in a mixture with other chemicals that could influence absorption potential?
2. What is the source of exposure?
    a. How is the chemical handled at the facility or relevant use scenario?
    b. Does the use scenario affirm or preclude the potential for skin contact?
    c. What is the duration and frequency of exposure?
3. Who is at risk?
    a. What occupational exposure groups or SEGs may be potentially exposed?
    b. What Are the sensitive populations (i.e., pregnant women), if any?
4. How is exposure expected to occur in the facility?
    a. What Is the potential for direct skin exposure (splash, dip of hands into vat)?
    b. What Is the potential for indirect skin exposure (i.e., touching a contaminated surface)?
    c. Does the occupational exposure scenario suggest a potential for exposure that is acute, chronic or both?
    d. Is work clothing worn home?
5. Are there control strategies already in place?
    a. what process controls are in place related to chemical use and selection?
    b. What engineering controls are in place related to chemical use?
    c. What standard operating procedures are in place related to chemical use?
    d. Is a personal protective equipment program in place related to chemical use?

Appendix B: Dermal Exposure Assessment Resources some of the categories and examples of key resources relevant to the exposure assessment of chemicals following exposure by the dermal route:

- Agency and Professional Guidance
- Agency Test Guidelines
- Tools and Toolkits
- Agency Databases and Occupational Monitoring Data
- Peer-Reviewed Literature

In addition to Appendix B, there is an additional resource spreadsheet titled “Critical Review of Existing Literature” of existing literature relevant to dermal exposure, including agency guidance resources, peer-reviewed dermal tiered assessment and frameworks, peer-reviewed dermal sampling methods and protocols, and reviews of dermal modeling approaches. The spreadsheet includes annotations regarding whether the document provides general information on dermal risk assessment decision making and

frameworks, dermal exposure methods, dermal exposure assessment procedures and considerations, and use of dermal exposure data.

2.3 Assessment Questions and Plan

Based on the rationale and goal of an assessment, the assessor can develop a very specific and attainable goal and an associated hypothesis or question. Consider an example problem formulation output: “This assessment is being conducted in response to a TSCA Section 4 test order for occupational dermal exposure data (i.e., skin loading) for chemical X. Based on initial scoping review of physicochemical properties and process information, the use of this chemical in processing is expected to have some dermal exposure potential during loading and unloading, and mixing, but the magnitude of exposure is not known.”

The key questions of this example assessment are thus:

- What is the external dermal loading dose associated with individual tasks, as well as full-shift tasks, with anticipated dermal exposure potential?
- What is the most effective sampling or model-based assessment method to estimate exposure given chemical properties and facility processes?
- What is the estimated internal dose based on the exposure data?
- How effective is PPE at protecting the workers from dermal exposure?

The problem formulation step should also culminate in a general plan for the assessment to answer the questions and meet the defined goal of the assessment.

3 Exposure Assessment Approaches

3.1 Overarching Tiered Approach to Dermal Exposure Assessment

Following initial problem formulation and data gathering, a dermal exposure assessment plan should be developed if a screening or refined risk assessment is warranted. Consistent with general approaches developed by the American Industrial Hygiene Association (AIHA), it is recommended that dermal exposure assessment methods follow a tiered approach. The early phases of the process include qualitative observations and data gathering to determine where dermal exposure potential is possible and rule out processes and tasks with no (or very limited) dermal exposure potential. This aspect of data collection would have been partially fulfilled in developing a refined problem formulation. Once scenarios/tasks with exposure are identified, screening level approaches may be useful prior to moving to a higher-tier dermal exposure assessment. The following section discusses the general components of a screening as well as refined dermal assessment approach and provides key questions and considerations to help the user determine when one approach is generally preferred.

Deciding whether a refined or screening-level versus refined dermal assessment is appropriate often relates to the need for refined information to have confidence in a risk informed decision. This is impacted by both the hazard and exposure assessments. This can be visualized as the potential margin between the dermal dose that causes adverse effects and the likely upper bound estimate of exposure for the occupational exposure scenario. The larger the margin the more likely a decision can be made with a screening assessment approach versus a more refined assessment.

With regard to exposure, low variability (in concentration and time) within a particular occupational group and exposures that are likely well below any dose of concern (e.g., minimal potential for skin contact) may suggest a screening approach is adequate. In contrast, highly variable exposure estimates within an occupational exposure group, such that high end estimates are close to a dose range of concern suggest the value in a refined assessment (unless one moves directly to risk management phases of the process).

Regarding the hazards of the chemical, availability of well-defined or conservative health benchmarks can support confidence in decisions using screening approaches. In addition, the consequences of not capturing an actual risk are often considered, thus effects that are of lesser overall concern (e.g., mild irritation and readily reversible systemic effects) are more likely to support a screening assessment than assessments related to effects such as reproductive toxicity, systemic toxicity, and direct irreversible skin effects.

Some examples of questions such as the following should be asked that affect confidence in understanding the potential dermal dose and application to the hazard and dose-response information:

1. Is exposure consistent, or does it vary throughout the day, or day to day?
2. Is exposure consistent throughout a work shift, or does it vary task by task?
3. what exposure controls are in place that impact degree and variability in dermal exposure?
4. Is the exposure expected to be sporadic (acute) or routine (chronic)? Should worst-case occupational exposure scenarios be evaluated?
5. What type of dermal exposure is expected? For example, direct contact with the chemical (immersion or splash), incidental (touching surfaces or containers that may be contaminated), vapor to skin deposition.
6. What are the adverse health effects associated with dermal exposure?

7. What level of confidence do we have that the medium, maximum, and 90th percentile exposure can be estimated?
8. Is there an occupational exposure limit or other benchmark to compare to? Can one be derived from existing information?

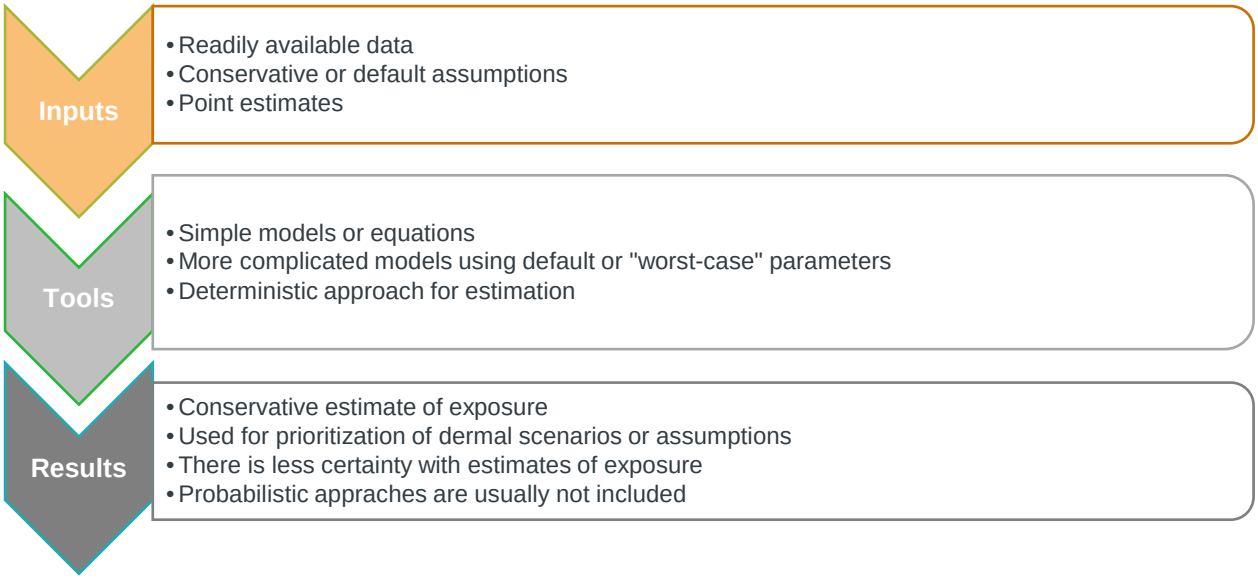
In most cases, direct contact with the chemical in will be unlikely. In many occupational settings, exposure potential is well-controlled, and it is more likely that incidental contact will occur via touching contaminated surfaces or containers, or when spills occur. In the case of responding to EPA TSCA Test orders, even in situations where dermal exposure is limited or unlikely due to the nature of the tasks performed, the use of PPE, and the implementation of closed manufacturing systems and other engineering controls or ventilation, monitoring data is still needed and/or required. As mentioned above, a purpose for performing a dermal assessment may be to show that the PPE and/or engineering controls being used are sufficient for reducing dermal exposures.

The exposure assessment decision framework and checklist tool can be used to determine when screening or refined assessments are more appropriate for the occupational exposure scenario of interest (**Appendix C – Dermal Occupational Hazard and Exposure Checklist**).

3.1.1 Screening Assessment

A screening level dermal exposure assessment may be needed based on the scope of the issue and what information is generated during the problem formulation and associated data gathering. Conservative or default assumptions are often used in a screening assessment to provide an initial conservative estimate of exposure. If it is determined that the exposure and the potential hazards are low or minimal, more advanced dermal exposure assessment may not be needed. If the substance is potentially highly toxic at low doses, a refined exposure assessment may be needed or risk management strategies may be used even if dermal exposures are minimal. There are several tools that can be used to perform a screening level assessment, such as exposure equations or simple modeling tools to identify potential exposure scenarios of concern or to prioritize which occupational scenarios may be of highest concern. Further, if little information is available to evaluate a particular chemical of concern or scenario of concern, read-across data can be used, such as data for a structurally similar compound, or equivalent/similar occupational task. If it is determined that there are insufficient data to assess the potential risk of dermal exposure following the screening level assessment, a data collection strategy may be needed to gather additional data regarding potential workplace exposures.

A summary of the types of inputs, tools, and results expected from a screening level assessment is shown below in Figure 2.



Source: https://www.epa.gov/expobox/exposure-assessment-tools-tiers-and-types-screening-level-and-refined

Figure 2. Schematic of Screening Dermal Exposure Assessment

Various tools exist that can help facilitate screening level assessments. One such tool is the AIHA Dermal Risk Assessment Model (DRAM). This Excel-based screening tool uses information on dermal hazard and exposure to calculate an overall dermal exposure rating. It can be used to prioritize scenarios with the highest potential risk of dermal exposure. The user can either perform a deterministic (single input values) or Monte Carlo type (distribution of input values) of assessment. First, a dermal hazard rating is assigned by a score (1-4) based on the potential for skin or systemic toxicity or skin sensitization. Dermal hazard is based on assigned GHS codes (which can be found on a chemical SDS) as well as toxicity data for the chemical of interest. The more likely a chemical is to cause skin or systemic toxicity or corrosivity and sensitization, and the lower the LD_{50} for a particular chemical, the higher the hazard rating. Next, a dermal exposure rating is assigned based on 5 categories of information (dermal contact area, dermal concentration or loading, dermal contact frequency, dermal retention time, and dermal penetration potential).

The following equation is used to determine the dermal exposure rating:

*Exposure Rating = CA * C * CF * RT * PP*

CA = Dermal Contact Area

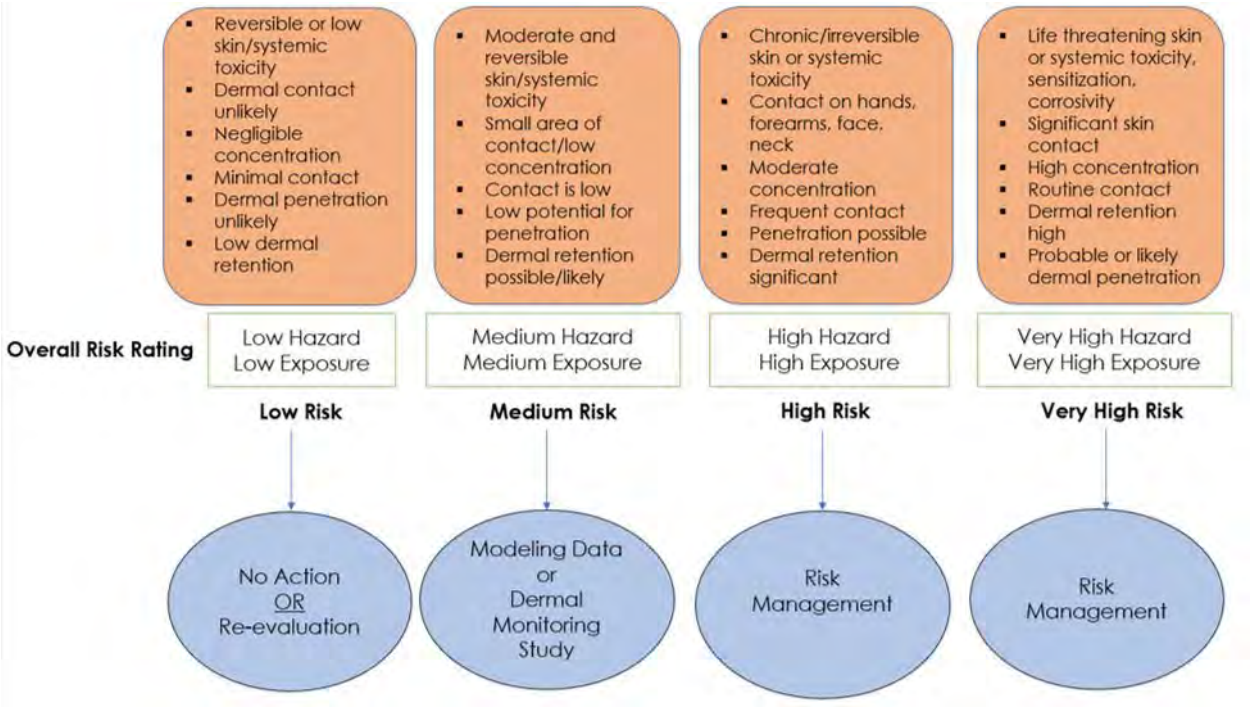
C = Dermal Concentration or Loading

CF = Dermal Contact Frequency

RT = Dermal Retention Time

PP = Dermal Penetration Potential

Most of the exposure ratings are qualitative in nature, and expert judgement may be required when scoring each exposure category in the context of available data and the relevant exposure scenario. Other methods also exist for categorizing and prioritizing hazard and exposure potential, such as occupational exposure banding.

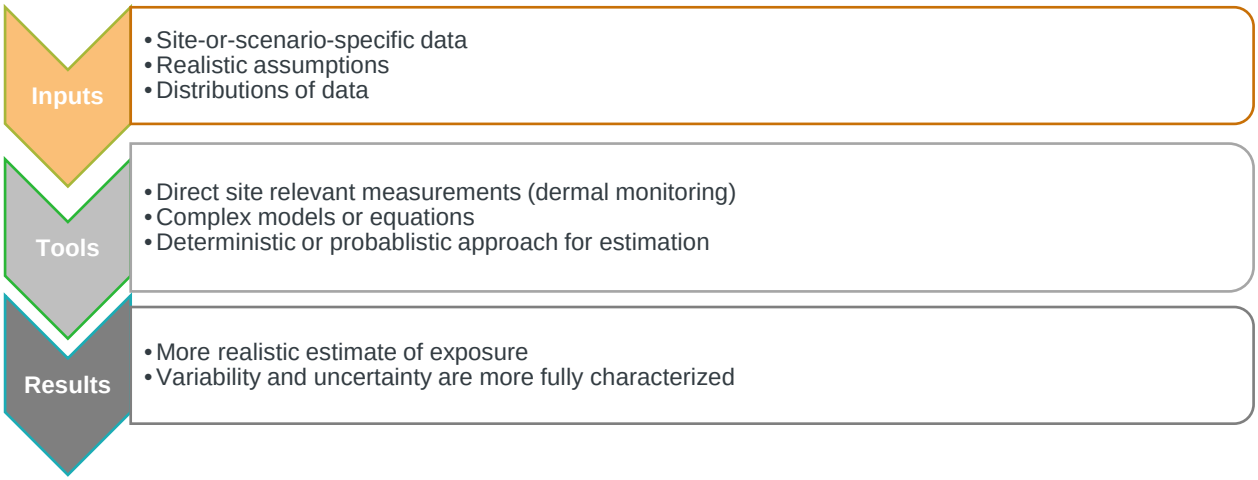


This tool is described in more detail in **Appendix D - Dermal Risk Rating Tool**.

Another useful screening level tool is ECETOC TRA. The ECETOC Targeted Risk Assessment (TRA) tool, with its conservative assumptions and low data requirements, has become a widely used and valuable method for conducting screening-level risk assessments of chemicals under the REACH regulation. By efficiently identifying substances that may need further evaluation, the TRA allows companies and regulators to prioritize resources and streamline the risk assessment process. Its widespread adoption, with over 80% of Chemical Safety Assessments in the first two REACH registration rounds relying on the TRA, highlights its critical role in enabling the screening of numerous chemicals. The TRA's practical approach has been instrumental in facilitating the compilation of Chemical Safety Assessments, making it a crucial tool for the successful implementation of REACH. Further information on this tool can be found in Appendix F.

3.1.2 Refined Assessment

A refined assessment should be performed given several different outcomes. First, if sufficient information is known just based on hazard information and the anticipated exposure scenario to definitively conclude a high probability for concern for health risk from dermal exposure, one may proceed directly to performing a refined assessment (Figure 1). Additionally, if a screening approach is conducted and suggests that the risk is uncertain, it is also recommended that a refined assessment be performed. In either case a screening assessment or refined assessment with more complete exposure assessments may be needed. If existing exposure data are not adequate for the scope of the assessment, a data collection strategy (whether modeled or empirical data or both) should be implemented. It should be noted that if insufficient data for the compound of interest is available to conduct modeling, but sufficient data is available for a structurally similar compound, a read-across approach can be used to estimate exposure. A refined exposure assessment will incorporate similar steps to the screening level assessment; however, a higher level of granularity will be required. There are also additional steps to evaluate IH data and conduct a dose response in order to enable a quantitative risk characterization that compares exposure estimates to a dermal occupational exposure benchmark (such as an OEL) or acceptable surface limit, if available. If a benchmark is unavailable, one may need to be developed; however, this process is not covered in this framework. Refer to Section 3.4.2. for more information on empirical data collection.



Source: https://www.epa.gov/expobox/exposure-assessment-tools-tiers-and-types-screening-level-and-refined

Figure 3. Schematic of Refined Dermal Exposure Assessment

3.2 Descriptive Workplace Assessment

A descriptive assessment of occupational processes and overall workflow allows one to document and collect information to develop SEGs and to guide the sampling strategy, if one is needed (i.e., where and to what extent dermal sampling is needed, to estimate exposure). Facility observations are critical to understanding and prioritizing occupational exposure scenarios with the greatest potential for dermal exposure, and thus guide where empirical monitoring should be performed. A primary goal of the qualitative process assessment is to exclude from further analysis the tasks that have no or minimal dermal exposure potential. For example, tasks associated with closed systems (process systems with equipment designed and operated such that the product is not exposed to the built environment; tasks that involve chemical handling that has hazards that limit potential skin contact - such as burns from heated liquids, etc.) will be excluded from further assessment. The information generated from this assessment can be used to define similar exposure groups (or SEGs), which is discussed in Section 3.3. This assessment should review operations at member facilities via informational interviews and facility observation to assess, collate and document:

- Task descriptions and duration of each task and existing task hazard analyses and operational standard operating procedures;
- Concentrations of chemicals in raw materials/formulations or products potentially; handled by workers, and bulk sampling data;
- Descriptions of exposure controls including PPE;
- Direct observations of exposure potential based on presence of the chemical for each process or handling task;
- Review of existing occupational monitoring data.

Appendix C outlines a dermal occupational hazard and exposure checklist that can be used to determine the potential for dermal risk in a particular facility and for the identified exposure scenario. It is meant to help prioritize tasks with the most exposure potential.

3.3 Development of Similar Exposure Groups (SEGs)

After conducting a descriptive workplace assessment, the information collected during this process will be used to identify similar exposure groups (SEGs) within the workplace(s) of interest. SEGs are groups of workers with the same general exposure potential based on the similarity of tasks they perform, the materials and processes with which they work, and the frequency and duration of their tasks. The workers in the SEG have a distribution of exposures which is often referred to as the exposure profile for the SEG. An OEHS professional should evaluate all relevant information from the descriptive workplace assessment and determine what factors to include to evaluate exposure potential. SEGs may be described by specific process(es), jobs, tasks, and chemicals involved among other factors. SEGs are a tool that allows OEHS professionals to target sampling efforts to characterize risk and make management decisions for larger groups of workers. The exposure profile for all members of a SEG are anticipated to experience a similar average exposure concentration and exposure distribution for the defined situation.

A more comprehensive identification of SEGs is needed if performing a refined exposure assessment. Recommended procedures for developing SEGs have been described by AIHA technical committees on exposure assessment (Jahn et al., 2015). Forms that can be used in the development of SEGs can be found in **Appendix E – SEG Development Forms**.

3.3.1 How are SEGs created?

A qualified Occupational Health and Safety (OEHS) professional determines SEGs by categorizing the employees believed to experience similar chemical or physical exposures based on the operational and process information reviewed about the workplace, workforce, and chemicals used. There is more than one right way to form SEGs, but it is important to establish a systematic approach to assessing information during formation. An observational approach, sampling approach, or a combination of both may be used to establish SEGs. The observational approach typically consists of a review of qualitative information from a workplace, after which an OEHS professional completes a basic characterization, splitting a generic workplace into discrete processes and jobs, then further into specific tasks. If quantitative exposure monitoring data is available, a sampling approach is preferred to assign workers to SEGs based on statistical analysis of the exposure data.

