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Workplace atmospheres – Assessment of dermal exposure —Part 1: Framework for Dermal exposure assessment

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Foreword

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This document was prepared by Technical Committee ISO/TC 146, Subcommittee SC 2, Workplace atmospheres, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 137, Assessment of workplace exposure to chemical and biological agents, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

A list of all parts in the ISO 13977 series can be found on the ISO website.

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Introduction

Dermal exposure assessment explores the dynamic interaction between environmental contaminants and the skin. For thousands of chemicals in the workplace, the contribution of the dermal route to total-body exposure has yet to be determined. Historically, the assessment of occupational exposure has focused on inhalation of chemical agents. However, evidence from studies investigating the exposure pattern for different occupational conditions indicates that dermal contact can serve as the primary route of exposure for many chemical substances.

The penetration and permeation of substances through the skin can cause local and systemic effects, respectively. Substances in contact with the skin may penetrate the stratum corneum to cause local effects (irritation, corrosion or sensitization). Substances may also permeate through the skin reaching systemic circulation leading to systemic effects, using different exposure pathways, namely 1) through sweat glands and hair follicles, 2) the intercellular route (around the cells), or 3) the intracellular pathway (through the cells).

Observational studies show that the most highly exposed body parts are the hands. However, deposition of airborne aerosols or direct contact with substances can also contaminate other body parts (e.g. forearms, chest and forehead). Location of the exposure is of particular interest, since both the thickness of the stratum corneum and the density of the hair follicles vary substantially between body locations. These are important parameters with regard to potential penetration and local effects through the skin but also for potential permeation and systemic effects. In addition to skin physiology, skin conditions and duration of contact, the actual contact site may also be relevant for potential inadvertent oral exposure due to hand-to-mouth contact.[1]

The development of a conceptual model was a major milestone in assessing dermal exposure.[2] The multicompartment model systematically describes the transport of contaminant mass from the source of exposure to the surface of the skin. The model consists of six compartments, eight mass transport processes and two barriers ,and provides a structure for both qualitatively and quantitatively evaluating dermal exposure. Many control banding tools, dermal exposure modelling tools and measurement methodologies are described in scientific and grey literature using this basic concept.

No legally binding dermal limit values (DLVs) for dermal exposure are established at the time of the publication of this document. However, Derived No Effect Levels (DNELs)[3] for the dermal route of exposure, Threshold Limit Value–Surface Limits (TLV–SLs)[4] and skin notations exist for many substances and should be considered in the risk assessment as prescribed in national regulations. For the assessment of, for example, biocides and plant protection products, (internal) reference values are determined. For example, the acute, medium and long-term Acceptable Exposure Level (AEL) is mainly referred to as the Acceptable Operator Exposure Level (AOEL) to indicate that it is a reference value for the whole human population.[5] As a common practice, the whole-body exposure *via* all relevant routes is assessed , but for many substances and exposure situations, one pathway (dermal, inhalation or ingestion) is typically dominant.

This document is aimed at industrial/occupational hygienists, human exposure scientists, researchers and health and safety professionals to assist recognition, evaluation and control of dermal exposure and its potential consequences.

This part of the document provides the framework introducing the approaches that can be applied to assess the risks linked to dermal exposure in the workplace. In addition, it is the basis for future parts of this document that will elaborate in more detail the methodologies and approaches that can be applied.

Workplace atmospheres – Assessment of dermal exposure —

Part 1:
Framework for Dermal exposure assessment

1 Scope

This document describes a framework introducing the approaches that can be applied to assess the risks linked to dermal exposure to chemical substances in the workplace. It provides guidance on the different steps to be taken when performing qualitative and quantitative dermal exposure assessments.

These assessments can be used for various purposes, such as:

— For the evaluation of exposure processes and pathways, in view of the human interface with workplace processes;

— For the evaluation of control measures or interventions for effectiveness of exposure reduction;

— For risk assessment, identifying hazardous agents that exhibit local effects and/or systemic health effects;

— For compliance purposes, where results are compared with existing or new established dermal OELVs;

— For epidemiological studies, requiring estimates of relevant exposure parameters.

NOTE *Ocular and mucous membranes exposure, biological agents, wet work and mechanical stressors are outside the scope of this document.*

It is acknowledged that in practice, other pathways like inhalation or ingestion are considered as well.