3.3.2 What determinants are considered when developing SEGs?

There are numerous determinants that may be considered when developing SEGs, however, only a handful may be needed to describe a unique SEG. These may include job classification, assignment, craft, or title; location or department; task or equipment assignment(s); input materials, byproducts, or products; process container, batch, or lot; ambient air concentrations.

When developing SEGs, it is important to interview workers and supervisors who are closely involved with the process(es) to understand any factors that may cause misclassification such as discrepancies in tasks, frequency of tasks, materials, processes, and how the work is performed.

3.3.3 Why form SEGs? How are SEGs used?

Developing an understanding of significant sources of exposure in a process and ways in which workers interact with these sources is a key step in exposure characterization. SEGs enable the OEHS professional to assess groups of workers at once rather than all individuals and tasks separately; therefore, reasonably saving time and effort and maximizing use of resources on those SEGs anticipated to experience the highest exposures. It is particularly useful to develop SEGs to focus on the task level so that gathered qualitative information can inform a greater understanding of points of potential exposure and the relevant exposure pathway. Additionally, understanding exposure potential, task frequency, and task duration for an SEG allows for comparison of sampling data to the appropriate health benchmark values, if they exist.

When applying the SEG methodology to develop exposure estimates, one must consider their intended use. Generally, SEGs are relatively granular and intend to define representative exposures over a relatively narrow set of exposure conditions. For example, a typical SEG is based on a single process unit or department and type of work performed (e.g., operator). While this is generally true, the OEHS professional should observe the process and interview relevant workers to determine if there are any other factors that could impact exposure potential. This level of specificity enables the IH to assess whether the facility needs customized exposure control and risk mitigation techniques (risk management) for a well-defined occupational exposure scenario(s). However, some assessments may cover chemical use and exposure across many departments, facilities, or even industrial sectors. An example of this broader definition of representative exposures is reflected in some occupational risk assessments for chemical registration regulations (e.g., EU REACH and EPA TSCA). Thus, a key consideration is documenting the intent of the assessment, the likelihood that it involves consolidating diverse data, and implications of the data analytics on the risk-informed decision process. Either the refined SEG or broad use approach can support decision making but the interpretation and application of the exposure estimations are likely to be different (e.g., for screening-level versus risk management decisions).

3.3.4 How can SEGs be applied across locations?

Location is one of many determinants that can be used to characterize an SEG, however, when there are similarities across locations, SEGs applicable industry-wide may be developed. Industries that have common processes, use similar or the same standard operating procedures, and have the same controls in place may be anticipated to have similar exposure profiles present across their locations. For example, a company may have 4 facilities across the country that creates that same product. An equipment operator at facility 1 would be anticipated to experience the same exposure profile as an operator at facility 2,3, and 4, so one equipment operator SEG industry-wide may be appropriate. The OEHS professional should evaluate all sites to determine if there are differences between site and select the site that would result in the worst-case exposure potential. Once a full sampling campaign has been conducted at that site, additional sampling could be conducted at the additional sites to confirm similar exposure profiles. The information needed for SEG development is shown below in Table 1.

Table 1. Information Needed for SEG Development

Job-specific or task-specific information	Process-specific information	Hazard-specific information
▪ Job classification ▪ Department ▪ Location ▪ Task duration ▪ Task frequency ▪ Task description	▪ Flow rate of process ▪ Engineering controls ▪ PPE ▪ Administration controls ▪ Weight fraction of chemical in process material	▪ Hazard description ▪ Potential exposure pathway

List of Key Resources for SEG Development:

- Job hazard analysis (JHA) program documentation
- Direct reading data
- Area monitoring data
- IH data
- Process flow diagrams
- Process safety management (PSM) program documentation
- Process standards or standard operating procedures (SOPs) for operations/maintenance
- Process hazard analysis documentation
- Engineering or purchasing records
- Government reporting submissions (e.g., U.S. EPA SARA reports)

SEG Resources

1. Jahn, S. D., Bullock, W. H., & Ignacio, J. S. (Eds.). (2015). A strategy for assessing and managing occupational exposures. Fairfax, VA: American Industrial Hygiene Association (AIHA). Chapter 4: Establishing Similar Exposure Groups.

2. Anna, D. H. (Ed.). (2011). The occupational environment: its evaluation, control and management. American Industrial Hygiene Association (AIHA). Chapter 9: Comprehensive Exposure Assessment.
3. Spear J.E. Industrial Hygiene Exposure Assessments, “Worst-Case” versus random sampling. Professional Safety, August 2005. Available from https://aeasseincludes.assp.org/professionalsafety/pastissues/050/08/030805as.pdf.
4. Stewart, P., & Stenzel, M. (2000). Exposure assessment in the occupational setting. Applied occupational and environmental hygiene, 15(5), 435-444.
5. Martha Waters, Lauralynn McKernan, Andrew Maier, Michael Jayjock, Val Schaeffer & Lisa Brosseau (2015) Exposure Estimation and Interpretation of Occupational Risk: Enhanced Information for the Occupational Risk Manager, Journal of Occupational and Environmental Hygiene, 12:sup1, S99-S111, DOI: 10.1080/15459624.2015.1084421.

3.4 Qualitative and Quantitative Estimations of Exposure

If the risk assessor determines that the data are not adequate to determine potential for risk after performing a screening-level assessment, development of a data collection strategy is needed. Data collection can occur using either empirical or modeled data, and sometimes a combination of the two methodologies. Numerous considerations are required before deciding whether modeling or empirical data collection is the most appropriate approach for dermal exposure estimation. Considerations such as the availability of a validated analytical method and the utility of modeling for the chemical and OES (e.g., strengths and limitations of various models, availability of data inputs for the models). Furthermore, the best approach in the end may be a combination of both approaches – e.g., dermal modeling validated by, or compared to, empirical data. Generally, measured data are preferred over modeled data, but the assessors must take care to interpret dermal monitoring data. Another consideration is that empirical dermal monitoring data may be available for a read-across compound, and such data could be used to extrapolate to other chemicals or occupational exposure scenario. Additional information regarding how to use existing data for a read-across evaluation can be found in Franken, et al. 2020.

For the tasks with the highest exposure potential (i.e., significant presence of the chemical on work surfaces, or low threshold for hazard), as identified by the screening or refined evaluation, there are two options for proceeding to the quantitative exposure estimate:

1. Provide the associated SEG and workflow information (e.g., task duration, frequency) to inform input of modeling. The information is expected to be an improvement over worst-case, default assumptions.
2. Initiate dermal exposure method development and validation efforts and conduct more refined dermal sampling of the high-exposure potential tasks.

This section is intended as a general guide to assist in providing guidance and key considerations needed when selecting qualitative or quantitative dermal modeling tools, or when developing a plan to collect empirical data. It is not meant to provide specific recommendations regarding which tool or procedure to use. However, the below components, at minimum, should be addressed when performing dermal modeling and/or conducting empirical data collection.

3.4.1 Model Selection

Exposure models may be useful for estimating exposure when empirical data are limited or absent. However, the number of validated dermal models is limited. While some models are qualitative in nature and provide exposure estimates in the form of exposure banding or exposure distribution percentiles. Others are qualitative in nature and provide estimates external or internal exposure doses. Available models represent a spectrum regarding ease of use, level of detail regarding inputs and outputs,

knowledge required to operate or use the model, and nature of the output values. Some models can generate a result with as few as three input parameters, while other models may require extensive input to build a repository of parameters that the modeling program uses to create predictive scenarios. Each model is highly situational, must be understood thoroughly, and paired with the appropriate use scenario to provide informative outputs. Pairing models with inappropriate OES will not provide meaningful data.

“Model” can be a misleading term, some “models” would more accurately be described as calculators. Rather than helping the user generate a conclusion based on input parameters, they simply transform input datapoints into different datapoints. For example, the NIOSH finite dose model inputs molecular weight of a compound, water octanol coefficient, and melting/boiling points, and calculates a steady state permeability coefficient for the given inputs. The permeability coefficient is effectively a transformed data point that the user can then use when drawing conclusions about risks or hazards. Conversely, some models use input parameters to provide a conclusion that ranks a set of parameters or outputs into categories such as a scenario as high or low risk.

Models used in dermal exposure assessment can be categorized based on two main criteria: the underlying approach (mechanistic or empirical) and the nature of the output (deterministic or probabilistic). Mechanistic models are built on mathematical equations that describe the mass balance and physical processes involved in the exposure scenario. Empirical models, on the other hand, rely on a set of rules or relationships derived from observations or experimental data to generate their output. Deterministic models provide a single, fixed output value for a given set of input parameters. In contrast, probabilistic (or stochastic) models incorporate variability and uncertainty by representing the input variables and the output as statistical distributions. Further information about commonly used chemical-specific parameters and operation/process specific parameters is described below.

Generally, models may generate estimates of exposure, however, the usefulness of the data can vary and the accuracy or robustness of outputs is reflective of accuracy and robustness of inputs. The accuracy and reliability of exposure models are influenced by two main factors: variability and uncertainty. Variability refers to the inherent differences in exposure levels from day to day, even when the exposure conditions remain the same. Uncertainty, on the other hand, arises from the lack of precise knowledge about the true value of a specific exposure parameter. Although both variability and uncertainty can affect the model's output in similar ways, it is essential to differentiate between them. Uncertainty can be reduced by collecting more data and improving our understanding of the exposure scenario, whereas variability is an intrinsic property of the system and can only be minimized by altering the way the substance is used or handled.

While certain models have been validated or designed using empirical data, some instead use simple equations to generate data. Each model will be optimized when input parameters cannot be improved further and will draw more meaningful conclusions with more complete inputs. The selected model ideally should be peer-reviewed and validated and should align with current industrial practices. However, there is no preferred or standardized model selected for use in dermal exposure modeling. A summary of some available models that can be used to estimate dermal exposure potential can be found in **Appendix F – Dermal Modeling Tools**.

3.4.1.1 List of Peer-Reviewed and/or Validated Models

Of the validated models reviewed, the three models in the table represent the most useful for a particular scenario.

Stoffenmanager is capable of creating and storing a very comprehensive inventory of chemicals and scenarios that can be reconfigured to assess different combinations of agents and tasks. Additionally, it also requires the user to pay fees to fully access the tool. ChemSTEER provides the most rigorous assessment of dermal exposures, however, has a higher barrier of entry and requires the most extensive input. However, it is limited in scope and unable to be used for more complicated exposure scenarios.

IH SkinPerm is a spreadsheet-based model for estimating dermal absorption of chemicals. It uses physicochemical properties such as molecular weight, octanol/water partition coefficient, vapor pressure, and water solubility to predict the permeation and absorption of a substance through the skin. The model considers various exposure scenarios, including instantaneous deposition, deposition over time, vapor exposure, and absorption from aqueous solutions. It accounts for the transport of chemicals through the stratum corneum and into the blood, as well as evaporation from the skin surface. The model employs a set of differential equations to calculate the mass of the substance on the skin surface, in the stratum corneum, and the amount absorbed into the blood over time. IH SkinPerm provides a user-friendly interface for inputting exposure scenarios and substance properties, and generates a detailed report with graphical representations of the absorption process (IH Skin Perm 2017). By using IH SkinPerm, assessors can account for the incomplete dermal uptake of a substance, which may be dose-dependent. This means that the fraction of the substance absorbed through the skin may vary depending on the applied dose. IH SkinPerm can help to quantify this dose-dependent absorption, providing a more refined estimate of the systemic dose resulting from dermal exposure. Incorporating the dermal absorption estimates from IH SkinPerm into the overall exposure assessment can lead to a more accurate comparison with the systemic dose derived from inhalation exposure.

ConsExpo is a validated model that can be used to estimate dermal exposure to chemicals from consumer products. It considers product composition, use patterns, and skin permeability. However, it may not be appropriate or applicable to occupational exposure scenarios. An overview of these four modeling tools is provided in Table 2.

Table 2. Overview of Key Peer-Reviewed and/or Validated Models

Model Name	Brief Overview	Key Takeaway
Stoffenmanager	A web-based tool available for a fee that consists of several modules including a control banding section (qualitative dermal and inhalation).	Stoffenmanager allows for the most comprehensive exposure/scenario inventory creation for assessment of large-scale operations, though analysis for dermal exposures is less thorough than ChemSTEER.
ChemSTEER	An interactive downloadable application that generates screening level estimated for environmental release of and worker exposure to chemicals in industrial settings.	Most thorough and developed tool for dermal assessment, contains the most models, and covers the most input parameters. However, requires the most data gathered during problem formulation stage, leading to a higher barrier of entry.
IH SkinPerm	Estimates absorption from as a result of different occupational exposure scenarios (such as instantaneous deposition, deposition over time, or from airborne vapors).	While more of a calculator than a model, this very easy to use tool can provide outputs directly comparable to OELs for risk assessment purposes. Lower barrier of entry, but less comprehensive than ChemSTEER.
ConsExpo	ConsExpo is a validated model and web-based tool developed by the Dutch National Institute for Public Health and the Environment (RIVM) that can be	ConsExpo provides a comprehensive and reliable framework for estimating realistic consumer dermal exposures,

	used to estimate dermal exposure to chemicals from consumer products, considering various factors such as product composition, use patterns, and skin permeability.	making it a valuable tool widely accepted by regulatory agencies and risk assessors for dermal exposure assessments, although it may require more detailed input data compared to simpler screening-level tools.

3.4.1.2 Modeling Inputs and Outputs

Chemical-Specific Parameters

- Substance Information (IUPAC name, CAS Number, molecular weight, vapor pressure, solubility, viscosity, K_{ow}, biodegradability)
- Weight fraction of chemical
- Concentration of chemical in mixture or article handled
- Fractional absorption
- Skin loading or transfer efficiency (from surface or textile to skin)
    - Can be found in empirical data sources – typically measured in an amount of chemical loaded per unit of surface area of skin or per event
    - Loading can vary based on type of exposure scenario (e.g., splash vs. immersion) or chemical form (e.g., liquid vs. solid)
- Maximum skin adherence

Operation or Process Specific-Parameters

- Operation Parameters
- Operations (sources/activities, site information)
- Dermal loading per event/activity
- Affected skin area (e.g., hands, face, neck, forearms based on task/process)
- Frequency of contact (events/day)
- Exposure duration
- Influence of PPE (clothing or gloves)

Example: Dermal Exposure Inputs used by ChemSTEER

- Task Duration

ChemSTEER models do not include default task-based durations. For models with daily durations, ChemSTEER defaults to an 8-hour workday. In the EPA OPPTS 2-hand model as applied under TSCA, task duration is not included, and the assumption is that there is one event/day, essentially equivalent to an “infinite dose” scenario when applied to an occluded exposure (i.e., under gloves).

- Adherence of Solids to Skin

ChemSTEER worker dermal exposure models include a parameter reflecting the amount of solids adhering to skin after dermal contact, which is calculated as the surface area of contact (S; cm^2) *

quantity remaining on the skin (Qu; mg/cm^2-event). As such, the units for this parameter are provided in mg/event. As a parameter, adherence of solids to skin (provided in mass/cm^2 as shown above) is most directly analogous to the ChemSTEER parameter Qu; however, the ChemSTEER user guide does not provide the specific values of Qu that are used to derive its default values for the amount of solids adhering to skin.

The EPA/ OPPT Direct 2-Hand Dermal Contact with Solids Model uses a default value of 3,100 mg/event to represent the total amount of solids remaining on hands after a variety of activities, including loading and unloading of solids into transport containers/ vessels, cleaning solid residuals from transport containers/ vessels, and sampling solids (ChemSTEER User Guide, 2015, p. 264).

The EPA/OPPT 2-Hand Contact with Container Surfaces Model uses a default value of 1,100 mg/event to represent the total amount of solids remaining on hands after contact with a container surface (ChemSTEER User Guide, 2015, p. 264).

- Qu and Film Thickness on the Skin

As discussed in the separate dermal modeling section, ChemSTEER provides default models for calculating worker dermal exposure to a liquid chemical based on different use scenarios by incorporating the following parameters: surface area of contact (cm^2), quantity remaining on skin (mg/cm^2-event), weight fraction of chemical in the liquid (unitless), and frequency of events (events/worker-day). The surface area of contact can be based on one hand or two hands (535 cm^2 or 1070 cm^2, respectively). The defaults for the amount retained on the skin, or Qu (mg/cm^2) (0.7 mg/cm^2 for the low end and 2.1 mg/cm^2 for the high-end) appears to be based on Cinalli et al. (1992), described above. In several EPA risk evaluations for existing chemicals (namely, the chlorinated liquids), the central tendency value, 1.4 mg/cm^2, was applied instead of the low-end Qu value.

Model Outputs

IH SkinPerm, Stoffenmanager, and ChemSTEER are three distinct models used to assess dermal exposure to chemicals, each with different input parameters and modeling approaches. While Stoffenmanager and ChemSTEER primarily rely on external measurements of exposure, such as the concentration of the chemical in the air or on surfaces, IH SkinPerm differentiates itself by focusing on the internal dose of a chemical based on dermal exposure. This unique feature of IH SkinPerm allows for a more comprehensive understanding of the potential health risks associated with dermal exposure, as it considers the absorption and distribution of the chemical within the body, rather than solely relying on external exposure measurements. The model output is important when considering comparison to occupational exposure limits, as these typically are related to external dose (rather than internal exposure), and therefore, may not be directly comparable.

3.4.1.3 Key Resources for Model Selection

1. U.S. EPA. Guidance on the Development, Evaluation, and Application of Environmental Models. Office of the Science Advisor, Council for Regulatory Environmental Modeling. March 2009.

3.4.2 Empirical Data Collection

If empirical data are lacking, the modeling data indicate a potential risk, or are not sufficient to evaluate dermal exposure with sufficient confidence using existing models, it may be necessary to collect empirical data in a representative worker population. The following sections will outline the considerations and components needed to a) develop and validate a robust dermal measurement methodology and protocol, b) outline potential data collection protocols (refer to Appendix I), and c) describe how to conduct in-field sampling of representative worker populations. The following are key questions that should be answered prior to deciding upon an empirical data collection strategy:

1. What is the anticipated exposure pathway (e.g., direct contact with the chemical or immersion, deposition onto skin, uptake of vapor, or contact with contaminated surfaces (transfer)?
2. Is there a published dermal sampling method for the chemical of interest, or a structurally similar chemical relevant to the exposure pathway?
3. If no published method exists, are there peer-reviewed published studies in which dermal sampling was performed for the chemical of interest (or a structurally similar compound)? (e.g., a field validation dermal sampling study in an occupational setting)

A target detection level should be determined prior to developing the analytical method, which will likely be informed by toxicological data and availability of OELs. Further, it should be considered whether dermal sampling should be paired with biological sample collection (e.g., blood, urine, or saliva) and analysis of biomarkers to assess internal dose.

3.4.2.1 Sampling Protocol Design

A clear research question and study objective(s) are necessary to determine sampling protocol design. All information gathered during problem formulation and any preliminary screening assessments should be used to inform the study objectives. For example, the chemical of interest, physical/chemical properties, occupational population characteristics, and tasks which represent the highest exposure potential should influence the study design. The objective should be informed by key hazard, health, and exposure information gathered during problem formulation, hazard assessment, exposure potential, or from work process evaluations. These types of sampling study designs may be considered:

1. A pilot or exploratory study in which a small subset of workers is sampled in order to evaluate potential for exposure. A more robust follow-up study may be needed to validate preliminary data.
2. A dermal or surface sampling study to validate an existing analytical method – the study protocol may already be published, but its applicability to the facility, exposure scenario, or chemical(s) may require in-field validation.
3. A full sampling campaign to understand dermal exposure across all workers within SEGs at a particular site, or multiple sites within the same industry.

Sampling Methods

Empirical data collection will involve in-field sampling of representative worker populations or sampling of work surfaces to which workers are anticipated or expected to come into contact with. Field-sampling may involve collection of surface, clothing (e.g., gloves or work clothing), or dermal samples. Various sampling methods involve the direct or indirect measurement of the potential dermal exposure of chemicals through different routes, such as direct contact with the chemical or immersion, deposition onto skin, uptake of vapor, or contact with contaminated surfaces (transfer). These data will be compared to an appropriate health-based dermal exposure benchmark, acceptable surface limit, or applied as “presence or absence” indicators to include or exclude a task from further assessment. Derivation of benchmarks are described below in the risk characterization, Section 4.

Numerous dermal sampling methods exist and are summarized below in Table 3. These methods primarily serve to provide information on the potential for dermal exposure, as measuring via an external dose. They may not be appropriate for assessing effectiveness of PPE or other controls, or for identification of the source of exposure. Additionally, these data will not provide an internal dose; thus, data on absorption may be necessary to estimate internal exposure doses. If dermal absorption data are not available or very limited, it may be necessary to use a modeling program to estimate the potential for dermal absorption. Refer to Table 2 for additional information regarding dermal absorption models, additional information can also be found in Appendix F. There are several ways to determine internal dose, such as through biomonitoring, but these such methods are beyond the scope of this framework.

Removal methods, such as wipe or tape stripping methods, typically remove a portion of the total mass of a contaminant or chemical that exist on the skin surface. A rinse method or UV fluorescent tracer method can measure the mass in the skin contaminant layer (as defined by Schneider et al. 1999). In some instances, it may be relevant to measure deposition from air to skin (e.g., charcoal cloth or silicone wristband) or transfer (using surrogate skin methods, such as pads or gloves). Additional considerations when choosing a sampling method can be found in Table 3.

Table 3. Summary of Select Dermal Sampling Methods

Sample Collection Method	Procedure Type	Exposure Type	Sampled Location	Description	Applicable Chemicals	Method Sampling Efficiency	Advantages	Disadvantages	References
Rinse Method	Removal	Air to Skin Direct Contact Surface to Skin	Skin	Exposed skin is rinsed with solvents	Lead; Pesticides	40-90%	A commonly used dermal sampling method assesses mass in the skin contaminant layer	May underestimate exposure due to absorption and removal efficiency	EPA 1992; Benford 1999; Van-Wendel-de-Joode et al. 2005
Wipe Method	Removal	Air to Skin Direct Contact Surface to Skin	Skin or Surface	Wipes soaked or impregnated with solvents used to wipe the skin or work surface	Flame Retardants; Lead; Pesticides	36-104% (median 51%)	A commonly used dermal sampling method	May underestimate exposure due to absorption and removal efficiency	EPA 1992; Van-Wendel-de-Joode et al. 2005; Brouwer 2000
Vacuum Method	Removal	Air to Skin	Skin	A vacuum is used to remove dust particles from the skin and collect them on a filter cassette	Pesticides	40-90% (<100%)	Non-invasive Simple construction	Difficult to deposit collected dust from the sampler to the filter for analysis; not a common method	Lundgren et al. 2006; Creek & Ashley 2014
Tape Stripping Method	Removal	Direct Contact Air to Skin	Skin or Surface	Adhesive tape used to remove residues from the outermost layer of skin or surface and the amount estimated by gravimetric procedures	Unspecified	Not available	Non-invasive Measures particle deposition	May underestimate exposure due to absorption and removal efficiency Might not work certain parts of the body	Benford 1999; EPA 1992; Van-Wendel-de-Joode et al. 2005; Lundgren et al. 2006; Lademann 2009
Patch/Pad Method	Collection Interception Transfer	Air to Skin	Skin or Clothing	Patch or pad placed on skin or clothing to collect chemical of interest	Pesticides, solvents, volatile compounds	>95% needed to be acceptable	Non-invasive Can measure deposition onto skin	Tend to overestimate exposure because they bind to receptor materials (activated charcoal) Does not differentiate between air deposition or liquid splashes	Benford 1999; EPA 1992; Van-Wendel-de-Joode et al. 2005; Soutar 2000
Glove Method	Collection Interception Surrogate Skin	Direct Contact Surface to Skin	Skin or Clothing	Absorbent or cotton gloves collect contaminants that come in contact with hands	Pesticides	Not well studied	Minimization of chemical-skin contact	Tend to overestimate exposure because they bind to receptor materials (cotton) Breakthrough is common	EPA 1992; Van-Wendel-de-Joode et al. 2005; Cherrie et al., 2004
Silicone Wristbands	Interception	Air to Skin	Skin	Silicone wristbands are placed on the wrist and passively absorb chemicals the individual is exposed to. Aerosolized and volatile compounds as well as physical contact with contaminants will permeate the wristband	Flame retardants, PCBs, EDCs, PAH pesticides, (S)VOCs	Extraction efficiency: >96%	Non-invasive Individual exposure Wide array of chemicals Relatively inexpensive	Skin compounds are absorbed and need to separate from chemical exposure Does not differentiate origin of exposure (ex: volatile vs physical contact with compound) Can be "oversaturated" which ends sampling and does not represent the exposure period	O'Connell 2014; Anderson 2017; Wang 2019
Whole Body Dosimetry	Collection Interception	Air to Skin	Clothing	Use clothing to trap contaminants	Pesticides	Lower than patch method	Larger surface area compared to patches	Difficult to extract residues	EPA 1992; Soutar 2000; Lee et al., 2018
Fluorescent Tracers	Tracer compound added to "agricultural spray mix" or compound being evaluated	Air to Skin Direct Contact Surface to Skin	Clothing or Skin	Use fluorescent tracer on compound to identify/quantify how it contacts the skin	Pesticides (agricultural work specifically)		Tracers strongly bind to skin Assess the non-uniformity of exposure	May overestimate exposure due to reduction of loss from skin through evaporation or washing Not able to differentiate between skin contaminant layer and SC	Benford 1999; EPA 1992; Van-Wendel-de-Joode et al. 2005; Fenske et al., 1985

Sample Collection Method	Procedure Type	Exposure Type	Sampled Location	Description	Applicable Chemicals	Method Sampling Efficiency	Advantages	Disadvantages	References
Fourier Transform infrared spectrometry (FTIR)	In situ method	Air to Skin Direct Contact Surface to Skin	Skin	Laboratory procedure analyzing infrared spectra different from skin from compounds with unique chemical moieties	Pesticides, Isocyanates (VOCs)	More volatile compounds are lost in analysis	Rapidly identifies and quantifies pesticide residue on skin *in vivo* Good for optically dense materials like lubricants, pastes, or food products	Suffers from variable background changes in the infrared absorption spectra of skin	Boeniger 2015; Yost & Fenske 2015

Key Considerations to Inform Study Design

- Who should be sampled?
  - > Determine the population of interest
  - > Use a determination of similar exposure groups (SEG) to identify worker populations with the highest risk
- Location of body to be sampled
  - > Need to understand exposure potential (splash vs. touching contaminated surface) which will influence where exposure might occur
- Timing of sampling
  - > A baseline concentration might need to be established, such as pre-shift sample, or a sample collected after hand washing prior to beginning a task
  - > Consider when sampling should occur (e.g., mid-shift or post-shift)
  - > How many days of sampling are needed to establish an appropriate determination of exposure mean and range?
- Who will perform the sampling?
  - > An external IH professional/researcher
  - > Internal IH or safety professional
  - > Self-collection by workers with supervision by a researcher or IH professional
- Protocol specifics
  - > Select the sampling method based on chemical of interest, whether the exposure route is anticipated to be via direct contact, or occur via deposition onto skin, or from contact with contaminated surfaces, clothing, or gloves
  - > Consider the location on the body where skin should be sampled
  - > A throughout review of peer-reviewed literature to identify studies in which dermal sampling has been conducted for the chemical or scenario of interest
  - > Reduce and prevent contamination (e.g., researchers should wear gloves during collection)
  - > Consider incompatibilities between chemical of interest and sampling procedure (e.g., solvents used)
  - > Will any environmental conditions impact sample collection (e.g., temperature, relative humidity, etc.)
  - > Are there any procedures that need to be standardized? For example, use of uniform pressure or wiping procedure.
- Collection of worker-specific behavioral and medical information
  - > Any personal data collected should be securely maintained, and personal identification removed
  - > A questionnaire may be used to collect data on job title, common job tasks, task duration and frequency, housekeeping procedures, use of PPE such as gloves and changeout procedures, as well as handwashing behaviors
- How will the data be used?

- How will the results be communicated to employees?

Appendix H – Empirical Data Collection Sheet is a dermal data collection sheet that provides relevant information categories when performing empirical data collection.

3.4.2.2 Other Considerations

There may be factors that can influence potential for dermal exposure that will not be measured in a dermal sampling study. For example, chemical absorption into the skin can be influenced by skin condition, environmental conditions (such as humidity), the physical/chemical properties of the chemical, worker personal hygiene practices, use of protective clothing, and other workplace conditions (Drexler, 2003; Grandjean et al., 1988). Dermal absorption data can be found within skin notation documentation and also within the peer-reviewed literature.

Note that, even with additional well-validated dermal wipe sampling data and empirical absorption information, translating data on mass loading, deposition, or transfer to skin into estimates of internal dose still require calculations that will involve some level of uncertainty stemming from a number of factors, including but not limited to the representativeness of experimental conditions in absorption studies (e.g., duration of exposure and the concentration of chemical used (de Sandt et al. 2007). Further, estimates of internal dose will need to be compared to toxicologically relevant endpoints and dermal or surface limits, if available. Please see Risk Characterization Section 4.1.4 regarding a discussion of dermal OELs.

In the absence of an occupational exposure limit (short term or long-term), it can be challenging to understand how the dermal data should be used or interpreted. In some cases, it may only be necessary to understand if a worker population has the potential for exposure, and the study only needs to show the presence or absence of a hazard. However, in the cases where quantitative data is required (such as for TSCA compliance), it may be necessary to develop an OEL for comparison, or a health benchmark to compare to.

3.4.2.3 Key Resources

1. EPA. 2007a. A Literature Review of Wipe Sampling Methods for Chemical Warfare Agents and Toxic Industrial Chemicals. EPA/600/R-11/079. January 2007.
2. EPA. 2007b. Dermal Exposure Assessment: A Summary of EPA Approaches. National Center for Environmental Assessment, Office of Research and Development. EPA 600/R-07/040F. September 2007.
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5. Standard Practice for Field Collection of Organic Compounds from Surfaces Using Wipe Sampling, American Society for Testing and Materials, West Conshohocken, Pennsylvania, ATSM International, D6661-10.
6. Surface Analysis Using Wipes for the Determination of Nitrogen Mustard Degradation Products by Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS), Sampling and Analytical Procedure for Analysis of Surfaces using Wipes Revision 2, EPA and NIOSH, 2011.
7. Code of Federal Regulations, 40 CFR Part 136, Appendix B. Definition and Procedure for the Determination of the Method Detection Limit – Revision 1.11.

8. Standard Practices for Preparation of Sample Containers and for Preservation of Organic Constituents, American Society for Testing and Materials, Philadelphia. ASTM Annual Book of Standards, Part 31, D3694-78.
9. OECD. 1997. Series on Testing and Assessment No. 9: Guidance Document for the Conduct of Studies of Occupational Exposure to Pesticides During Agricultural Application. OECD /GD(97)148.
10. OECD. 1999. GLP Consensus Document: QUALITY ASSURANCE AND GLP; Number 4 (revised). OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring. Paris, 1999.
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12. Surface samples – NIOSH Method 1902

Published Analytical/Sampling Methods

Dermal Sampling Guidance Documents

1. OECD. (1997). Organisation for Economic Co-operation and Development; Guidance document for the conduct of occupational exposure to pesticides during agricultural application; OECD Environmental and Safety Publications, Series on Testing and Assessment no. 9, OECD/GD (97) 148, Paris, France.
2. US EPA. (1986). Pesticide assessment guidelines, subdivision U: applicator exposure monitoring: PB87-133286/EPA/540/9–87/127. Washington, DC: US Environmental Protection Agency.
3. ISO. (2011). ISO/TR 14294:2011 Workplace atmospheres—Measurement of dermal exposure—Principles and methods. International Organisation for Standardisation. London, UK: BSI.

Reviews/Overviews of Dermal Sampling Methods

3.4.2.4 Analytical Method Development

A published and validated analytical method may not be available for the chemical and sampling method of interest. Therefore, it may be necessary to develop a laboratory analytical method for the sampling method or media selected. Prior to developing an analytical method, the assessor should determine if a.) an existing method has been published by the organizations in the resources listed above, or if a method that has not been fully independently validated has been published in the peer reviewed literature. Next, it should be determined if there are laboratories that have developed analytical methods for a structurally similar chemical or using sampling media (if known).

A clear research question and study objective(s) are necessary to determine experimental design. For example, the chemical of interest, occupational population characteristics, tasks which represent the highest exposure potential all need considered. The objective should be informed by key hazard, health, and exposure information gathered during problem formulation or from work process evaluations. A target detection level should be determined prior to developing the analytical method.

Some Key Considerations include:

- What quantification method should be used? Is there any potential for contamination or interference from other compounds present in the workplace, as a result of the proposed methods, or from other factors (e.g., sweat, solvent type, sampling media)?
- What should the LOD/LOQ of the study be? How low can it feasibly be based on the proposed instrumentation and equipment available in the laboratory?

- How many samples are needed for a statistically robust method development study?
- Is the type of equipment available sensitive enough to determine exposure potential at relevant levels?
- Is the analytical method feasible for large-scale sampling and is it able to be employed in accredited laboratories?

In general, method development may comprise of various steps, including selection of measurement techniques, recovery efficiency from the sampling media, stability of the analyte on the medium, method evaluation, and field evaluation of the method (NIOSH, 2020). A robust analytical method will also include information on storage procedures, equipment and supplies needed, instrument calibration procedures, considerations of quality control and sample stability, the limit of detection or quantification (LOD/LOQ), data analytics, and metrics of method accuracy, precision, and performance. There will likely be collaboration and discussion between the risk assessor/IH professional and the analytical chemist/laboratory.

Additional considerations and resources for developing an analytical method are found in **Appendix I – Sampling and Analytical Method Development**.

3.4.3 Data Analysis of Occupational Exposure Data

The U.S. EPA has published a guidance document for the statistical analysis of occupational exposure data, specifically focus on air monitoring, but the concepts are applicable to dermal monitoring data (EPA 1994). This document outlines the types of occupational monitoring data and assessments, the variability in exposure data, how to identify data needs, identify parameters affective exposure, as well as how to identify uncertainties, assumptions, and biases. It provides further guidance on how to define groups for analysis, how to treat and perform descriptive statistics on the data, and present the results.

Following laboratory analysis, dermal sample results should be analyzed using a variety of statistical methods. The main objectives of data analysis should involve:

1) Describe the overall structure of the data
2) Account for measurements below the LOD
3) Identify potential outliers
4) Assess the distribution of the data
5) Characterize the measured and modeled exposure profile for each SEG by COU
6) Recommend exposure estimates (descriptive statistics) for comparison to appropriate OELs or dermal DNELs for workers

Unless it is statistically reasonable to combine measurements among COUs, all steps above are executed for each sample type (e.g., full shift, task length) by COU.

3.4.3.1 Variability of Exposure Data

Although random sampling is preferred, it is more typical to conduct “worst case” sampling campaigns for regulatory compliance (EPA 1994). Regardless of the method of sampling, occupational exposure data has high variability (EPA 1994).

3.4.3.2 Summary Statistics

With any dataset, it is important to understand the overall structure of the data, summary statistics, including sample size, mean and standard deviation (SD), geometric mean (GM) and geometric standard

deviation (GSD), median, minimum, maximum, and high-end estimates (95th percentile) were calculated for each sample type (i.e., full shift, task length) by COU.

3.4.3.3 Data Below LOD

Next, any data below the LOD (i.e., non-detects or ND) should be accounted for and there are numerous methods to handle these types of data. For example, the analytical method LOD can be divided by 2 (DL/2), or other methods, such as regression on order statistics (ROS), Kaplan Meier (KM), and Bayesian methods. EPA uses DL/2 in TSCA risk evaluations, and this method is generally recommended for highly skewed data sets (such as with a GSD of 3.0 or greater) (IT Environmental Programs, Inc., 1994). However, other publications suggest that this method is not recommended (ProUCL 5.2 Technical Guide).

3.4.3.4 Outliers

In order to identify outliers in the dataset, graphical examination and Rosner's test can be used for raw data and log-transformed measurements (Rosner 1983). Full-shift samples and task-length samples for each COU should be assessed separately to identify potential outliers at 1% and 5% confidence levels.

3.4.3.5 Distribution of Data

The distribution of the data can be assessed using lognormal distribution (Q-Q-plot) and statistical GOF tests (Shapiro-Wilk, Shapiro-Francia). The purpose of assessing the distribution is to test the null hypothesis that the lognormal model is adequate for data within each sampling type (full shift and task length) by COU.

3.4.3.6 Assessment of Exposure Profiles for SEGs

Nested analysis of variance (ANOVA) followed by pairwise comparisons (Tukey post-hoc tests) of log transformed concentration measurements stratified within SEG can be used to assess differences among COUs. Estimates of central tendency, the arithmetic mean risk or the median risk, and high-end, at or above the 90th percentile of a population distribution, exposures should be calculated for each SEG by COU.

For each sample type (i.e., full shift, task length), the proportion of non-detected values, GSD and the distribution of the data can be used to inform selection of the appropriate methodology for treatment of non-detected values. Estimates of central tendency (mean, GM, median) and high-end (95th percentile) exposures are computed for each SEG by COU. Bayesian estimation with non-informed priors for central tendency and high-end exposure estimates (95th percentile) are used to simulate underlying distributions for the measured concentration by each SEG within COU.

3.4.3.7 Key Resources

1. U.S. EPA. Guidelines for Statistical Analysis of Occupational Exposure Data. Office of Pollution Prevention and Toxics. August 1994. Available at stat_guide_occ.pdf (epa.gov).
2. IT Environmental Programs, Inc., ICK Kaiser Incorporated. (1994). Guidelines for Statistical Analysis of Occupational Exposure Data. Final. Contract No. 68-D2-0064, Work Assignment No. 006. Office of Pollution Prevention and Toxics, August 1994. https://www.epa.gov/sites/default/files/2015-09/documents/stat_guide_occ.pdf
3. Rosner, B. (1983). Percentage Points for a Generalized ESD Many-Outlier Procedure. Technometrics, 25(2), 165–172. https://doi.org/10.2307/1268549

4 Risk Characterization and Management

4.1 Risk Characterization

The risk characterization step provides for the integrated consideration of the exposure estimate in the context of an exposure benchmark. Risk characterization includes metrics as well as narratives. The overall risk characterization should ensure transparency and clarity for all intended stakeholders. These principles apply to the data and methods used, the evidence integration procedures, metrics that inform conclusions, and limitations and uncertainties (NRC, 2009).

There are general guidelines regarding risk characterization approaches that are similar among chemical health assessment related agencies and organizations. While any of the approaches have been developed or our most readily available for occupational inhalation exposures – the same concepts would apply to dermal route exposures.

4.1.1 Category-based approaches

For many screening risk characterizations, a categorical approach is applied to inform decision making. This is typically developed in the context of an exposure potential category and a hazard category. In many cases the assignment of a scenario and chemical use case then yields an overall risk category based on a risk matrix of the exposure and hazard categories. Appendix D is an example system developed for dermal risk ranking within the set of AIHA tools. However, many other frameworks and algorithms exist. The nature of the criteria and number of categories vary and can also be refined to increasing levels of complexity. The NIOSH occupational exposure banding approach provides an example of a five-band system with assignments to bands dependent on the nature of the available data and the depth of data review – but the NIOSH framework is currently only published for inhalation exposures. The risk categories are also often linked directly to control categories or recommendations using tools that are often described as control banding. There are many examples of this approach built into occupational risk screening tools (e.g., UK HSE COSHH Essentials and Stoffenmanager, among others). Zalk et al have described many aspects of these banding methodologies.

4.1.2 Approaches for effects with threshold-like responses

For non-cancer effects or effects that are likely to have effects that can be estimated as having population onset doses or estimated threshold like behaviors a procedure that evaluates the ratio of exposure and health benchmark is common. Different organizations define the ratio differently. Note that none of these methods provide precise lines between concern and no concern and none of them provide a probability of effect occurrence as one reaches and exceeds the benchmark. Common examples include:

- Margin of exposure (MOE): the health effect POD is divided by the scenario adjusted exposure estimate. In this case the larger the value the less of a concern. The “adequacy” or target margin is usually defined with the method use context. This approach has particular value in its flexibility given alternative POD choices for different use scenarios. This approach is used in the TSCA risk evaluation and OPP risk assessments.
- Margin of safety (MOS): the health benchmark including assessment or uncertainty factors is divided by the adjusted exposure estimate. This metric has a similar directional interpretation as the MOE but requires less judgment from users regarding the desired margin. Generally, as values exceed a value of one there is less concern for adverse effects. This methodology has similar benefits of flexibility for various scenarios but can be easier to interpret for some stakeholders. This approach is common for consumer product risk assessments.

- Hazard quotient: the scenario adjusted exposure estimate is divided by the occupational health benchmark. This is similar to the MS – but the inverse equation. The approach works well for well-defined and standardized heath benchmark application scenarios. For example, for OELs setting a value as a full-shift time weighted average is fairly standard – so the duration and scenario flexibility building into the MOE approach is less necessary. In this case, as one reaches and exceeds a value of unity, the level of concern is increased.