There is a relationship between skin contamination and inadvertent ingestion.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 78-2, *Chemistry — Layouts for standards — Part 2: Methods of chemical analysis*

ISO 18158, *Workplace air — Terminology*

ISO 20581, *Workplace air — General requirements for the performance of procedures for the measurement of chemical agents*

EN 689, *Workplace exposure - Measurement of exposure by inhalation to chemical agents - Strategy for testing compliance with occupational exposure limit values*

EN 1540, *Workplace exposure - Terminology*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 18158and EN 1540, as well as the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— IEC Electropedia: available at http://www.electropedia.org/

— ISO Online browsing platform: available at http://www.iso.org/obp

3.1
contaminant layer compartment
layers that contain a contaminant or chemical agent

Note 1 to entry: The contaminant layer compartment is characterized by a volume of unknown depth.

Note 2 to entry: Compartments include source, air, surface, skin, inner and outer clothing contaminant layers (see Annex A)

3.2
dermal contact volume
volume containing the mass of the chemical agent present on the **dermal exposure surface area**

Note 1 to entry: This theoretical term is equivalent to the volume of the *skin contaminant layer (SCL) compartment* (3.15); however, for practical reasons, it is defined by the mass of all substances present on the SCL.

3.3
dermal exposure assessment
estimation (qualitative or quantitative) of the magnitude, frequency, duration,and extent of exposure to a chemical agent via the dermal route

3.4
dermal exposure concentration
concentration of the chemical agent contained within the

skin contaminant layer (SCL) compartment (3.15)

Note 1 to entry: The dermal exposure concentration is the *dermal exposure mass* (3.6) divided by the *dermal contact volume* (3.2) or the *dermal exposure mass* (3.6) divided by the mass contained in the *skin contaminant layer (SCL) compartment* (3.15)*compartment*.

3.5
dermal exposure loading
dermal exposure mass (3.6) divided by the *dermal exposure surface area* (3.7)

Note 1 to entry: For practical reasons, dermal exposure loading can be expressed as mass of the chemical agent in an exposed part of the *skin contaminant layer (SCL) compartment* (3.15) divided by the surface area of that part, expressed for example in milligrams per centimetre squared.

3.6
dermal exposure mass
mass of chemical agent present in the *dermal contact volume* (3.2)

Note 1 to entry: For practical reasons, dermal exposure mass is defined by the amount of the chemical agent present in the *skin contaminant layer (SCL) compartment* (3.15)

3.7
dermal exposure surface area
skin surface area where a chemical agent is present

Note 1 to entry: For practical reasons, the dermal exposure surface is represented by a two-dimensional representation of the *skin contaminant layer (SCL) compartment* (3.15), expressed in centimetres squared

3.8
dermal hazard assessment
process to identify and characterize the adverse effects of a chemical agent to which individuals could be exposed via the dermal route

Note 1 to entry: Effects should be assessed adverse only if they affect the viability and normal function of the organism under test.

3.9
dermal limit value (DLV)
level of exposure to the skin that is not expected to result in adverse biological effects

Note 1 to entry:

3.10
dermal risk assessment
overall process comprising a *dermal hazard assessment* (3.8) and a *dermal exposure assessment* (3.3)

Note 1 to entry: A risk assessment usually includes risk mitigation, but this is outside the scope of this document

3.11
local dermal effect
effect that involves the skin (stratum corneum, epidermis and derma). It can be after acute or chronic exposure

3.12
penetration
occurs when a substance enters into the skin

3.13
permeation
occurs when a substance pass through the skin

3.14
potential dermal exposure
dermal exposure expected to occur on the unprotected skin or clothes

Note 1 to entry: all substance mass that could reach the body without any exposure reducing methods being applied

3.15
skin contaminant layer (SCL) compartment
compartment on top of the stratum corneum of the human skin formed by sebum lipids, sweat and additional water from transepidermal water loss, also including products from cornification and unshed corneocytes

Note 1 to entry: More information can be found in Annex AA.

Note 2 to entry: The SCL compartment is characterized by a volume of unknown depth.