4.1.3 Approaches for effects with no assumed threshold like response

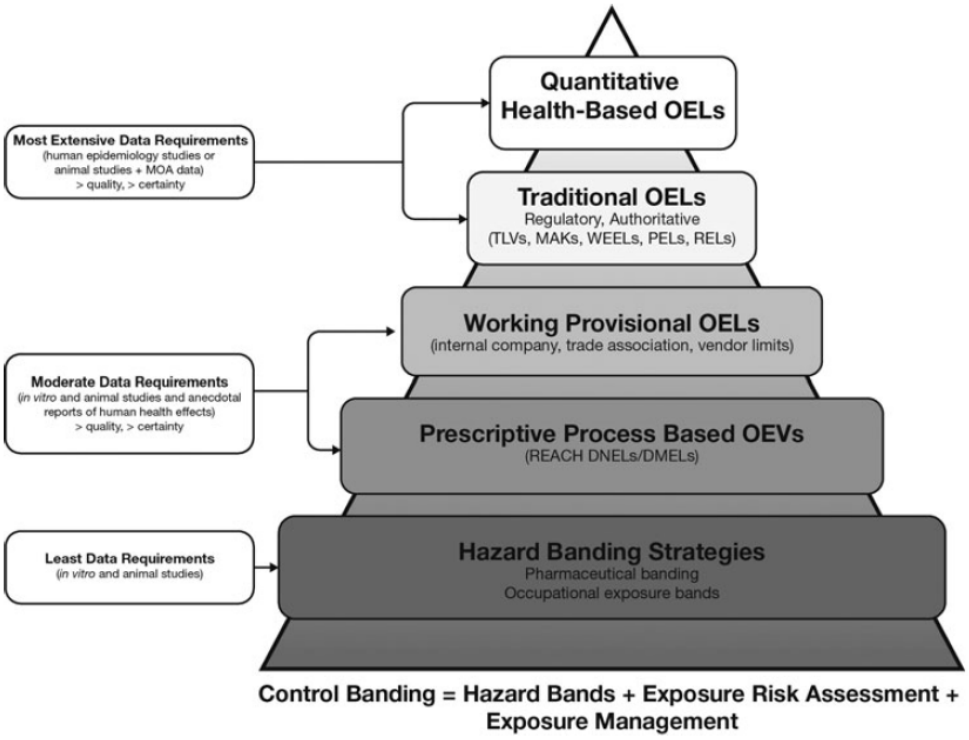
For effects that are not presumed to have a threshold like response an alternative method that involves extrapolation of a line (or curve) to background exposures are common. This method is most common for direct acting carcinogens but has also been applied to some chemicals for non-cancer effects. Since the data at very low residual risk levels are usually sparse and the method is one of dose extrapolation linear extrapolation method are most common unless detailed information is available (e.g., detailed mechanistic toxicology knowledge). The result of the method is a “slope factor” when applied to dermal data (or route-adjusted data). The slope factor is the degree of extra effect risk per unit dose and describes the effect potency. Multiplying the exposure estimate by the slope factor provides an estimate of the scenario related extra risk.

Regardless of which of these risk characterization metrics is applied, a definition of the interpretation of acceptable versus not acceptable risk and connection to risk informed decision for risk management is required as part of the process.

4.1.4 OEL Derivation

Occupational exposure limits (OELs) serve as benchmarks to be compared against measured or estimated airborne exposure levels in the workplace (Deveau et al. 2015; Laszcz-Davis et al. 2014). Some OELs are entirely health-based, whereas others account for the technical and economic feasibility of implementing controls There are multiple types of OELs, as illustrated by the hierarchy of OELs concept (see Figure 5) and as described, in brief, below:

- *Quantitative health-based OELs* - incorporate the probability of health risk, and require the most extensive data (e.g., epidemiology datasets for dose-response modeling).
- *Health based OELs* - identify critical health effects, evaluate dose-response behavior, and extrapolate these data, accounting for uncertainties, to estimate a level intended to protect worker health. OELs in this category are typically derived by expert committees that include formal peer review.
- *Working or provisional health-based OELs* – set by companies for internal purposes; may incorporate proprietary data not available to external groups and are not peer reviewed. Prescriptive or process-based occupational exposure benchmarks and guidance values (OEVs) and occupational exposure hazard bands may serve as alternative quantitative exposure benchmarks where data are insufficient to develop OELs; however, they are not generally equivalent in level of evidence integration to formal health-based OELs (Laszcz-Davis 2014).



Source: Deveau et al. 2015

Figure 4. Hierarchy of OELs

4.1.4.1 Dermal OELs

In contrast to the inhalation route of exposure, managing the occupational health risk of potential dermal exposure to substances with relatively high uptake via skin has typically taken a qualitative approach with the use of skin notations, rather than quantitative dermal occupational exposure limits (Naumann and Arnold 2019). Different skin notations have been published that vary in the criteria used to assignment of the notations and the nature of the effects addressed. U.S. NIOSH has published a methodology (NIOSH, 2009) that incorporates a decision framework for integration evidence related to potential for systemic effects from dermal contact with chemicals that considers dermal route systemic toxicity data, toxicity data from other routes, and empirical or estimated dermal absorption potential. The NIOSH methods also include notation relevant for direct skin effects. Other organizations that establish inhalation-based occupational exposure limits have procedures for assigning skin notations. These notations generally are provided to reflect the potential for absorption of toxicologically relevant doses such that aggregate exposure via the dermal route need considered in interpreting the level of protection afforded by the inhalation OEL. For example, the American Conference of Governmental Industrial Hygienists (ACGIH) designates “skin” under “notations” for chemicals that have the potential for “significant contribution” to an individual’s overall exposure by the cutaneous route (ACGIH TLVs and BEIs 2021). The Workplace Environmental Exposure Levels (WEEL) Committee, and other international OEL derivation groups establish similar procedures.

Application of acceptable surface limits for dermal route chemical risk assessment has a long history of use. For example, risk assessments for assessing inorganic lead contamination include surface limit testing. In addition, surface limit methods have been a well-accepted risk characterization tool in the pharmaceutical industry (Kimmel et al. 2011). Some organizations have proposed including surface limit values as a means to provide quantitative guidance for controlling dermal exposures (Naumann and Arnold 2019; ACGIH TLVs and BEIs 2021) to augment traditional inhalation based OELs. For example,

ACGIH sets threshold limit values-surface limits (TLVs®-SLs), defined as "[t]he concentration on workplace equipment and facility surfaces that is not likely to result in adverse effects following direct or indirect contact" (ACGIH TLVs and BEIs 2021). These surface limits are intended to serve as a supplement to airborne TLVs®, particularly those which have been designated as having skin, dermal sensitization, and/or respiratory sensitization notations. In these methods, the general procedure is to define a point of departure for an effective systemic dose and adjust that dose through application of assessment factors that address uncertainties in the data extrapolation, biological variability assumptions, and systemic dose route bioavailability for tested routes versus dermal routes (Dankovic et al., 2015; Wheeler et al., 2015). The result dose limit can then be converted to a surface limit in mass/surface area units – usually based on dividing the acceptable dose by assumptions regarding had or palmar surface areas. This type of assessment has regulatory, or compliance precents for various EPA scenarios as well as in meeting consensus standards in protecting health care and pharmaceutical workers (USP 800).

In addition, in certain instances, it may be feasible to derive a dermal safe dose or equivalent dose from the health effects and toxicology literature. The same general principles of dose-response assessment applied for other routes apply to dermal risk assessment as well. When direct dermal testing data are available a health-based exposure limit is often developed directly. More commonly the same general procedure can be used with the addition of a factor to adjust for extrapolation from data derived from one of exposure (often oral dosing for industrial chemicals) versus the route of interest (dermal in this case). A chemical specific route bioavailability factor is often used if route specific toxicokinetic data are available. In the absence of such data modeled estimates for uptake or default values are used. This procedure is routine in the context of U.S. EPA assessments for dermal risk screening levels, and for chemical registration for occupational procedures using the DNEL methodology. This process has also been applied in the context of EPA TSCA risk evaluations. Similar principles have been applied to develop dermal equivalent values of OELs. For example, an inhalation OEL may be converted to a total systemic dose in order to evaluate the equivalent dose via dermal absorption in circumstances where the basis of an OEL is to prevent a systemic toxicological effect (Tibaldi et al. 2013). Tibaldi et al. (2013) provides an illustrative example of such a scenario, in which the recommended OEL for NMP is 10 ppm (40.5 mg/m^3), which equates to a total allowable occupational dose of 405 mg (40.5 mg/m^3 x 10 m^3 (respiratory volume for 8-hour work shift)).

4.1.4.2 Biological Exposure Indices (BEIs)

The ACGIH BEI Committee (and international counterparts) have a longstanding and continuing effort to develop Biological Exposure Indices (BEIs). In most cases, BEIs are derived using regression-based correlations from occupational epidemiology and exposure data to estimate the quantitative relationship between the inhalation exposure and the appropriate biological marker (exhaled air, urine, blood levels). The BEI is then presented as the level in biological media that equates to the level of protection afforded by the TLV (inhalation OEL). The "safe dose" is essentially connected to the TLV dose. For chemicals with a BEI (or equivalent limit), most occupational exposure assessments favor measurement of chemical concentrations in the breathing zone of the worker coupled with a skin notation for warning of the other main occupational pathway of exposure. Traditionally, biological exposure monitoring has been limited to specific chemicals that have a regulatory limit (e.g., blood lead). Even for most chemicals that have chemical specific OSHA standards, measurement of chemicals (or metabolites) is typically only required (or done) under cases where there is suspected external exposure exceedances. Several standards also include biological effect monitoring in such cases. Despite the traditional limited application of the technique there are some additional ways to think about OELs based on internal dose metrics that we expect to increase in use. This generally reflects two points:

1. Increased drive to consider aggregate exposures (from EPA) and from cumulative risks (emphasis in NIOSH TWH programs).

2. Increased access to toxicokinetic modeling tools that make translation of the results or modeled estimates better linked to external dose scenarios.

As the desire for setting new limits has increased and toxicokinetic models have improved the push to set "internal dose" based limits has also increased. This has the advantage of using the toxicology data more directly (since most chemicals do not have occupational epidemiology that is quantitative). It also allows for back extrapolating to different exposure routes, and thus can support cumulative (or aggregate) risk assessments more fully. In these cases, the point of departure on an internal dose basis is the center point for the risk assessment and then reverse kinetic assumptions can be used to set a route specific exposure target, such as is the case with the development of dermal OELs. This general approach will continue to grow as we use more commonly HTTK (high throughput toxicokinetics) – already available via NIEHS OPERA.

Recently another application has evolved that is particularly pertinent for carcinogens and has been applied for metals such as nickel and cobalt. The approach involves developing a general population internal dose reference level for a biomarker to benchmark against a worker's total dose. Based on the statistical distribution of the general population variability in the biomarker of choice, a biomarker level "limit" is then developed to reflect occupational exposure exceeding general population levels. In the EU these are call biological guidance values (BGVs) (Bolt and Thier, 2006; European Commission, 2014).

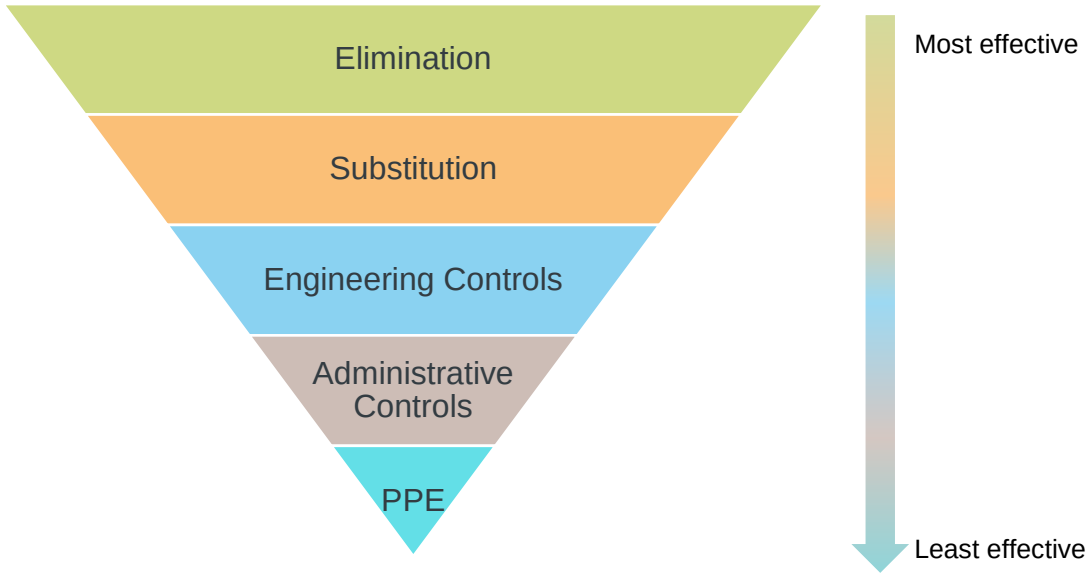
One of the more common uses of biomonitoring is geared for risk management, in particular medical surveillance. This can take the form of exposure biomarkers or effect biomarkers (e.g., IgE testing for detection of sensitization).

It is also worth noting that while ambient sampling is generally preferred from a pragmatic view (less invasive, etc.) there are likely to be some situations driven by decreased LOD requirements or use scenarios with sampling complications for which having a biomonitoring operation could give some flexibility in addressing regulatory requests for empirical evidence of low exposure. Thus, the combination of increased focus on aggregate exposure, lower LODs that generate practical sampling problems, and very low risk limits (e.g., for some carcinogens) all could increase the value of viable biomonitoring approaches.

In many cases dermal exposure in the workplace does not occur in the absence of potential inhalation exposures. Thus, biological monitoring is also an approach that can be reconsidered.

4.2 Risk Management

Risk management is a process by which identified risks are mitigated or remediated using various control strategies. A hazard and exposure both must be present to constitute a risk. Based on the previous steps identified in this framework, it may be determined that a risk for dermal exposure is unacceptable or presents a clear concern, and a risk management strategy will need to be outlined and documented to reduce or eliminate the potential risks. The types of controls used will depend on the occupational exposure scenario and what is feasible for the facility of interest. As depicted in Figure 5, there is a recommended hierarchy of controls that should be implemented to mitigate risks. From the most to least effective, these controls include Elimination, Substitution, Engineering Controls, Administrative Controls, and PPE. Each of these controls will be described in greater detail in this section.



Source: https://www.cdc.gov/niosh/topics/skin/recommendations.html

Figure 5 Hierarchy of Controls Pyramid

4.2.1 Elimination

Elimination is the preferred method of controlling exposures in the workplace. Elimination includes the removal of a hazard and therefore prevents any exposure to the hazard. Thus, there is no risk. Regarding dermal exposures, elimination would entail the removal of a substance that poses a dermal exposure risk (for example, a substance with an ACGIH skin notation) from a work process. If the substance cannot be feasibly removed from the work process, potential substitution of the hazardous substance would then be evaluated.

4.2.2 Substitution

Substitution is the replacement of a hazardous substance with an appropriate alternative that is less hazardous and therefore poses comparatively less health risk in the event of exposure. Substitution must include an assessment for any potential new risks; specific considerations should be given to the replacement substance's toxicity and volatility. For example, a substance that is recognized to be a dermal sensitizer may be replaced by another substance that is not a dermal sensitizer but is still able to achieve the intended effect in the work process as the sensitizing substance.

4.2.3 Engineering Controls

When elimination and substitution are not feasible, engineering controls should be enacted to isolate workers from the hazard, thereby mitigating hazardous conditions from the workplace. Engineering controls often include equipment or workspace modifications, as well as the installation and use of protective barriers, ventilation, and other controls. Examples of engineering controls as they pertain to dermal exposures include (re-)designing a work process to avoid splashing or immersion of a worker's hand during a transfer process. Engineering controls are most effective when they are easily implemented and are minimally impacted by human factors (e.g., interference by users). According to NIOSH, the most effective engineering controls are those which (NIOSH 2023):

- Are part of the original equipment design;
- Remove or block the hazard at the source (prior to contact);
- Prevent workers from modifying or interfering with the control;

- Needs minimal user input;
- Can operate correctly without interfering with or complicating the work process.

4.2.4 Administrative Controls

Following any implementation of engineering controls, administrative controls should then be considered. The purpose of administrative controls is to "establish work practices that reduce the duration, frequency of intensity of exposure to hazards" (NIOSH 2023). Administrative controls involve changing the way people work through the establishment of work practices and procedures, education and training, hygiene, and housekeeping. As they pertain to dermal exposures, administrative controls may include training programs educating workers on the hazards associated with a substance with which they may come into contact in the workplace, on proper PPE that should be selected for a certain task, and on best housekeeping practices. It could also mean that certain workers are given rest breaks, are rotated between jobs to reduce frequency of certain tasks, or access to areas where hazardous materials are located are limited (NIOSH 2023).

4.2.5 Personal Protective Equipment (PPE)

Personal protective equipment (PPE) is the last line of defense for controlling workplace exposures and should only be relied upon when feasible workplace control measures are unavailable or ineffective at reducing hazardous exposures to levels below the available occupational exposure limits. Employees wear PPE to minimize exposure to hazards and is ideally utilized in conjunction with other workplace controls. PPE worn to protect against dermal exposures may include gloves, aprons, goggles, face shields, chemical suits, and boot covers.

The following are examples of some factors that may influence the selection of protective garments for a workplace: type of chemicals handled, nature of contact (total immersion, splash, etc.), duration of contact, concentration and temperature of chemical, area requiring protection (hand only, forearm, arm, eyes, etc.), dexterity requirements, grip requirements (dry, wet, oily), glove features (e.g., cuff edge, lining, color), thermal protection, size and comfort, abrasion/resistance requirements, and price (OSHA 2023). Proper garment and material selection are critical to creating a protective barrier between the skin and dermal hazards. Table 4, below, offers guidance on selecting proper garment types for dermal protection.

Table 4. PPE Garment Guidance

	Protection From			
PPE	**Contact**	**Splash**	**Vapor/Aerosol Deposition**	**Additional Considerations**
Gloves	Hand Only	Hand Only	Hand Only	Impact on Dexterity, Cut Protection, Thermal Protection
Boots	Feet Only	Feet Only	Feet Only	Slip/Toe Protection, Electrical Safety
Sleeves	Arms Only	Arms Only	Arms Only	Must be Fitted and Contiguous with Gloves
Apron	Partial Body	Partial Body	Not Significant	Splash Protection is Directional
Safety Glasses	Eyes Only	Partial Eye Protection	Not Significant	Ballistics Protection
Safety Goggles	Eyes Only	Eyes Only	Partial Eye	Splash/Vapor Protection Depends on Construction

PPE	Protection From			Additional Considerations
	Contact	Splash	Vapor/Aerosol Deposition	
Full-face Shield	Eyes Only	Eyes Only	Not Significant	
Two Piece Chemical Protective Suit	Full Body	Limited Full Body	Limited Full Body Protection	Protection Limited at Seams/Gaps
Overalls (One Piece)	Full Body	More Comprehensive Full Body	More Comprehensive Full Body	May Increase Heat Stress
Hooded Overalls	Full Body and Head	Full Body and Head	More Comprehensive Full Body and Head	May Increase Heat Stress
Fully Enclosed HAZMAT suit	Most Comprehensive Full Body Head	Most Comprehensive Full Body and Head	Most Comprehensive Full Body and Head	May Increase Heat Stress, Requires SCBA

Additionally, garments may be made of different base materials that offer differing levels of protection from specific chemicals. Protective materials may degrade at different rates or provide different levels of permeation and penetration protection. Please see Table 5, below, for general guidance regarding material selection. In general, gloves should be selected based on the intended use, the chemical being handled and the physicochemical properties of that chemical. Several types of chemical-resistant glove materials are available, such as butyl, latex (rubber), neoprene, nitrile, fluorocarbon (Viton), as well as various plastics like polyvinyl chloride (PVC), polyvinyl alcohol and polyethylene. Glove types should also be selected with skin sensitivities or allergies of the working individual in mind. The appropriate usage of each depends on chemical attributes and specificity of the task and nature of the work. OSHA provides some information on factors which can influence which gloves are selected, including nature of the contact (immersion, splash), duration of contact, skin contact area, grip requirements, thermal protection, size and comfort, and abrasion/resistance (OSHA 2004). It may be prudent to consider laboratory testing to validate the ability of a chosen glove material to resist permeation of the chemical of interest.

Other considerations should be made when selecting PPE, such as design and quality, ease of maintenance, fit and comfort for employees, and compatibility if combining multiple types of PPE. Regardless of the PPE selected, all workers should receive training on the proper use, disposal, and replacement of PPE.

Table 5. General Base Material Guidance for PPE

Base Material	Intended Use	Good For	Poor For
Latex	Incidental contact	Water based and biological materials	Organic solvents and chemicals
Nitrile	Incidental and extended contact	Chlorinated solvents, oils, grease, acids, caustics, alcohols	Oxidizing agents, aromatic solvents, ketones, acetates
Butyl Rubber	Extended contact	Ketones, esters, strong acids & bases, peroxides	Gasoline, aliphatic, aromatic and halogenated hydrocarbons
Neoprene	Extended contact	Acids, bases, alcohols, fuels, phenols	Halogenated and aromatic hydrocarbons

Norfoil	Extended contact	Most hazardous chemicals	Poor fit
Viton	Extended contact	Chlorinated and aromatic solvents	Ketones
PVC	Specific use	Acids, bases, oils, fats, peroxides, amines	Organic solvents
PVA	Specific use	Aromatic and chlorinated solvents	Water-based solutions

Table 5 is not a comprehensive review of all material and chemical combinations. Table 4 of the U.S. Department of Energy Occupational Safety and Health Technical Reference Manual provides comprehensive protection ratings of each glove type versus specific chemicals (OSHA 2023; ,3).

PPE efficacy depends on 1) permeation of a chemical through the glove and 2) exposure related to the use of the garment (e.g., spillage around the cuff of a glove and direct contact while removing the garment). The total protection factor is thus a combination of these two pathways of skin contact. With regard to glove selection, vendors test according to ASTM F739-20 and provide these results for each of their products (ASTM 2020). The ASTM method includes measures of breakthrough detection time, standardized breakthrough time, permeation rate, and cumulative permeation. Companies also report overall chemical compatibility (e.g., if a chemical is expected to break down the glove material).