3.16
systemic dermal effect
systemic toxicity occurs when skin exposure contributes to the overall body burden, resulting in other organ toxicities

[Source Andersen & Meade (2014)]

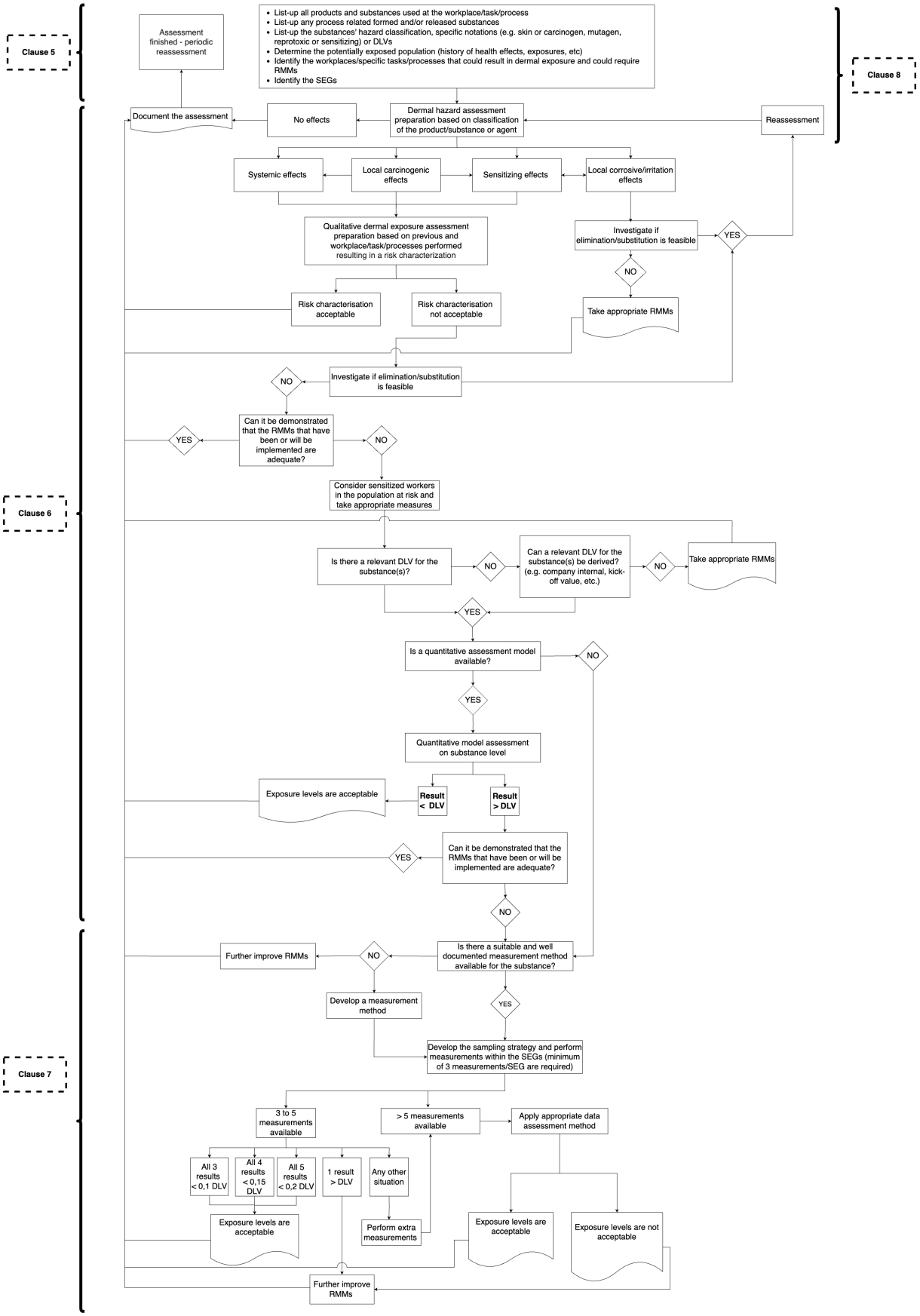
[6]

3.17
uptake
concentration-driven transport of a chemical agent from the *skin contaminant layer (SCL) compartment* (3.15)into the skin, i.e. crossing the interface between the skin contaminant layer (exposure surface) and the stratum corneum (absorption barrier)

Note 1 to entry: The time-exposure concentration profile for an identified area of the skin contaminant layer over a defined period of time is relevant for uptake.

4 Schematic overview of the framework for dermal exposure assessment

The assessment of dermal occupational exposure to chemical agents starts with general substance information gathering, identification of the population at risk, description of the workplace (e.g. Use of risk management measures (RMMs)) and the identification of similar exposure groups (SEGs)Clause 5. This is followed by a dermal exposure risk assessment based on the classification of the product, substance or agentClause 6 and when required by a quantitative assessment when a method and DLV is available6.3. The dermal exposure assessments shall be documented and periodic reassessments shall be conducted when significant changes occur at the workplace that may affect the dermal exposure and for evaluations where no safe situation can be obtained. An annual interval for reassessment is recommended, whatever the outcome isClause 7. Figure 1 provides a schematic overview of the framework for dermal exposure assessment.



NOTE DLV can be an OELV, DNEL, TLV, etc. and is used for evaluating the results

Figure 1 — Schematic overview of the framework for dermal exposure assessment

5 Information gathering

5.1 General

Information shall be obtained to:

— List all products and their constituants used in the activities and process generated substances potentially released during the activities so that toxicological endpoints for effect related to dermal exposure, skin notations and/or DLVs can be identified.

— Determine the population at risk.

— Identify the workplaces, activities and / or processes at risk and the RMMs currently in place.

— Identify SEGs.

5.2 Substance-related information

The preparation of a list of all substances in the workplace and the relevant information concerned is an essential step to the identification of the potential for exposure. The products' safety data sheets (SDSs) and other available information are useful to establish the list. The list shall include any of the following:

— raw materials, primary products, impurities, intermediates, final products, reaction and process products and by-products, etc;

— the individual substances, identified with chemical registration numbers (e.g. Chemical Abstracts Service Number, European Commission Number), including process generated emissions;

— classification and labelling, e.g. the health hazard (H) statements a shall be evaluated to identify those which may be relevant;

— substance properties that affect dermal absorption and toxicokinetics, e.g octanol/water partition coefficient (log Pow), molecular size, ionizatio and particle size / dustiness [7], as well as product characteristics, e.g. vehicle used, dilution rate, and partitioning between vehicle and stratum corneum;

— appropriate limit values and additional notations (e.g. 'skin', 'D'(dermal), 'C' (carcinogen), 'M' (mutagen), 'Sk' (skin), 'DSEN' (dermal sensitization notation)) and additional relevant toxicological endpoints for effect;

— additional information such as amount used, vapour pressure, temperature, saturation and concentration.

To determine whether any potential dermal exposure might be of concern, information regarding the hazardous classification of the substances handled should be retrieved. The H statements as presented in the products SDS should be reviewed to identify those which may be of relevant to the dermal route (see Table 1, Table 2, Table 3).Due to local restrictions other statements may also be relevant, for instance EUH statements (these being additional labelling information used in the European Union (EU)) related to skin or allergic effects.[8]

Table 1 — List of hazard statements relevant to dermal exposure – local corrosive/irritation effects

Code	Hazard Statement
H314	Causes severe skin burns and eye damage
H315	Causes skin irritation

Table 2 — List of hazard statements relevant to dermal exposure – sensitizing effects

Code	Hazard Statement
H317	May cause an allergic skin reaction

Table 3 — List of hazard statements relevant to dermal exposure – systemic effects

Code	Hazard Statement
H310	Fatal in contact with skin
H311	Toxic in contact with skin
H312	Harmful in contact with skin
H313	May be harmful in contact with skin
H340	May cause genetic defects
H341	Suspected of causing genetic defects
H350	May cause cancer
H351	Suspected of causing cancer
H360	May damage fertility or the unborn child
H360D	May damage the unborn child
H360Df	May damage the unborn child. Suspected of damaging fertility
H360F	May damage fertility
H360FD	May damage fertility. May damage the unborn child
H360Fd	May damage fertility. Suspected of damaging the unborn child
H361	Suspected of damaging fertility or the unborn child
H361d	Suspected of damaging the unborn child
H361f	Suspected of damaging fertility
H361fd	Suspected of damaging fertility. Suspected of damaging the unborn child
H362	May cause harm to breast-fed children
H370	Causes damage to organs
H371	May cause damage to organs
H372	Causes damage to organs through prolonged or repeated exposure
H373	May cause damage to organs through prolonged or repeated exposure

These shall then be checked in publicly available databases such as the “Information on Chemicals” platform in the ECHA website.[9]