Protective gloves should be inspected before each use to ensure that they are not torn, punctured, or made ineffective in any way. A visual inspection will help detect cuts or tears but a more thorough inspection by filling the gloves with water and tightly rolling the cuff towards the fingers will help reveal any pinhole leaks. Gloves that are discolored or stiff may also indicate deficiencies caused by excessive use or degradation from chemical exposure. Any gloves with impaired protective ability should be discarded and replaced. Reuse of chemical-resistant gloves should be evaluated carefully, taking into consideration the absorptive qualities of the gloves. In some cases, particular contaminants of interest may penetrate or diffuse into the glove material even after decontamination (Jester 1991). The Reuse of chemically exposed gloves is generally discouraged, but if done, one should take into consideration the toxicity of the chemicals involved and factors such as duration of exposure, storage and temperature (OSHA 2023).

According to OSHA, employee should be trained to understand a.) when PPE is necessary, b.) what PPE is necessary, c.) How to properly don, doff, and adjust the PPE, d.) the limitations of the PPE, and e.) the proper care, maintenance, lifespan, and disposal procedures for the PPE (OSHA 2023). Additional resources for assistance with glove section are described below.

Key Resources:

1. OSHA Personal Protective Equipment, OSHA 3151-02R 2023. Accessed at https://www.osha.gov/sites/default/files/publications/osha3151.pdf.
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3. https://www.cdc.gov/niosh/ncpc/azncpc.html#
4. ASTM Standard Test Method (F739-20) for Permeation of Liquids and Gases Through Protective Clothing Materials Under Conditions of Continuous Contact. 2020. Accessed at https://www.astm.org/f0739-20.html.
5. Risk management for Existing Chemicals Under TSCA: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/risk-management-existing-chemicals-under-tsca
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19. OSHA [1997]. Assessing the need for personal protective equipment: A guide for small business employers. Occupational Safety and Health Administration No. 3151. Washington, DC: U.S. Government Printing Office.
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21. Sanson EB, Tewari YB [1978]. The permeability of laboratory gloves to selected solvents. Am Ind Hyg Assoc J 39:169-174.
20. https://www.osha.gov/dermal-exposure/control-prevention
21. https://www.cdc.gov/niosh/topics/skin/recommendations.html
22. https://ohsonline.com/Articles/2003/01/Effective-Dermal-Protection.aspx

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APPENDIX A

DERMAL HAZARD RESOURCES

Appendix A – Dermal Hazard Resources

The objective of this Appendix is to describe some of the categories and examples of key resources relevant to the hazard assessment of chemicals following exposure by the dermal route. There are numerous challenges in developing such assessments that reflect the current landscape of information resources. There is no single best resource for developing a comprehensive dermal hazard assessment. For this reason, a systematic literature identification workflow is recommended. Such a workflow would incorporate key elements of the problem formulation as described in other sections of this dermal framework document.

The workflow included in this section reflects a balance of ease of use, degree of data completeness, likelihood for the data to be updated and current, and uniqueness of a resource. A similar strategy was employed by NIOSH in developing a library of dermal risk assessment resources for emergency response by NIOSH researchers (Hudson et al., 2015).

1. Information Resource Categories and Selected Resources

1.1 Health Effects and Toxicological Data:

The following are commonly searched hazard and toxicological summary resources typically collated and searchable by chemical. Note that these are compiled resources websites that draw data from various sources as referenced and since they are organized by chemical provide an easy-to-use way to find a large amount of chemical specific data in summarized formats. The selected resources are not a comprehensive list, but rather provide some of the most commonly used resources among human health risk assessment scientists. The resources here do not preclude the potential value of conducting primary literature searches.

- EPA Chemistry Dashboard: This resource provides access to hazard related data in several sections of the individual chemical file. The physical and chemical properties tab can provide information that supports hazard potential. The hazard data tab provides information of point of departure and toxicity values annotated by source and route of exposure. The database also is notable for inclusion of in vitro hazard assay data that may have some relevance for dermal hazard assessment depending on the nature of effects that are of concern. An example would be the analysis of bioassay data relevant to skin sensitization, reproductive toxicity modes of action, neurotoxicity, etc. The resource also has a tab for GHS data (which are pulled from PubChem) and thus may not be the latest harmonized classifications (as provided in the ECHA database). The resource includes two methods for identifying data for related chemicals is a chemical read across methodology is desired. With regard to facilitated literature searching there is a tab for conduct of a primary literature search with access to an abstract sorting tool. The resource also has a well-developed links page to other key resources.
- PubChem: This resource combines content from many of the databases previously include in the NLM TOXNET set of resources. It is easy to navigate and provides tabs for hazard, regulations, and toxicity data tables. Toxicology abstracts are also provided. This resource (because it provides the abstracts from HSDB) can provide a bit deeper information than the annotated lists present in the EPA Chemistry Dashboard, but the quality and reliability of the information varies by abstract and originating source. GHS classifications are provided but may not be the latest harmonized classifications (as provided in the ECHA database).

- ECHA REACH Database: This resource is particularly helpful for providing “robust” summaries of manufacturer supplied toxicology data and hazard assessments. The detailed profiles have tables for health-based limits and data summaries for physical and toxicological endpoints. The ECHA profile includes a description of the hazard classification and harmonized codes.

There are variety of other resources many of which have data incorporated in the resources above. For direct access some include:

- EPA Integrated Risk Information System (IRIS): This resource is a database with potential human health effects resulting from various chemical exposures, including individual chemicals, groups of chemicals, or chemical mixtures. These data are often used by EPA and other agencies to inform toxicity information.
- OECD ToolBox: This resource provides data in a tabular endpoint format, similar to ECHA REACH Database. The OECD Toolbox also provides additional QSAR tools as well as tool for chemical read across.
- ATSDR Toxicological Profiles: The Agency for Toxic Substances and Disease Registry compiles toxicological data for various substances. The chemical profiles contain information on health effects, chemical and physical information, potential for human exposure, among other information.
- eChemPortal: This resource is a global resource for information on chemical substances maintained by OECD. Chemical information can be searched using CAS number and other identifiers. The portal provides information on physical and chemical properties, toxicity, classification and labeling, and exposure and use.
- SDS/MSDS: Safety Data Sheets (SDSs) and Material Safety Data Sheets (MSDSs) contain information on physical data, health effects, and other information useful for hazard identification and assessment.
- SRC Database: This database combines information on chemical and toxicological data from various resources to inform hazard and exposure assessments. A key difference is that this resource has a database compiling information on unpublished technical reports submitted by industry to EPA under TSCA.
- ECHA C&L Inventory: Database to search for chemicals and labeling information, classifications for any substance on the EU market, and labelling requirements.
- Dupont Verisk 3E Database: This toolkit provides information on occupational exposure limits, toxicity classifications, GHS information, and information on whether a particular compound is listed by OSHA, IARC, NTP, California Prop 65, and NIOSH.

1.2 Hazard Notations and Classifications:

In some cases, information might be available in the form of a detailed hazard assessment that has been developed specifically to address the potential for toxicologically relevant dermal effects or systemic effects by the dermal route for worker scenarios. It is important in reviewing such resources the definitions and criteria used to assig various notations. The criteria and meaning can vary among organizations that establish such notations.

- NIOSH Skin Notation Profiles: NIOSH developed an updated protocol for assign skin hazard notations. The assessments for individual chemicals are provided as skin

notation profiles that include consideration of direct effects on the skin as well as systemic effects from skin exposure in the workplace. The direct effects categories include skin corrosion/irritation as well as sensitization. For systemic effects the degree of absorption and available dermal toxicity data are considered in the notation assignment.

- HBEL related notations: Most of the major expert groups that publish occupational exposure limits (see category below) include a hazard notation system that addressed systemic effects and sensitization effects. For systemic effects the majority of these expert committees assign a “skin” notation to reflect that upon contact (or in some cases vapor phase exposure) the chemical can be absorbed dermally in sufficient amounts and at sufficient rates to yield toxicologically relevant levels of systemic exposure. This the intent is to identify an important potential route of exposure for total dose reduction and to alert the user of the inhalation based OEL that concurrent skin exposure would reduce the level of protection afforded by the OEL. These same expert committees generally have another separate notation for skin sensitization potential.

- GHS hazard classifications: The Global Harmonized System (GHS) classification incorporate hazard codes (H-code) specific to the exposure route for some endpoints. H-codes can vary for the same chemical based on the source. They are found on the SDS as well as most of the hazard data compiled resources noted above. There are separate codes for dermal acute toxicity, irritation, sensitization. Note that in most resources that provide H-codes the provision of a code is an indication that the data based on a specific criterion or weight of evidence has met the definition for that code. However, the absence of a code in many cases reflects absence of endpoint specific data rather than an absence of that hazard. Thus, reliance only on H-codes is not recommended for a complete hazard assessment.

1.3 Health-based exposure limits:

The process of deriving a quantitative health related benchmark requires critical evaluation of the health effects information to identify potential route relevant adverse health effects and estimated onset doses (point of departure estimates) for those endpoints. Thus, such derivation documents typically provide a hazard summary and information of potency. For dermal route risk assessment such health-based exposure limits for dermal risk assessment may be available as workplace surface limits, skin surface limits or associated estimated doses, or internal doses. Each type of value has advantages for the occupational risk assessor. Unfortunately to date there is not a large library of such limits, and thus, the amount of chemicals with such limits is small. Some examples of key resources are noted below.

- ECHA DNELs: To our knowledge the most complete set of dermal workplace limits are the derived no effect levels (DNELs) published as part of the chemical profiles in support of the registration process for chemical use in the EU. The chemical safer report requires an assessment of risk by the dermal pathway (when relevant to that chemical’s uses). A dermal route DNEL can be derived for this assessment. When the data are available from dermal dosing studies the DNEL can be derived directly using the point of departure and relevant “adjustment factors” using a prescribed derivation approach. Many of the available dermal DNELs are derived using route extrapolation from oral dosing toxicology studies and the related uncertainties should be carefully considered.

In addition, the level of peer review and auditing of the derivations can vary – as the dossiers are submitted by private entities. A useful resource for fining GHS codes, DNELs, and other OELs is the GESTIS database.

- EPA NCELs and ECELs and EPA Pesticide Risk Assessments: The U.S. EPA as part of the chemical registration process develops dermal route risk assessments relevant to the chemical's uses. For new and existing chemicals in general commerce this takes the form of duration relevant dermal point of departure benchmarks modified by uncertainty factors. A similar process is used for registration of pesticides. These values are available in the public release documents of the individual chemical assessments. There are individual with other U.S. EPA surface specific limits (e.g., lead).

- Other individually published limits: Few of the non-governmental expert committees have derived a large portfolio of individual chemical dermal route OELs. There are recent proposals and work group efforts to develop such limits via the American Conference of Governmental Industrial Hygienists Threshold Limit Value Committee (ACGIH TLV®) and an American Industrial Hygiene Association (AIHA®) technical working group effort. Some TLVs exist for concentrations of chemicals on equipment or surfaces that can help inform dermal workplace limits following direct or indirect contact for sensitizers.

- Biological Exposure Indices: The ACGIH publishes Biological Exposure Indices (BEI®) and some European organizations also have such limits for selected chemicals. These limits are not designed for dermal route only – rather they provide an internal dose benchmark that can be used a metric for occupational risk assessment that provides similar levels of protection as inferred in the inhalation OEL (in the case of the BEI) or that relates to measures of indications of an increase in exposure via the occupational route (the EU BLV would be an example of this application).

2. Dermal Hazard Assessment Workflow Considerations:

The optimum workflow reflects a strategy to identify the most complete and scenario relevant data most efficiently. There is no single best approach, but documenting a systemic approach is recommended. The following are potential suggested steps in the process of identifying relevant hazard assessment data for conducting a dermal risk assessment for occupational scenarios.

1. Verify chemical identification. Note that this can be a challenge for mixed exposures and handling of formulated product for which each chemical ingredient may not be known. A list of chemicals for the hazard data queries in compiled at this step. Consider searching by CAS RN. Note that in some cases other international chemical descriptors might be needed for data poor compounds.

2. If the chemical is a pesticide or a high-volume chemical an existing assessment document is most likely. Consider starting with the relevant agency website for a toxicology review or profile or search the EPA Chemistry Dashboard Toxicity Values. If the data are not from a high volume or highly regulated use category chemical, consider a dual search for availability of existing authoritative assessments in the EPA chemistry dashboard and the ECHA database. This step is intended to identify sources with both a health-based dose-response value AND a summary of dermal route hazards with interpretation of relevance.

3. If no authoritative assessments are available (or they are not current) then search for hazard data summaries. We typically search at least four sources: 1) the SDS for manufacturer's general interpretations, 2) EPA Chemistry Dashboard (for listed *in vivo* toxicity data by route), 3) A sub-list of common OELs to search for skin hazard notations, 4) the ECHA database for additional non-published data and harmonized classifications. None of these sources are complete individually so this data source grouping approach is recommended.
4. Develop a weight of evidence assessment for the potential for direct and indirect skin effects for the use scenario integrated with the exposure assessment. This will take into account the potential for various effects to manifest from differing exposure patterns as described in the risk characterization section.

APPENDIX B

DERMAL EXPOSURE ASSESSMENT RESOURCES

Appendix B – Dermal Exposure Assessment Resources

The objective of this Appendix is to describe some of the categories and examples of key resources relevant to the exposure assessment of chemicals following exposure by the dermal route. There are numerous challenges in developing such assessments that reflect the evolving science and understanding of the many factors that affect both dermal exposure potential and the methods to measure such exposures, including environmental (e.g., temperature), chemical (e.g., chemical form), scenario-driven (e.g., pressure and duration of hand-to-surface contact), and physiological (e.g., the presence of sweat, the condition of the skin). There is no single standard or comprehensive resource guiding conduct of dermal exposure assessments. For this reason, a workflow incorporating review of a combination of available agency assessments and guidance and peer-reviewed literature review is recommended.

1. Agency and Professional Organization Guidance for Exposure Assessment:

The first step in a dermal exposure assessment is to research and select the most appropriate methodology. There are numerous Agency and independent resources available to design an assessment strategy as well as lists of available tools for all phases of exposure (and in some cases, risk) assessment. Key examples are provided below.

- American Industrial Hygiene Association (AIHA): The Occupational Environment: Its Evaluation, Control, and Management, 3rd edition ("White Book"), Chapter 20: "The Skin and the Work Environment." Overview of tiered approach to skin exposure assessments in the workplace. Review of dermal hazards, monitoring methods, dermal absorption calculations, and chemical-specific case studies.

- American Industrial Hygiene Association (AIHA): A Strategy for Assessing and Managing Occupational Exposure, 4th edition. This resource provides guidance on how to establish an exposure assessment strategy, develop SEGs, evaluate exposure profiles, quantitative exposure data interpretation and analysis, and methods to evaluate and validate exposure assessments.

- Dermal Exposure Assessment: A Summary of EPA Approaches: 2007 report describing approaches across the Agency, including The Office of Pollution Prevention and Toxics (OPPT), the Office of Water (OW), the Office of Solid Waste and Emergency Response (OSWER). (https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=183584)

- US EPA Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment). This document is the fifth annex of RAGS Volume I, the authoritative guidance for human health risk assessment at Superfund sites in the US. It is focused on environmental, rather than occupational exposures, but contains some information relevant to both applications, such as permeability coefficients, dermal absorbed dose equations, etc. Available online at https://epa-prgs.ornl.gov/chemicals/help/documents/RAGS_E_EPA540R99005.pdf

- EPA Exposure Assessment Tools by Lifestages and Populations - Occupational Workers: Lists numerous internal and external resources for data, models, and information on occupational exposures. The descriptions for each resource describe

where applicable to the dermal route. Available at: https://www.epa.gov/expobox/exposure-assessment-tools-lifestages-and-populations-occupational-workers.

- European Food Safety Authority (EFSA): Guidance on dermal absorption: Developed for plant protection products but contains information on skin and properties affecting dermal absorption and provides general guidance on study design and interpretation, including *in vitro* absorption studies, and reporting. Available online at: https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2017.4873

- RISKOFDERM toolkit – While no longer being updated, provides a useful decision-tree to evaluate the potential for dermal hazard and exposure. See: Oppl et al. (2003) and https://echa.europa.eu/documents/10162/19680902/calculator_riskofderm_enl.xls/9e0c3fa8-4764-4a18-95f9-8fbccf3acf2a

- The Dermal Advanced REACH Tool (dART): Tool to estimate dermal exposure to the hands for non-volatile and solid-in-liquid products. Peer-reviewed paper available at: https://academic.oup.com/annweh/article/66/5/602/6490538

- IHSkinPerm 2.0 – Tool for estimating dermal doses; see AIHA website and Tibaldi et al. (2014) Dermal Absorption of Chemicals: Estimation by IH SkinPerm, *Journal of Occupational and Environmental Hygiene*, 11:1, 19-31, DOI: 10.1080/15459624.2013.831983; additional information provided in Appendix F.

- European Food Safety Authority (EFSA): "Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products." Provides information on the tiered approach used to assess pesticide exposure, including methods for the field trials informing the guidance (e.g., handwash and wipe samples).

2. Agency Test Guidelines

- Occupational and Residential Exposure Test Guidelines OPPTS 875.1200 Dermal Exposure— Indoor. EPA 712–C–96–209, 1996. This test guideline was developed for pesticide exposure studies, but provides general guidance on dermal sampling, including wipe and hand rinse methodology, laboratory method validation, chemical stability testing on stored wipes, extraction efficiency testing, etc.

- Indoor Exposure Product Testing Protocols Version 2.0 (epa.gov) – Exposure protocol 9: migration to sweat (dermal exposure)

3. Compendia of Tools and Toolkits:

- CDC/NIOSH Dermal eToolkit: List of dermal exposure and risk assessment resources, including exposure and hazard, emergency response, decontamination, etc. https://chemm.hhs.gov/dermal/resources.html

- AIHA Risk Assessment Tools: Includes background reference documents on occupational exposure assessment, an exposure scenario tool (IH/OEHS Exposure Scenario Tool), an exposure assessment sampling templates and qualitative checklists, modeling tools, and statistical tools. Available online at: https://www.aiha.org/public-resources/consumer-resources/apps-and-tools-resource-center/aiha-risk-assessment-tools

4. Agency Resources with Exposure Data:

There are several US agency databases that contain occupational monitoring data. These data are sometimes found within agency exposure or health assessments, or as raw data (as in the case of the OSHA database). While not exhaustive, the below list represents the major sources of such information.

- NIOSH Health Hazard Evaluations (HHEs): This NIOSH program provides comprehensive evaluation of new and recurring workplace health hazards in a variety of specific occupational scenarios across an array of industries. In some instances, HHEs will include collection of dermal exposure data. Available at: CDC - NIOSH Health Hazard Evaluations (HHEs) - Search.
- NIOSHTIC-2: Searchable database containing various NIOSH publications including occupational safety and health publications, documents, and other communication products supported at least partially by NIOSH. For example, this database includes peer-reviewed research conducted with NIOSH co-authors/with NIOSH funding. Available at: NIOSHTIC-2 Publications Basic Search | CDC/NIOSH.
- OSHA incident reporting: OSHA gathers industrial hygiene samples as part of its compliance monitoring program, which are available in an online, searchable database. However, as noted on the website, OSHA compliance officers do not routinely visit every business, attempt to take representative samples, or always obtain samples for entire 8-hour shifts. OSHA often focuses data collection efforts on chemicals based on the existence of emphasis programs. OSHA notes that OSHA compliance officers "Use professional judgment and often attempt to evaluate worse case chemical exposure scenarios." Further, some of the data are collected in response to employee complaints. OSHA's chemical exposure database includes personal, area, and bulk samples for various airborne contaminants reported to OSHA. Currently housed at: https://www.osha.gov/opengov/health-samples
- EPA Chemical Data Reporting (CDR): Contains information provided by manufacturers (including importers) under TSCA on a four-year cycle starting in 1986. Includes company and site information, manufacturing (including import) information, production volume, and processing and use data. Can include occupational and environmental monitoring data, health and safety studies, ecotoxicity, and human health hazard information, where submitted. Available at: https://www.epa.gov/chemical-data-reporting/access-cdr-data

5. Peer-Reviewed Literature Searches

After consulting Agency sources, searching the peer-reviewed literature is a next logical step to identify publications on relevant methodologies and exposure data. For example, peer-

reviewed literature may contain dermal wipe sampling method validation, studies of dermal wipe sampling for specific chemicals, method validation,

The following are commonly searched databases for peer-reviewed articles on environmental health, including exposure assessment. There is a substantial amount of overlap in coverage of journals across these databases, but there are some differences that may warrant searching two or more of them to ensure information is not missed. The selected resources are not a comprehensive list, but rather provide some of the most commonly used resources among human health risk assessment scientists. All of the following databases have features to identify "related citations" or "find similar", and "cited by" options to enable targeting forward searching.