Next, information regarding the potential of dermal absorption shall be retrieved in order to assess the relevance of systemic exposure following the exposure *via* the dermal route. Measured dermal absorption data is preferred to be used as an estimate of uptake but may not be available. In absence of this data, the substance properties that affect dermal absorption can be evaluated, including the octanol/water partition coefficient (log Pow), the molecular size, the ionisation and the particle size (e.g. for powders).[7] It shall be noted that the dermal absorption rate for a specific substance can differ significantly depending on the vehicle that is used, the dilution rate, the partitioning between solvent and stratum corneum and workplace factors, see 5.4

Considering the high relevance of dermal exposure for many products, such as pesticides and biocides, a high number of *in vitro* and *in vivo* dermal absorption studies have been conducted during the last decades. Based

on these data, a significant impact of the substance concentration on dermal absorption and formulation category has been reported for pesticides.[10]

Additional characteristics, such as the physicochemical properties of the substances or products handled, shall be considered on a case-by-case basis. For example, when handling liquid products at the workplace, e.g. by means of stirring or spraying, droplets or aerosols can be formed. Depending on the volatility of the substance, these droplets can easily evaporate or stay in the air for a relatively long period and can even increase in volume over time due to condensation processes.[11] When these droplets come into contact with the skin (resulting in moistening of the skin), the chemical composition of the liquid, its skin-damaging properties and percutaneous absorption characteristics shall be taken into account, regardless of the droplets' original dimensions.

Furthermore, the existence of a DLV or skin notation for the substance under consideration shall be checked. For dermal exposure, different limit values can be available and shall be identified. In the simplest case, a DLV exists which can directly used for compliance testing, without considering other exposure pathways. However, for pesticides and biocides reference values referring to an internal body burden are common. These limit values are usually indicated as mass of substance per body weight and day, and considered relevant for risk assessment related to systemic exposure resulting from all relevant exposure pathways, i.e., inhalation, dermal and, if applicable, oral exposure. Similarly, for industrial chemicals limit values such as DNELs exist, which can refer to different exposure pathways. In this case, for risk assessment purposes, exposure indices (exposure divided by limit value) are calculated for all pathways and then summed to conclude whether the exposure levels are acceptable (i.e. resulting sum is <1). For such limit values, assessment of the dermal pathway according to this document requires that the exposure levels resulting from all other relevant pathways shall be established. The acceptable exposure level remaining for the dermal route shall then be derived and considered further as the relevant limit value for the this route.

5.3 Population at risk

The population at risk shall be identified. Pre-employment health questionnaires and company health surveillance, if available, can help identify susceptible individuals or those with existing skin complaints. Any occurrence of skin disease or health effects can indicate potential dermal exposures. For more information on local and/or systemic dermal health effects, see Annex B.

Disruption of the skin decreases the barrier function of the stratum corneum and is thus important to consider when establishing the population at risk. The integrity of stratum corneum and its damage due to pre-existing disease and other work-related conditions (e.g. wet work and abrasion) can be assessed relatively easily. Assessment of skin condition can be made by visual examination, which may include questionnaires or scoring systems, like the Nordic Occupational Skin Questionnaire (NOSQ-2002) [12], the Hand Eczema Severity Index (HECSI) [13] [14], the Manuscore [15], the Osnabrück Hand Eczema Severity Index (OHSI) [15], and Hand Eczema Score for Occupational Screenings (HEROS).[13] Furthermore, there are a number of biophysical parameters that can be used to objectively assess skin condition, like transepidermal water loss (TEWL) from the skin surface, skin hydration and quantitative measurement of skin colour.[16] It should be noted that what is observed at the individual worker level cannot be directly translated to an assessment of skin disruption on a group level as it is. It is also important to take into account accidental damage of the skin that might or might not be work-related. On the other hand, combining data generated on an individual level may generate valuable information on a group level. It is advised to document and retain these (anonymised) observations at company and/or industry level to be able to identify any group level issues of concern .

5.4 Workplaces, tasks and / or processes at risk and RMMs in place

To determine if exposure *via* the dermal route is of relevance based on the workplace environment, a description of all worker activities should be available, as well as details of how the worker directly or indirectly interacts with the substance. The conceptual dermal model [2]shall be used to identify the processes by which substances from the source of exposure can be transported to the surface of the skin, e.g. emission, deposition, transfer and removal. Further information on the conceptual model, is provided inAnnex A.