- PubMed: This free database is run by the National Library of Medicine (NLM) and includes biomedical literature pertaining to medicine, dentistry, nursing, veterinary medicine, and environmental health. It includes more than 34 million publication abstracts. PubMed has a few subsections: MEDLINE, articles indexed by medical subject headings (MeSH terms), PubMed Central (PMC, a curated full-text archive), and Bookshelf (archive of books, reports and some individual book chapters). PubMed is easy to search using Boolean search terms, and the interface is clean; allows for exportation of search results into various formats (Excel CSV, Word document with titles only, title + abstracts, etc.). Some issues with quality of PMC evidence because NIH funded articles do not always undergo editorial review. MEDLINE indexes about 6,200 journals.
- Scopus: Large, subscription-based multidisciplinary database run by Elsevier. Includes trade journals, books, patent records, and conference publications. Indexes MEDLINE with 25,000 total journals indexed. Includes many journals published outside of the United States and articles published in foreign languages. May be beneficial for broader environmental science topics, relative to PubMed alone.
- Web of Science: This is a subscription-based citation indexing service run by Thomson Reuters. Indexes MEDLINE, but broader content that includes engineering, social sciences, arts, and humanities. In-house editors curate and evaluate include journals. Includes 21,000 journal titles.
- Embase: Elsevier subscription-based biomedical database that covers topics in PubMed/MEDLINE, but also has a focus on drugs/pharmacology, medical devices, and clinical medicine. Journals are screened by an editorial committee.

APPENDIX C

DERMAL OCCUPATIONAL HAZARD AND EXPOSURE CHECKLIST

DERMAL OCCUPATIONAL HAZARD AND EXPOSURE CHECKLIST

General Instructions:

The goal of this document is to guide users in identifying and collating hazard and exposure information needed to determine the potential for dermal risk for a given facility and exposure scenario. Answering the questions provided below will also help tasks with the most exposure potential. The information gathered for these checklists can be used to populate a categorical risk matrix to guide decision-making, as presented in Appendix D.

Company Name:	
Company Contact Information: (Name, Email, Phone #)	
Surveyor Name:	
Survey Date:	
Jobsite/Work Unit:	
Area/Room:	

Section 1: Occupational Scenario Characterization and Key Considerations

Provide a concise description of the following components of the occupational scenario being assessed and the key considerations identified.

Company Name	
Industry	
Department	
General Facility or Work Area Description	
Key Questions	
1. What is the general nature of workplace or built environment in the area of the handling operation? Room size and shape, general ventilation, degree of openness to the ambient environment, etc.?	
2. Is the work generally performed inside or outside?	

3. Does the general maintenance and appearance of the space suggest the potential for re-entrainment of dust onto contact work surfaces or workers' skin?	
Worker Classification and Health	
Key Questions	
1. What work group (i.e., similar exposure group profile) is involved in the handling operation or task?	
2. Are there any sensitive populations?	
3. Have there been incidences of skin irritation, or other dermal or systemic health effects reported?	
4. Are there any dermal screening protocols in place? How often does this occur?	
Process Description	
Key Questions	
1. What handling operations or tasks are involved?	
2. What are the discrete tasks where the chemical is handled? (e.g., manual additions, handing loading hoses, collecting samples, sample analysis, filter cleaning, maintenance)	

3. What equipment is being used during this task?	
4. Are there work handling practices (such as open liquid pouring/transfer, heating open top vessels, spraying tasks) that would be expected to generate surface contamination that might yield dermal exposures?	
5. Are there chemosensory indicators (odors, visible haze, etc.) of airborne exposures that could result in direct skin contact or settling on surfaces that are contacted?	
6. Is the material visibly present on task related equipment, tools, or frequent contact surfaces?	
7. Do observations suggest direct contact with the chemical(s) such as presence of the chemical(s) on workers' clothing? If so, please describe.	
Risk Management	
Key Questions	
1. What exposure controls are being implemented? [e.g. process controls (purging/clearing equipment prior to opening), engineering controls (local exhaust, engineered sampling points, dry disconnect/dripless fittings), standard operating procedures (SOPs), PPE (gloves)]	

2. Are the workforce personnel wearing PPE designed to prevent direct dermal exposure? Is the material compatible with the chemical(s)?	
3. Describe the recommended PPE for this chemical(s).	
4. Are there observable workforce personnel implemented equipment or handling modifications (e.g., taped on barriers, use of gloves or other protective equipment outside a formal program, etc.?)	
5. Is the chemical or material visibly present on PPE that will be reused (e.g., gloves or aprons)?	
6. What is the frequency of changeout for PPE?	
7. Where is used PPE discarded or stored?	
Product or Chemical Description	
Key Considerations	
1. Is there a scenario-relevant chemical use inventory for the operation or facility? If so, collate the list of relevant chemical(s).	
2. What is the chemical form (solid, liquid, vapor)?	
3. Is the chemical neat or in a solution/mixture?	

Hazard and Toxicology Information *(Please refer to Appendix A: Dermal Hazard Resources)*	
1. Please describe relevant physical/chemical properties (e.g., molecular weight, pH, boiling point, viscosity, vapor pressure, water solubility, log K_{ow}, etc.)	
2. Does the chemical(s) have physical or chemical properties suggestive of a potential for direct (liquid or solid material contact) or indirect skin exposure (deposition via airborne chemical or contact with contaminated surfaces)?	
3. Does the chemical(s) have physical or chemical properties that inform the likelihood of dermal absorption? (e.g., high molecular weight, high volatility)	
4. What are the identified hazards?	
5. Does the chemical have a GHS classification for skin irritation or dermal toxicity?	
6. Does the chemical(s) have a skin notation?	
5. Does the chemical have a dermal LD_{50}?	
6. Is the chemical considered to corrosive or irritating to the skin?	

7. Is the chemical considered to be mutagenic or carcinogenic?	
8. Is the chemical a reproductive toxicant or cause teratogenicity?	
9. What is the target organ(s)?	
10. What are the symptoms of exposure?	
11. Based on the nature of the chemical(s), are the health effects likely to be a.) temporary or permanent, b.) direct (at point of contact), systemic, sensitization, or a combination?	
12. Are the anticipated health effects likely to arise from acute, acute delayed, or chronic exposure?	
13. Does the chemical have an occupational exposure limit (inhalation or dermal)?	
Source Description	
Key Considerations	
1. How many sources are present? Please describe them.	
2. What is the chemical usage (kg/day)?	
3. What is the volume of chemical being handled/applied?	
4. What is the concentration of the chemical in the mixture (if applicable)?	
5. At what temperature is the chemical/mixture being handled or applied?	

6. Is the chemical found in a mixture? What are the other components of the mixture?	
Exposure Characterization *Please refer to Appendix B: Dermal Exposure Assessment Resources for additional information.*	
Key Considerations	
1. What is the route for dermal exposure? (e.g., direct (liquid or solid material contact), vapor to skin, indirect (contact with contaminated surfaces)	
2. What area of the body is affected? (e.g., hands, forearms, whole body)	
3. What is the duration of the potential exposure?	
4. What duration of the workday is spent performing the tasks in which exposure is possible?	
5. In observing the task, are there clear opportunities for direct dermal exposure – (e.g., active contact with chemical(s), minimal contact, surface contact versus immersion)? What is the frequency of dermal contact while performing the task?	
6. Are there aspects of the handling or operation that preclude the potential for dermal exposure? (e.g., closed system; thermal considerations)	
7. Do worker interviews indicate potential for contacting chemicals during the completion of daily tasks?	
8. Are validated sampling methods available to	

assess dermal exposures?	
9. Do surface sampling techniques exist for the chemical(s)?	
10. Do occupational exposure limits exist or have safe handling limits been established?	
Occupational Health Assessment	
1. During interactions with workforce personnel have they noted any specific health-related concerns relevant to chemical exposures?	
2. Are there any observations of the workforce personnel that are suggestive of or consistent with health hazards of the chemical(s) being handled? (Presence of rash, etc.). Please note any potential incidences of direct, systemic, or sensitization effects.	
3. Has an occupational health care provider observed health effects (such as rashes or sensitization) in the worker population?	
4. Does the occupational health care provider have any dermal screening protocols in place? How frequently are these performed?	

Section 2: Data Availability Assessment

Please select "yes" or "no" for relevant document/resource availability. Refer to Appendices A and B for a list of useful resources that can be used to inform this section.

Scenario Relevant Documentation Review		
Please check "Yes" or "No" depending on whether the listed information is available. If checked "No", please add to the data gap/uncertainties section below.	**Yes**	**No**
1. Are current manufacturer-supplied SDS sheets available for the chemical(s)?		
2. Are there any relevant GHS classifications for this chemical?		
3. Are there existing regulatory assessment or toxicology review for the chemical(s)?		
4. Are there any hazard data summaries available?		
5. Does the chemical have an occupational exposure limit (OEL)?		
6. Does the chemical have a NIOSH skin notation profile?		
7. Have OSHA inspections, NIOSH Hazard Evaluations or other agency or expert group assessments exposure assessments been published for similar chemical handling operations that provide useful information for consideration?		
8. Are there prior internal industrial hygiene or other assessments available for the handing operation that assessed the potential for exposure?		
9. Are there any reports or records related to the health experience of the workforce in this handling operation (e.g., employee medical records, OSHA injury and illness logs, etc.)		
10. Is there a current relevant job hazard analysis or similar assessment document that documents the potential for dermal exposures for the chemical(s) of interest? This includes documentation of the degree of exposure and exposure frequency and duration by task.		
11. Has a literature search been performed to identify additional hazard and/or exposure data?		
12. Are validated sampling methods available to assess dermal exposures?		
13. Do surface sampling techniques exist for the chemical(s)?		

14. Do skin sampling techniques exist for the chemical (s)?		
15. Are there data from exposure modeling tools suggestive of the potential for dermal exposure? (See Appendix F for description of modeling tools).		
16. Are there any biological monitoring data available?		

Section 3: Identifying Data Gaps or Areas of Uncertainty

Please list any key questions in which the answer was "no" from the sections above here. This will help identify any potential data gaps (such as the need for a validated sampling method), or potential areas of uncertainty where more information is needed, or a risk mitigation strategy should be employed. In the notes section, please describe data collection or mitigation strategies.

Data Gap Identified	Notes

Signature of Surveyor: _____ Date:_____

APPENDIX D

DERMAL RISK RATING TOOL

Appendix D – Dermal Risk Rating Tool

		Low (Score 1)	Medium (Score 2)	High (Score 3)	Very High (Score 4)
Step 1: Dermal Hazard Rating[1]	Dermal Hazard Score	Reversible or very low skin or systemic toxicity	Moderate but reversible skin or systemic toxicity	Irreversible/chronic skin or systemic toxicity or sensitization	Life threatening skin or systemic toxicity, sensitization, or severe corrosivity
	GHS Classification	H313, H316 No GHS Carcinogenicity Category	H312, R21: Harmful in contact with skin	H314, H315, R38: Irritating to the skin R35: Causes severe burns (corrosive) R34:Causes burns (corrosive) R43: May cause sensitization by skin contact	H310, R27: Very toxic in contact with skin R43: May cause sensitization by skin contact
	Dermal Toxicology	LD50 (2000 - 5000 mg/kg)	LD50 (>1000 -<2000 mg/kg)	LD50 (>200 -≤1000 mg/kg)	LD50 (≤50 mg/kg)
	Dermal Symptoms	May be harmful in contact with skin; mild irritation; not likely to be an allergic sensitizer or corrosive to skin	Harmful in contact with skin; may cause irritation; low potential for allergic sensitization	Toxic in contact with skin; irritant; corrosive; may cause allergic sensitization	Highly toxic in contact with skin; high potential for allergic sensitization; severe irritation; highly corrosive
Step 2: Dermal Exposure Rating	Dermal Contact Area (CA)	Unexpected/unlikely	Very small area of contact	Contact possible to smaller areas of skin (hands, forearms, face, neck)	Contact possible to significant area of skin
	Parameters Impacting Contact Area	1. Reliable controls are in place 2. Small volumes (mL or mg) handled infrequently with good handling technique 3. Up to part of fingertips rarely exposed	1. Contact possible with small volumes (mL or mg) 2. Fingertips only or small amounts on other body parts	Contact possible to parts of hands, hands, and parts of forearms	1. Contact possible to significant area of skin (more than hands and forearms) 2. May have significant contamination of clothing (inside gloves, aprons, coveralls, or other garments)
	Dermal Concentration or Loading (C)	Negligible concentration of chemical likely to contact or load onto skin	Low concentration of chemical likely to contact or load onto skin	Moderate concentration of chemical likely to contact or load onto skin	High concentration of chemical likely to contact or load onto skin
	Parameters Impacting Concentration or Loading	1. Less than 1 µg/cm^2 adherent loading 2. Not likely to permeate from vehicle or substance matrix	1. Low viscosity carrier unlikely to remain as a film on skin 2. In the range of µg/cm2 adherent loading 3. Total daily concentration giving cause for concern: dust 500 mg, liquid 10 mg	Total daily concentration giving cause for concern: dust 50 mg, liquid 1 mg	Any amount of dust or liquid is cause for concern

		Low (Score 1)	Medium (Score 2)	High (Score 3)	Very High (Score 4)
	Dermal Contact Frequency (CF)	Minimal contact with skin; one or two incidental contacts; contact during less than 5% of task	Up to 10 incidental contacts with skin; contact during less than 10% of task	Up to 50 incidental contacts with skin; contact during less than 50% of task	Routine incidental contact with skin throughout shift; contact during 50-100% of task
	Dermal Retention Time (RT)	Amount transferred unlikely to remain on skin for any period of time	Amount transferred may remain on skin for some time	Amount transferred is likely to remain on skin for a significant period of time	Amount transferred very likely to remain on skin
	Parameters Impacting Retention Time	1. High volatility chemical (vapor pressure >5 hPa) (unless occlusion is expected) 2. Dry and powdery compound	1. Some volatility (semi-volatile, vapor pressure 0.1-5 hPa) 2. Damp powder or moist skin	1. Low volatility 2. High MW 3. Sticky or consolidated on skin	1. Non-volatile chemical (vapor pressure <0.1 hPa) 2. MW>100 3. Substance likely to stick to skin
	Dermal Penetration Potential (PP)	Not likely	Low potential	Possible or slow	Probably or likely
	Parameters Impacting Penetration Potential	1. Physical-chemical properties not compatible with skin permeation 2. MW>500 Daltons 3. log Kow outside of range -1-4	1. Small insoluble particles < 1 micron 2. Poor lipid solubility 3. Poor water solubility	1. Very small insoluble particles < 1 micron 2. Some lipid solubility 3. Some water solubility 4. Marginal skin health	1. Good lipid solubility 2. Good water solubility 3. Poor skin health 4. Solvents or other mixture components that may enhance absorption or present as dermal hazards themselves

Exposure Rating = CA * C * CF * RT * PP (see Figure below for scoring)

References:

1 Globally Harmonized System of Classification and Labelling of Chemicals (GHS)

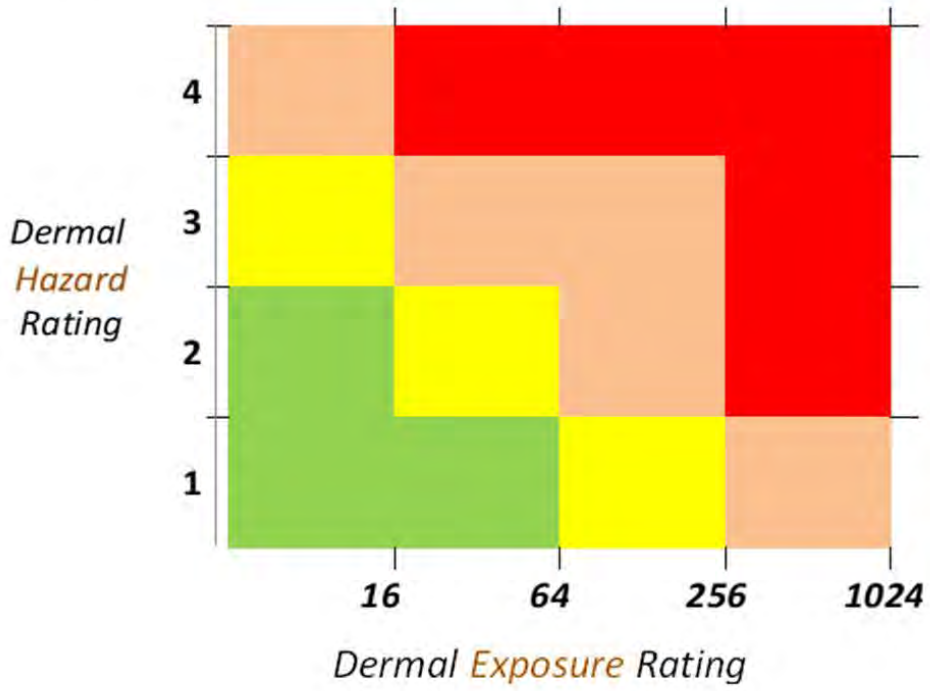
2 AIHA Dermal Exposure Tool (DRAM);

3 Garrod, A & Rajan-Sithamparanadarajah, R. (2003). Developing COSHH Essentials: Dermal Exposure, Personal Protective Equipment and First Aid. The Annals of occupational hygiene. 47. 577-88. 10.1093/annhyg/meg089.

4 Committee on the Design and Evaluation of Safer Chemical Substitutions: A Framework to Inform Government and Industry Decision; Board on Chemical Sciences and Technology; Board on Environmental Studies and Toxicology; Division on Earth and Life Studies; National Research Council. A Framework to Guide Selection of Chemical Alternatives. Washington (DC): National Academies Press (US); 2014 Oct 29. Appendix D, Overview of the GHS Classification Scheme in Hazard Classification. Available from: https://www.ncbi.nlm.nih.gov/books/NBK253967/

Step 3

Results



*Exposure Rating = CA * C * CF * RT * PP =*

APPENDIX E

SEG DEVELOPMENT FORMS

Appendix E – SEG Development Forms

Table 1: Example of Compiled Task-Level Detail for Hypothetical Process Technician (Based off JHA Below)

Job Title: **Process Technician** **Facility:** _____ **Department:** **Reactor**

							Process Parameters		Hazard Controls				
Task #	Task Description	Task Frequency	Duration (hr)	Routine/ Non-Routine	Potential Exposure Type	Hazard Description	Flow Rate (kg/hr)	Weight Fraction (%)	Engineering	Administrative	PPE	Existing Full-Shift Monitoring Data?	Existing Task Length Monitoring Data?
1	Collect sample from process line	1/week	0.25	Routine	Inhalation; Dermal	Liquid	100	100%	Closed-loop sample collection	Written operating procedure developed for use of closed-loop sample stations; Signs in area with PPE requirements	Chemical impervious clothing, gloves, boots, splash-proof goggles	No	No
2	Check and maintain process controls, unit equipment	1/day	3	Routine	Inhalation	Liquid	N/A	N/A	General ventilation (outdoors)	Process area access restricted to operators and maintenance personnel	Chemical impervious clothing, gloves, boots, splash-proof goggles	Yes	No

							Process Parameters		Hazard Controls				
Task #	Task Description	Task Frequency	Duration (hr)	Routine/ Non-Routine	Potential Exposure Type	Hazard Description	Flow Rate (kg/hr)	Weight Fraction (%)	Engineering	Administrative	PPE	Existing Full-Shift Monitoring Data?	Existing Task Length Monitoring Data?
3	Load raw chemical into hopper	1/week	1	Routine	Inhalation; Dermal	Liquid	50	100%	General ventilation and LEV (indoors)	Written operating procedure developed for loading; Signs in area with PPE requirements	Half-face APR; chemical impervious clothing, gloves, boots, splash-proof goggles	No	Yes
4	Work in Control Room	1/day	4	Routine	None	N/A	N/A	N/A	N/A	N/A	Steel Toed Boots	Yes	No

Note: Rows would continue to build out all tasks performed by the process technician on a routine and non-routine basis, with associated hazard description, process parameters, and hazard control information.

Table 2: Example Industry-Wide SEG Designations based on Task-Level Exposure Information (for Epoxy Resin Manufacturing)

Process Area	Job Title	Task Description	Frequency	Potential Exposure Type	Exposure Data Available (type)?
Reactor	Process Technician	Routine operations at process unit includes, maintaining and monitoring process controls, unit equipment and gauge recordings	Daily	Inhalation	Yes (Full-shift, inhalation)
Reactor	Process Technician	Collect sample from high concentration process line %; closed-loop sample collection.	Weekly	Inhalation; Dermal	Yes (Task, inhalation)
Reactor	Process Technician	Collect samples from intermediate lines with low-moderate concentration %; closed-loop sample collection.	Weekly	Inhalation; Dermal	Yes (Task, inhalation)
Reactor	Process Technician	Check strainers in process line between weight hopper and reactor	Monthly	Inhalation, Dermal	No
Reactor	Process Technician	Prepare equipment for maintenance (block/ bleed lines; drain process lines)	Weekly	Inhalation	Yes (Task, inhalation)
Reactor	Maintenance Technician	Line breaking and equipment opening to perform preventive maintenance tasks	Weekly	Inhalation, Dermal	Yes (Task, inhalation)
Loading/Transport	Logistics/Distribution Technician	Sampling, moving, spotting, and loading bulk chemicals for transfer to laminator	Daily	Inhalation, Dermal	No
Wastewater / Air Treatment	Utility Technician	Routine operations including sample collection, chemical addition, monitoring operations, and equipment inspection.	Daily	Inhalation	Yes (Full-shift, inhalation)
Laboratory	Lab Technician	Routine operations in laboratory, including performing chemical and physical laboratory tests, prepare chemical solutions, and writing technical reports.	Daily	Inhalation	Yes (Full-shift, inhalation)

Sample Blank JHA Form (adapted from OSHA 2002)

*** NOTE: Companies may already have PSM and/or JHA documentation that documents this level of detail on specific tasks. This form is not a requirement, rather provided as an example of the granularity in task-specific information requested.*

<table>
<tr><td>Job Title:</td><td colspan="2">Job Location:
• Facility:
• Department:
• Sub-Department:
• Equipment Number:</td><td>Date:</td></tr>
<tr><td colspan="4">Task #:
Task Description:
Task Frequency:
Task Duration:
Routine/ Not Routine:</td></tr>
<tr><td>Potential Exposure Type (check):
☐ Inhalation
☐ Dermal</td><td>Hazard Description:
Physical State (check):
☐ Solid
☐ Liquid
☐ Emulsion
☐ Particulate
☐ Gas
Notes:</td><td colspan="2">Process Parameters (at location):
Flow Rate of Process (kg/hr):

Weight Fraction of chemical:

Attach or draw below diagram of process layout with note where in process this task occurs</td></tr>
<tr><td colspan="2" rowspan="3">Existing Monitoring Data (check)?
☐ Yes
☐ No
☐ Unknown

Notes:</td><td colspan="2">Hazard Controls
Engineering:</td></tr>
<tr><td colspan="2">Administrative:</td></tr>
<tr><td colspan="2">Personal Protective Equipment:</td></tr>
<tr><td colspan="4">Rationale or Comments:</td></tr>
</table>

APPENDIX F

DERMAL MODELING TOOLS

Appendix F – Dermal Modeling Tools

Dermal Model	Developed by?	Model Type	Applicable Use Scenario	Brief Overview	Input Parameters	Pros	Cons	Validated?
ECETOC TRA	ECHA REACH	Quantitative	1.) Hand and forearm only exposures 2.) Liquids and solids	Tier 2 Dermal exposure model that estimates dermal exposures from low volatile liquid products and solids in liquid to the hands, and in some cases, parts of the forearms. It builds upon the existing ART framework and incorporates elements of the ART model for estimating dermal contamination by aerosol deposition. It follows source-receptor approach and uses modifying factors to refine the model.	1.) PROC 2.) Type of setting (industrial vs. professional) 3.) Dustiness of solids (High medium low) 4.) Vapor pressure of liquids 5.) Duration of exposure 6.) Ventilation 7.) Concentration of substance in mixture 8.) Use of dermal PPE	1.) Relatively simple setup 2.) Does not require many inputs or include many exposure modifiers	1.) Limited flexibility with operational conditions and risk management measures 2.) Clear bias towards (severe) overestimation of dermal exposure at low measured exposure values - an effect of built-in underestimation of PPE protection values 3.) Apparent underestimation of dermal exposure at high exposure values 4.) Sampling method (interception vs. removal) had effects on the exposure estimation of the models	Corroborated using independently measured exposure data in Marquart et al. (2017)

Dermal Model	Developed by?	Model Type	Applicable Use Scenario	Brief Overview	Input Parameters	Pros	Cons	Validated?
Dermal Advanced REACH Tool (dART)	Jointly funded by HSE, the Dutch Government, the AFSSET, the CEFIC LRI, Shell, Eurometaux, the BOHS and GSK. Developed by scientists at six European research organizations	Qualitative	1.) Hand only exposures 2.) Low-volatile liquids 3.) Various exposure routes - deposition from air, direct emission and direct contact, and transfer from surfaces	Based on an existing inhalation model (ART), a mechanistic model based on the source-receptor approach. The dART model is a mechanistic and statistical modeling. framework. This model assigns a multiplier or score which is calibrated to measurement data. Exposure estimates can be adjusted based on modifying factors like surface area, direct emission, and transfer potential. The model can be used to estimate a TWA for a single task in a work day or shift. Additionally included inter-worker variability.	1.) Deposition rate of product onto hands per minute 2.) Unspecified parameters previously included in ART model *model is not incorporated into existing ART online software, parameters subject to change	1.) Easy to use web-based tool; 2.) Takes into account occupational activities, operational conditions, and risk management measures for liquids or solids; 3.) Scenario-specific exposure data is not needed; 4.) Model was calibrated with measured data; 5.) Combines mechanistic model with measured data in a Bayesian statistical process; 6.) Provides exposure distribution percentiles	1.) Compared to other Tier 1 models, it requires a lot of information; 2.) Expert judgement may be needed to select input parameters; 3.) Does not predict dermal exposures; 4.) Unable to estimate exposures to other body areas (other than hands); 5.) Cannot estimate exposure to fumes, gases, or fibers; 6.) Does not include removal processes like handwashing; 7.) Unable to combine multiple activities into one work shift; 8.) Difficult to convert factors driving exposure estimate into operational conditions and risk management	Not yet validated. Based on existing ART framework and incorporates elements of ART model for estimating dermal exposure via aerosol deposition.

Dermal Model	Developed by?	Model Type	Applicable Use Scenario	Brief Overview	Input Parameters	Pros	Cons	Validated?
Bayesian Exposure Assessment Tool (BEAT)	United Kingdom HSE with European Biocidal Products Directive (has since been replaced by the biocidal products regulation [BPR])	Quantitative	1.) Hand and body exposures 2.) Solid/liquid exposures 3.) Various task-based parameters (spraying, automated, partially automated)	Dermal model that provides dermal exposure as mass rate for the hands and potential exposure to the body for a specific defined area od the skin and a specific application rate presented in the database. Developed in 2002 by the UK's HSE for undertaking regulatory risk assessment. BEAT provides the option to search for appropriate generic data based on task, and a hierarchical Bayesian model for probabilistic predictions.	1.) Physical state 2.) Particle size 3.) Particle wetness 4.) Viscosity 5.) Volatility 6.) Work environment (confined, restricted, open) 7.) Automation level (partial, fully) 8.) Type of ventilation 9.) Whether liquid bases dust control is used 10). High/low energy process 11.) Spray pressure (high pressure, shower) 12.) Segregation of worker from source 13.) Surface area of contact 14.) Level of contamination 15.) Frequency of skin contact 16.) Application use rate (L or Kg/min) 17.) Distance to source 18.) Length of tool handle 19.) Orientation (overhead, level) 20.) Duration of exposure (minutes)	1.) Provides dermal exposure to hands and potential exposure to other areas of the body 2.) Web tool (may or may not still be active, could not find a working link) 3.) Combines measured data from database with Bayesian models 4.) High resolution input parameters allow for detailed task description 5.) Users are not restricted to data extracted from database and may input other data	1.) Details regarding underlying algorithm are not publicly available 2). Web tool may no longer be functional	Not Validated.

Dermal Model	Developed by?	Model Type	Applicable Use Scenario	Brief Overview	Input Parameters	Pros	Cons	Validated?
RISKOFDERM	European 5th framework programme project	Quantitative	1.) Estimating dermal exposure in generic risk assessment for single chemicals 2.) Risk assessment and management in small-medium sized enterprises	This quantitative conceptual model to estimate risk for regulatory purposes, such as registration of new chemicals, and simple-to-use toolkit for assessment and management of risks from dermal exposure. The tool translates information input by the user into broad data categories of hazard and exposure that lead to a rough estimate of health risk from dermal exposure.	1.) Type of skin contact 2.) Frequency of skin contact 3.) Type of product handled 4.) Viscosity of the product 5.) Volatility of the product 6.) Dustiness of the product 7.) Use rate of the product 8.) Formation of aerosols 9.) Manual or automated tasks 10.) Direction of application 11.) Tools used 5 12.) Quality of ventilation 13.) Direction of airflow 14.) Segregation of worker from source 15.) Distance of worker from sources	1.) Easy to use 2.) Task based model that takes into account different handling types/processes 3.) Can evaluate potential exposure of hands and body 4.) Data driven (based on large set of dermal exposure data); 5.) Can use conservative inputs to account for limit information	1.) Not ideal for handling powders or for very volatile substances; 2.) Information needed may not be available to assessor (use rate etc..); 3.) Cannot evaluate exposure on specific parts of the body besides hands; 4.) Does not take into account clothing or glove protection; 5.) Data set may be heterogeneous; 6.) Probabilistic assessments are not possible; 7.) Cannot combine estimates for separate tasks to full shift estimates	Not validated with independent data; however, model has been validated for similar exposure scenarios measured in the data set used to build the model (Warren 2006)

Dermal Model	Developed by?	Model Type	Applicable Use Scenario	Brief Overview	Input Parameters	Pros	Cons	Validated?
Dermal Exposure Assessment Method (DREAM)	Peer-reviewed paper, based on the theoretical model (Schneider et al. 1999). Paid for by the Dutch Ministry of Social Affairs and Employment/ South Africa Netherlands Research Program on Alternatives in Development.	Semi-quantitative	1.) Solid/liquid exposures 2). Direct contact and contaminated surface exposures 3.) Decontamination of skin scenarios 4.) Task/job ranking	This semi-quantitative model evaluates potential occupational exposure to chemicals for any given occupational situation. It is a useful tool for tiered approach for initial assessments of dermal exposure for the purposes for hazard evaluation or hazard control.	1.) Source present 2.) Contaminant layer present 3.) Decontamination of contaminant layer 4.) Source strength, emission evaporation, decontamination 5.) Decontamination of skin 6.) Event per unit time 7.) Probability and intensity of dermal exposure routes (per body part) 8.) Use of clothing (per body part)	1.) Consists of two parts, inventory and evaluation 2.) Inventory addresses general info (company, department, job, task, and exposure) 3.) Evaluation addresses dermal exposure assessment determinants 4.) Evaluates both potential exposure (clothing and uncovered skin), and actual exposure (exposure on skin); 5.) A model that is good for initial assessments of dermal exposure for tasks, or groups of workers to help inform hazard evaluation or control	1.) Not ideal for regulatory use; 2.) Limited information exists for dermal exposure determinants, so values are assigned with professional judgement or assumptions; 3.) Potential variability in assigning tasks based on different observers; 4.) Time-consuming	The accuracy and reliability have been evaluated.

Dermal Model	Developed by?	Model Type	Applicable Use Scenario	Brief Overview	Input Parameters	Pros	Cons	Validated?
IH Skin Perm	American Industrial Hygiene Association (AIHA) in collaboration with the original model creator Dr. Wil ten Berge	Quantitative	1.) Can be used for any skin location, exposure is based on surface area; 2.) Undamaged skin 3.) Not to be used for irritants; 4.) Applicable for substances with log Kow -3 to 6 and molecular weight (MW) < 600.; 5.) Might need to consider whether chemical has enhanced absorption (higher than in water)	Estimates absorption from as a result of different occupational exposure scenarios (such as instantaneous deposition, deposition over time, or from airborne vapors).	1.) Data source (database, user data) 2.) Scenario parameters (instantaneous vs. deposition over time vs. vapor to skin) 3.) Dose 4.) Affected skin area 5.) Thickness of stagnant air 6.) Chemical 7.) Timing parameters 8.) Report parameters	1.) The tool is easy to use 2.) The library contains 100 chemicals which have skin notations; 3.) Estimates can be compared to OELs for risk assessment purposes; 3.) Provides estimate of lag time until steady state loading, which is helpful to understand when to implement handwashing and other removal behaviors	1.) Model assumes healthy undamaged skin; 2.) Substances that may irritate or cause structural damage to the skin are not a good fit for this model; 3.) Unable to determine influence of solvents or other additives that may potentially increase dermal absorption; 4.) Should only be used for chemicals that have specific properties, not applicable to high molecular weight compounds, or anything with a Kow >6	Yes, validated compared to observed absorption data from published human studies

Dermal Model	Developed by?	Model Type	Applicable Use Scenario	Brief Overview	Input Parameters	Pros	Cons	Validated?
Stoffenmanager	Dutch ECHA REACH	Qualitative (for dermal only - Inhalation portion of model has quantitative	1.) Estimating task-based exposure levels (inhalational only) 2.) Control banding for dermal exposure scenarios (no quantitative results)	A web-based tool that consists of several modules: a control banding section (qualitative dermal and inhalation), and a general quantitative and REACH-oriented quantitative section that are both inhalation only. Dermal inputs and outputs are significantly less developed and comprehensive that the inhalation modules. Exposure assessments are limited to inhalation, dermal parameters are limited to control banding.	1.) Physical state of the substance (solid or liquid) 2.) Whether there are activities that may cause emission of dust. 3.) Vapor pressure of liquids or dustiness (solid articles, firm granules or flakes, granules or flakes, coarse dust, fine dust, extremely dusty products) 4.) Type of dust emitted from solid objects 5.) Percentage of the substance(s) in the product 6.) Level of dilution of liquid products with water 7.) Handling category 8.) Duration and frequency 9.) Local controls (including local exhaust ventilation (LEV) and containment) 10.) Distance of the worker from the source 11.) Presence of secondary emission sources 12.) Room volume 13.) General ventilation 14.) Emission control measures (such as control rooms) 15.) Respiratory protective equipment (RPE) used 16.) Information on whether the work area is regularly cleaned 17.) Information on whether machinery and equipment are regularly inspected and kept in good order.	1.) Online tool is intuitive and easy to use 2.) User can create an inventory of chemicals and tasks to create different risk assessment scenarios	1.) Dermal modelling is not the focus of the software 2.) Very robust tool with significant predictive power 3.) Conservative enough for a REACH tier 1 tool 4.) Extensive input is required to build the site and exposure profile before the tool can be used for risk assessment 5.) The user must pay a fee to access full capabilities	Has been validated and refined in several publications and the ISAB guarantees the tool complies with regulations.

Dermal Model	Developed by?	Model Type	Applicable Use Scenario	Brief Overview	Input Parameters	Pros	Cons	Validated?
AIHA DRAM (Dermal Risk Assessment Model)	AIHA	Qualitative	1.) Estimating dermal exposure risk for predetermined skin areas during specific scenarios 2.) Hand/forearm or significant skin contact area scenarios	An interactive macro-enabled excel workbook, that allows the user to calculate exposure ratings based on input parameters and either Monte Carlo or deterministic simulations.	1.) Dermal contact area 2.) Dermal loading/concentration 3.) Contact frequency 4.) Dermal Retention Time 5.) Dermal penetration potential 6.) Dermal hazard rating	1.) Extremely easy to use 2.) Fast, free download with relatively simple input parameters 3.) Immediate qualitative risk rating generated	1.) Simple qualitative output: dermal hazard rating of 1-4 2.) User cannot save scenarios or agents 3.) Requires qualitative hazard judgement as input parameters (user must understand penetration potential, general hazard levels)	Not validated.
ChemSTEER	EPA	Quantitative	1.) 1-hand dermal contact with liquids 2.) 2-hand dermal contact with liquids 3.) 2-hand immersion in liquids 4.) 2-hand dermal contact with solids 5.) 2-hand contact with contaminated surfaces 6.) User defined scenarios can be created	An interactive downloadable application that generates screening level estimated for environmental releases and worker exposure to chemicals in industrial settings. ChemSTEER is intended for use when worker exposure data are not available. ChemSTEER contains some generic scenarios for correlating exposure scenarios with a task.	1.) Surface area of contact 2.) Quantity remaining on skin 3.) Weight fraction of chemical (for liquids) 4.) Frequency of events	1.) Contains pre-defined scenarios which minimize effort required to prepare an assessment 2.) Includes several dermal and inhalation exposure models 3.) Includes peer-reviewed mathematical models 4.) User can use preloaded scenarios; build assessment 5.) Software limitations have already been identified and described	1.) Requires significant amount of knowledge and input to generate scenarios. 2.) "Screening levels" of results are intended to be conservative and are likely higher than average compared to real world scenarios. 2.) Requires that the user be familiar with the tool, process chemical information (chemical/physical properties), amount of chemical used in processes, relationship with supplier-customer operations, best estimate of fraction of chemical devoted to each operation	EPA states that ChemSTEER models have been extensively reviewed and validated, but few public publications are available to confirm this.

Dermal Model	Developed by?	Model Type	Applicable Use Scenario	Brief Overview	Input Parameters	Pros	Cons	Validated?
NIOSH Finite Dose Model	NIOSH	Quantitative	1.) Calculating steady state permeability from aqueous solutions of infinite volumes corresponding to typical occupational exposure scenarios	This calculator estimates fluxes, skin concentrations, and amounts of compound absorbed from any size dose applied to partially or fully hydrated skin.	1.) Molecular weight 2.) log Kow 3.) Melt/boiling point	1.) Free downloadable tool 2.) Chemical parameter data widely available	1.) Requires Java runtime environment 2.) Requires known chemical data, will not work for novel chemicals	Mathematical models have been evaluated; however overall model has not been compared with occupational exposure data.
ConsExpo	Dutch National Institute for Public Health and the Environment (RIVM)	Quantitative	Estimating dermal exposure from consumer products	ConsExpo is a validated model and web-based tool that can be used to estimate dermal exposure to chemicals from consumer products, taking into account various factors such as product composition, use patterns, and skin permeability.	1.) Body weight (defaults) 2.) Body surface area (defaults) 3.) Contact rate (specific to product type and scenario) 4.) Release duration (specific to product type and scenario) 5.) Exposed area (specific to product type and scenario) 6.) Product use amount (specific to product type and scenario)	1.) Web based tool 2.) Takes into account product use scenario for parameters	1.) Applicable to consumer exposure scenarios but not occupational scenarios 2.) Requires more detailed assessment for input data	Has been validated

Dermal Model	Developed by?	Model Type	Applicable Use Scenario	Brief Overview	Input Parameters	Pros	Cons	Validated?
DustX	Netherlands National Institute for Public Health and the Environment	Quantitative	1.) Calculating human exposures to semi-volatile dusts	While intended for exposure to off-gassed and dust exposures in residential settings, the model estimates exposures to dust and semi-volatile solids on skin	1.) Room volume, ventilation rate 2.) Substance properties (Log Koa, MW, mass transfer coefficient, transdermal permeability coefficient) 3.) Product/emission parameters (surface area, volume, concentration) 4.) Dust parameters (organic matter content, loading, density, elimination rate from environment) 5.) Indoor surface parameters (surface area, total surface area for sorption, surface/air partitioning) 6.) surface layer thickness 7.) Airborne particulate matter parameters (air concentration, density, mass transfer coefficients, organic matter content) 8.) Exposed population parameters (adult/child, inhalation rate, body weight, skin surface area, ingestion rate) 9.) simulation parameters (simulation duration, exposure frequency, exposure duration) Exposure parameters (oral absorption fraction, inhalation absorption fraction	1.) Free, easy to use web-browser tool 2.) Parameter scenarios can be exported and saved and imported later 3.) Captures dermal contact, inhalation, and ingestion parameters for total body burden calculation 4.) Includes parameter guides to help user choose inputs based on published literature	1.) Intended for non-occupational scenarios 2.) Does not include parameters for PPE, tasks, any occupational scenarios 3.) Requires significant amount of input parameters	Individual model parameters have been evaluated but the total model has not been validated.

APPENDIX G

IH DATA ANALYTICS STRATEGY

Appendix G – IH Data Analytics Strategy

1. SOP for Combining Data

When attempting to standardize data from multiple sources (such as different facilities and workplaces) it is critical that information collected is as consistent as possible. Below is a table of the most critical data elements that need to be collected in order to facilitate the combination of data from different sources.

Table 1. Data Elements Needed to Combine Data

Data Element	Description
Facility Code	Anonymized code for each facility
Date	Date of data collection (YYYY-MM-DD)
Sample Number	Number that links back to a specific sample
Sample Media	Type of media that a sample is collected on (e.g., tape, wipe, etc.)
Sample Surface	Type of surface that a sample is collected from (e.g., skin, metal, clothing)
Surface Area	Surface area (m^2) of the sample collection
Chemical	IUPAC Chemical Name
Job Title	Job title assigned to an employee
Task Description	Description of the task undertaken by an employee
Process Information	Information on the large process associated with the worker's task
PPE	Personal protection equipment used

This data can easily be tabulated into a spreadsheet to be combined with other data for analysis. Broman & Woo (2018) outlined important steps that can help ensure that data is entered in a way that minimizes the amount of data cleaning necessary to conduct an analysis.

1. Be consistent – the more consistent the entries are the easier it is to analyze the data.
2. Be thoughtful in how things are named – try to avoid generic terms that could be confused later on.
3. Write dates according to ISO 8601 (YYYY-MM-DD) – this makes it easier to combine data from companies located outside of the United States.
4. Do not leave cells empty. If information is missing or unknown, indicate that with a standardized value such as "NA".
5. Put one piece of information in a cell. It is better to have more columns of data than squeezing multiple pieces of data in to one cell. For example, if a measurement is <0.01

it is better to express this information in two columns, one for the less than symbol and one for the numeric value.

6. Create a data dictionary. Avoid putting notes in the spreadsheet containing the data. Instead make new document that contains the descriptions and definitions of any codes.
7. Do not perform any calculations in your dataset. This has the potential to confuse a data analysis and lead to erroneous results.
8. Do not use fonts or highlights to indicate information. If the spreadsheet is loaded into statistical software (R, Stata, SPSS, SAS, etc.) any formatting information from the spreadsheet will be lost.
9. Make sure to back up your data. Preferably with a version saved on the cloud to avoid data loss.

2. Data Analytics Strategy

2.1 Descriptive Statistics and Plots

Descriptive statistics and plots are useful tools for understanding a dataset. The following descriptive statistics will be calculated in order to understand the characteristics of a dataset: Minimum value, the 25^{th}, 50^{th}, 75^{th}, 95^{th}, and 99^{th} percentiles, maximum value, arithmetic mean, standard deviation, geometric mean, and geometric standard deviation. These values should be calculated for the overall dataset, but also stratified by important factors (e.g., facility, task, job title, etc.) that may have a latent effect on the distribution of measurements. Descriptive plots will also be used to describe the distribution of the data, including box and whisker plots, scatterplots and histograms.

2.2 Measurements Below the Level of Detection (LOD)

It is not uncommon for a certain percentage of measurements to be below the level of detection (LOD). Even within the same SEG the reported LODs can vary. The most conservative approach for handling measurements below the LOD is to simply assume that the reported LODs are accurate estimates of exposure. This method is one possible approach because it is straight forward and allows for a comparison to other methods to determine the potential impact of left-censoring on the dataset. However, this approach reduces variability and will impart a positive bias on measures of central tendency (Hewwtt & Gasner 2007). By far, the most commonly employed method for adjusting values below the LOD is substituting the reported LOD by dividing by the value of 2 or the square root of 2 (Finkelstein & Verma 2001). However, EPA's Guidance for Data Quality Assessment (EPA 2000) notes that this approach is only appropriate for datasets where 15% or less of the data is below the LOD. For this dataset, EPA suggests that Trimmed mean, Cohen's adjustment, or Winsorized mean and standard deviation be used (EPA 2000).

The trimmed mean method involves removing a set percentage if measurements in the tails of the exposure distribution. EPA (2000) states that it is "also possible to trim the data only to replace the nondetects". However, this approach will result in a positive bias in measurements and reduces the total sample size of the dataset. The Winsorized method is similar to the trimmed mean method only the most extreme values in the exposure distribution are replaced with the next most extreme values. The two main differences between this method and the trimmed mean method is that values are replaced and not dropped from the analysis and the replacement is done based on a count of extreme values in each tail, so that the replacement is symmetrical on each side of the distribution. This avoids both data loss and minimizes the positive bias on the mean.

Cohen's Method utilizes a maximum likelihood estimation (MLE) approach to calculate adjust mean and standard deviations for measurements below the LOD. However, Cohen's Method can only be used when a single LOD is present, which is often not the case. Another method recommended by EPA (2009) and commonly employed is the Kaplan-Meier method. This method involves fitting the left-censored data to a known distribution (most commonly the normal or log-normal) distribution and estimating an adjusted-mean and standard deviation for the population. However, this approach only allows for the calculation of an adjust-mean and standard deviation for a group of measurements, which greatly limits the utility of this method. To get around this issue, we suggest the use of robust regression on order statistics (ROS), which is also recommended by EPA (2009). This method uses a statistical model to impute (i.e. estimate) individual values below the LOD, based on a defined underlying probability distribution (in this case a log-normal distribution).

Regardless of which method is used, it is advisable to conduct a sensitivity analysis to determine the impact a chosen approach will have on the final results.

2.3 Potential Outliers

Outliers are values that are not representative of the overall distribution (EPA 2000). However, for log-normal data it is important to distinguish between true outlier values and values that are expected to occupy the right tail of the distribution. In order to assess the presence of potential outliers in the dataset the measurements must first be standardized to the same sample period. Reported measurements were standardized to an 8-hr TWA using Equation 1 (AIHA 2015).

$$8hr\ TWA = Concentration\ \times \frac{sampling\ duration\ (\min)}{480\ min}$$

Equation 1. Calculation of an 8-hr TWA

There are numerous approaches for identifying potential outliers. The most basic approach is to use the underlying exposure distribution to calculate a threshold where any values above the threshold are considered outliers. This can be done by using Equation 2, where Q3 is the third quartile (75th Percentile) and the IQR is the interquartile range (75th percentile-25th percentile). This approach as the advantage of being simple to calculate, but risks over classifying outliers when the underlying data follows a log-normal distribution. However, because the simplicity of this method, it was chosen as one of the possible methods for identifying outliers.

$$Threshold = Q_3 + 1.5 \times IQR$$

Equation 2. Calculation for the Upper Threshold

Another approach involves using hypothesis testing to determine if a measurement or group of measurements are outliers. The most commonly employed hypothesis test is the Grubbs Test. However, this test is only suitable to detect a single outlier. While this test could be run multiple times by continuously excluding each identified outlier, this would inflate the type 1 error rate (false positive) of the hypothesis test. Another commonly used test is the Tietjen-Moore test which works for multiple outliers but requires the suspected number of outliers to be specified before running the test. However, the results of the tests should be based on the data itself, thus the Tietjen-Moore test is not ideal for this situation. The Generalized Extreme Student zed Deviation (ESD) test, otherwise known as the Rosner's Test, is a more general form of the Grubbs test which allows for the detection of multiple outliers, by adjusting the critical value used on the hypothesis test based on the number of outliers being evaluated. Because this is

one of the more robust hypothesis tests for detecting outliers it was chosen as a possible method for evaluating potential outliers.

Regression analysis can also be used for detecting potential outliers. The log-transformed measurements were regressed using Equation 3, where β_0 is the intercept, β_1 is the regression coefficient for each SEG, and ϵ is the error term. The regression equation can be used to look for measurements that are outliers or exhibit high leverage or high influence on the model estimates. Cooks Distance provides a means to quickly identify influential measurements. By comparing the resulting distances to a threshold (4/N) it's possible to identify potential outliers.

$$\log(measurement) = \beta_0 + \beta_1 \times SEG_i + \epsilon$$

Equation 3. Regression Equation for SEGs

2.4 Statistical Assessment of SEGs

While there is not a single definition of what constitutes an SEG, one metric is to measure the amount of variability within each SEG is to the calculate fold-range difference for the middle 95% of an exposure distribution (Rappaport & Kupper 2008). This can be visualized by plotting the data from a specific SEG on a log-probability plot. Additionally, an analysis of variance (ANOVA) can be conducted on the log-transformed data to determine if a statistically difference in means exists between groups. Alternatively, a Kruskal-Wallis test (a non-parametric ANOVA) can also be employed to determine if there is a statistical difference between the medians of the SEGs. As both these are omni-bus tests specific post-hoc statistical tests can be employed to determine between which groups the statistically significant difference actually exists. While these statistical tests are useful, they must be used in conjunction with expert knowledge on the processes, jobs, and tasks that take place in a given workplace.

3. References

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APPENDIX H

EMPIRICAL DATA COLLECTION SHEET

Appendix H – Empirical Data Collection Sheet

FIELD SAMPLING DATA SHEET

General Information		
Project:		
Facility:		
Date Sampled:		
Sampled By (Industrial hygienist, employee etc.)**:**		
Sample Objective (check)**:**	☐Compliance ☐ Worst-case ☐Routine (Baseline)	
Product of Interest (include manufacturer)**:**		
Chemical of Interest:		
Facility/Sampling Location		
Location within Facility (process area, office, etc.)**:**		
Tasks to be performed during sampling:		
Weather Conditions (outdoor)	**Temperature** (F):	
	Relative Humidity (%):	
	Wind Direction:	
	Wind Speed:	
Employee Information		
Worker Name / ID # (if applicable):		
Job Title:		
Shift (check):	☐ First ☐ Second ☐ Third	
Shift Duration (check):	☐8 hour ☐10 hour ☐12 hour	
Employee Skin Condition:		

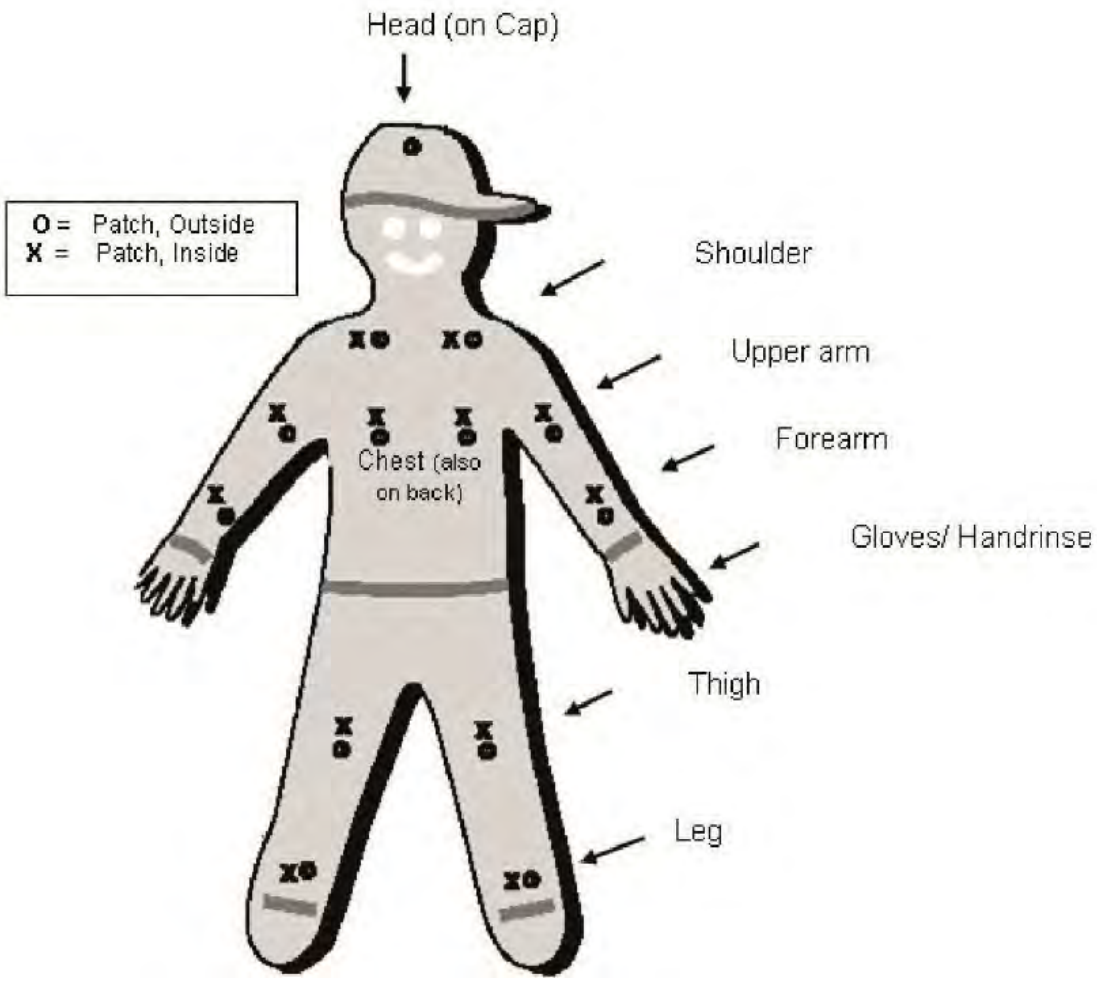
Sample Information	
Sample ID (match label)**:**	
Sampling Method (e.g., EPA/ASTM/NIOSH/OSHA):	
Sampling Method Type (check):	☐ Direct ☐ Indirect
Sample Collection Method (check):	☐ Rinse Method ☐ Wipe Method ☐ Tape Method ☐ Patch/Pad Method ☐ Glove Method ☐ Whole Body Dosimetry ☐ Fluorescent Tracers Method
Location of Sample Collection (check):	☐ Skin ☐ Surface ☐ Clothing
Skin Location (if applicable):	
Sample Collection Media and manufacturer (e.g., tape, hand rinse, dermal/surface wipes, skin patches, tracer/dye, cloth, pad, clothing, etc.)**:**	
Sample Type (check):	☐ Full-Shift ☐ Task-Length
Sample Start Time:	
Sample Stop Time:	
Total Sample Duration (calculate Stop-Start; min):	
Notes on deviation from sampling method (e.g., patch fell off, etc.):	

Description of Activities/Tasks Performed During Sampling At least four (4) check-ins should be conducted during the sampling period. Record information on work practices, tasks/activities performed, PPE utilized (including condition during task), workplace controls (e.g., ventilation), etc.		
Check-in Number	**Time**	**Description of Activities**

Surface Wipe Sampling		
Sampling Media Type and manufacturer:		
List location(s) sampled (e.g., work surface, skin surface (e.g., hands, neck, face), clothing or glove, etc.):		
List Surface Area of locations for all samples collected (e.g., Sample 1 (Countertop) 100 cm^2):		
Patch Sampling		
Sampling Media Type and manufacturer:		

Tasks performed during sampling:

Mark location(s) of sample apparatus/media (e.g., body location on worker)**:**



Adapted from EPA Dermal Exposure Assessment Handbook

List Surface Area and location of all patches (e.g., Sample 1 (Left arm) 25 cm^2):

PPE Use	
Does worker require PPE?	
If Yes, specify PPE type, specifications, and manufacturer (e.g., half-face respirator, OVM cartridge,	

3M, faceshield, gloves, gown, apron, goggles, boot covers, etc.)**:**	
If Yes, specify tasks during which PPE is used:	
If Yes, describe condition of PPE:	
Workplace Control Use	
Does Process or Task Area have workplace controls?	
If Yes, specify control type, specifications, and manufacturer (e.g., mechanical ventilation, hood, enclosure, fan, etc.):	
If Yes, specify tasks during which controls are used	

Sample Analysis	
Analytical Method *(e.g., EPA/ASTM/NIOSH/OSHA)*	
Field Analysis Requirements (e.g., solvent type needed following sample collection, etc.):	
Analytical Laboratory	

APPENDIX I

SAMPLING AND ANALYTICAL METHOD DEVELOPMENT

Appendix I – Sampling and Analytical Method Development

This document is intended as a general guide to assist in providing key elements to develop a robust analytical method. It is not meant to provide specific recommendations regarding which analytical method or sampling study design is appropriate for the occupational exposure scenario of interest. However, the below components, at minimum, should be addressed in any analytical method development for the chosen sampling method (e.g., rinse, wipe, patch). These elements should ideally be developed in partnership with an accredited analytical laboratory. Prior to engaging a laboratory, a literature review should be performed first to identify any available methods (even if unvalidated) or similar sampling methods that can be adapted or modified.

1. Key Considerations

The following elements should be considered when developing or validating an analytical method:

- What is the overall objective of the method development or validation study?
- How many samples are needed to validate each phase of the method?
- What are the potential interferences or contamination sources?
- What will the limit of detection (LOD) or limit of quantification (LOQ) be?
- Is the proposed LOD/LOQ low enough for the purposes of the exposure assessment?
    - How does it compare to exposure levels at which toxic effects are seen?
    - How does it compare to occupational exposure levels?
    - Is it comparable to the proposed OEL, if available?
- Does the chosen laboratory follow good laboratory practices (GLP)?
- Is the laboratory accredited by AIHA?
- What QA/QC procedures will be followed?
- How will the precision, accuracy, and recovery of the method be evaluated/reported?
- How will the method be validated?

2. Objective and Scope

A clear study objective is needed to determine experimental design. Once a sampling method is decided upon, a proposed analytical method can be developed and validated prior to conducting in-field sampling on worker populations. The sample number will depend on the use of the data, and the scope of the study.

3. Study Design and Collection Method

Validation of an analytical method is inherently dependent upon the needs and design of the planned data collection method (e.g., wipe methods). As a result, it may be most efficient to validate both analytical and sampling methods concurrently. Specific elements that should be considered in the study design and collection method include:

- What chemical is being sampled?
    - Are there physicochemical properties that may influence which collection method is used?
    - Are there any potential interactions between the chemical and other analytes in the proposed method?
- What location is being sampled (skin, clothing, work surfaces)?
- What is the sample medium?
- What is the wetting agent?
- What is the collection technique?
- What does the published data suggest about the collection efficiency of the proposed collection method?
- Are serial or sequential samples needed (such as for wipes)?

The sample design will greatly impact the collection efficiency and the analytical results. It will be influenced by the physicochemical properties of the chemical being sampled for and the location/environment in which it is being sampled. If skin surfaces are being sampled, it should be considered which media, or solvents, are appropriate for use on human skin so as not to disturb or damage or influence potential exposure or absorption. Further, if it is expected that some damaged skin may exist, what effect, if any will the proposed collection method have on these individuals. If sampling a surface, the properties of the surface may impact study design, such as the hardness or porousness (NMAM). If clothing or PPE are being sampled, the collection method should not interference with or damage the PPE. Once a study design and analytical method is developed, the written sample collection procedure should be as detailed as possible.

4. Key Elements of the Analytical Method

The analytical method should include, but are not limited to, information regarding the following elements:

- Sample collection methods (if relevant, i.e. if validating analytical and wipe sampling methodology in surrogate skin)
- Sample/chemical storage and stability
- Analytical procedure (sample preparation, sample analysis, sample extraction, clean-up procedures)
- Equipment description and operation mode
- Target analytes
- Limit of detection (LOD) and limit of quantification (LOQ)
- Instrument calibration and standardization
- Quality control (good laboratory practices (GLP))
    - Precision and accuracy of the method
    - Detection and quantitation limits
    - Analytical recovery
    - Surrogate standards

- Quality assurance – field and laboratory blanks
- Data analysis
- Method performance (precision, accuracy, detection limits, recovery percentages, extraction efficiency, and potential issues)

5. Interference and Contamination

It is important to reduce the potential for interference during method development, from any study materials, laboratory equipment and from contamination due to the lab environment. All study materials (solvents, reagents, glassware, equipment, and apparatus) should be free from contamination which may influence the results or lead to interference with the proposed analytical method (NIOSH 2011). Some pre-washing or pre-cleaning steps may be needed for selected media or equipment/containers, depending on the method chosen.

Further, all study materials, whether it be sampling media, reagents, solvents, etc. should be purchased from reputable sources and be free of contamination.

6. Analytical Recovery

The accuracy of the analytical method can be determined by spiking known amounts of the chemical of interest onto the sample media and confirming that the developed analytical method can recover an acceptable concentration of the test compound. The laboratory should determine the extraction efficiency (or analytical method recovery) based on the specific sampling media, internal standards, reagents, and laboratory techniques that the laboratory may use. An acceptable concentration will be determined by the purpose of developing the method, and other considerations (such as regulatory requirements). This will be reported as a percent recovery of the known spiked analyte, or difference between the mean and accepted value (including confidence intervals) (ICH 1995). According to OECD (1997), average recovery of 70-120% and a coefficient of less than or equal to 20% are acceptable. Other recovery percentages of >90% have been suggested by OSHA, and between 60 and 125% has been suggested by EPA. The ability to recover the analyte from the sampling material should be determined prior to the initiation of any studies (including laboratory or field studies).

7. Stability Testing

It is important to establish the stability of the chemical of interest on the selected wipe material under typical or anticipated field, storage, and transport conditions (OECD 1997). Therefore, stability testing should be performed to validate the stability of the chemical on the appropriate media, using 1.) appropriate range of concentrations of the chemical or analyte of interest, 2.) variety of media types (if applicable) and solvent chosen for collection protocol, 3.) and using anticipated temperature ranges expected to be experienced in the laboratory or field setting during sampling and/or storage.

Field recovery samples are samples that are concurrently collected and transported with the experimental samples and provide information on the potential loss of analytes that may occur during any phase of sample collection, handling, storage, and transportation (OECD 1997). These samples can help to identify potential losses of analyte that may occur during sample shipment and storage.

8. Resources for Validated Sampling and Analytical Methods

ASTM International Standards - https://global.ihs.com/standards.cfm?publisher=ASTM&rid=Z56&mid=ASTM&utm_source=google&utm_medium=cpc&utm_campaign=astm&utm_content=&utm_term=astm%20standards%20for&gclid=Cj0KCQiAm5ycBhCXARIsAPldzoVUrcqVsbKpdbgowpIoPqAdH3MDastYBVQ3C-WKii4ifBV-nu0DpFkaAtPPEALw_wcB

OSHA - https://www.osha.gov/chemicaldata/sampling-analytical-methods

NIOSH Manual of Analytical Methods (NMAM) - https://www.cdc.gov/niosh/nmam/default.html

EPA Environmental Sampling and Analytical Methods (ESAM) Program - https://www.epa.gov/esam

9. Accredited Laboratories

AIHA accredited laboratory: https://www.aihaaccreditedlabs.org/

10. References

EN TR 15728, 2006, “Workplace Exposure—Strategy for Evaluation of Dermal Exposure,” European Committee for Standardization (CEN), Brussels.

Fenske, R. A., “Dermal Exposure Assessment Techniques,” Ann. Occup. Hyg., Vol. 37, 1993, pp. 687–706.

McArthur, B. (1992) Dermal Measurement and Wipe Sampling Methods: A Review, Applied Occupational and Environmental Hygiene, 7:9, 599-606, DOI: 10.1080/1047322X.1992.10388051

OECD. 1997. Series on Testing and Assessment No. 9: Guidance Document for the Conduct of Studies of Occupational Exposure to Pesticides During Agricultural Application. OECD /GD(97)148.

OSHA Index of Sampling and Analytical Methods - https://www.osha.gov/chemicaldata/sampling-analytical-methods

OSHA – Evaluation Guidelines for Surface Sampling Methods

NIOSH Surface Analysis Using Wipes for Determination of Nitrogen Mustard Degradation Products by Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS). EPA 600/R-11/143. November 2011.