The work processes and procedures shall be evaluated to gauge the exposure and the exposure profile to chemical agents by a detailed review of workplace factors, such as:

— work organization (job titles, activities, tasks, work shift system, job functions, etc.);

— processes and techniques (type of processes, temperature, pressure, etc.);

— amount of the substance that is used per shift/task/activity;

— workplace layout and configuration, including confined spaces, open air, etc.;

— safety precautions and procedures (restricted area, training, etc.);

— cleanliness and tidiness of workplace;

— ventilation installations, other forms of engineering control and any information on their performance;

— emission sources and locations of high concentrations;

— periods, frequencies and durations of exposure, considering variation of exposure with time of day and season of the year;

— work load;

— worker behaviour, or activity or production rate indicators;

— administrative controls and use of personal protective equipment (PPE).

Annex C provides a simple checklist of questions to be addressed and information to collect when visiting the workplace to determine if dermal exposure is relevant. Information on engineering controls, protective gloves and other PPE use is collected, as are details of the work practices and workers interaction with the substances of concern.

5.5 Identify similar exposure groups

SEGs rely on grouping workers and assessing their health risks based on similar exposure conditions. When determining SEGs consideration shall be given to various characteristics that influence exposure including, e.g. tasks and activities undertaken and equipment used. Further information on assigning SEGs can be found in EN 689, 5.2.1. However validation and constitution of SEG's might not be possible in all cases with dermal exposure measurement results.

6 Dermal risk assessment

6.1 Dermal hazard assessment

The first step in the dermal exposure risk assessment is to identify whether the subtances under assessment may produce any effects following exposure *via* the dermal route. The substance-related information retrieved within5.2 shall be reviewed in detail to conclude on the specific assessment required in relation to the hazardous properties. The different cases are summarised below:

— All information gathered assigned to the substances under assessment present no relevant effects and while there is also no DLV established; no further assessment is required (see 6.2.1).

— At least one of the H statements included in Table 1 or any other information gathered referring to any local corrosive/irritation effects is assigned to the substance under assessment; an assessment is required (see 6.2.2).

— At least the H statement included in Table 2or any other statement or skin notation referring to sensitizing effects is assigned to the substance under assessment; an assessment is required (see 6.2.3).

— At least one of the H statements included in Table 3or any other statement or skin notation referring to potential health effects related to dermal exposure, following absorption in the systemic circulation is assigned to the substance under assessment; an assessment is required (see 6.2.4).

— no H statement is assigned to the substance under assessment but local carcinogenic effects are identified (see Annex B.1.3); an assessment is required. (see 6.2.4).

—

The relevance of systemic effects is also indicated by the existence of reference/limit values for the chemical agent/product under assessment, independently of the classification.

It is noted that multiple statements can be assigned to the substances under assessment and thus multiple exposure risk assessments can be required, e.g. an assessment for both local and systemic effects may be required.

6.2 Qualitative dermal exposure assessment

Once the hazard evaluation has been performed, the qualitative dermal exposure assessment shall be performed in cases where effects relevant to dermal exposure have been identified. The qualitative exposure assessment shall consider workplace factors, workers tasks and the physical-chemical properties of the agent. This assessment can be performed on product, substance or process level. When the qualitative exposure assessment indicates that the risk characterisation result is not acceptable then an investigation of the possibilities for elimination or substitution shall be performed. If elimination or substitution is possible, the situation shall be reassessed, if not, a quantitative exposure assessment shall be performed to identify the exposure risk.

For the purposes of the qualitative dermal exposure assessment, several methods/tools are available depending on the level of detail needed to perform the analysis. These include approaches which require minimal information where easy to use spreadsheets can be used, to more sophisticated tools.

A typical, simplistic approach is based on the Kinney and Fine risk assessment method [17], which can be easily performed in a spreadsheet (see Annex D). Other examples are Control of Substances Hazardous to Health (COSHH) Essentials [18], Système d'évaluation et d'information sur les risques chimiques en milieu professionnel (Seirich) [19], and *Einfaches Maßnahmenkonzept Gefahrstoffe (*EMKG) [20] which are freely available. The lack of consideration of the exposed skin surface is the major disadvantage of these tools. Examples of tools which take into account the exposed skin surface and where results are expressed as categorical estimates of exposure, e.g. ever-never, yes-no or exposure classes (low, medium, high), are the Dermal Risk Assessment Method (DRAM) [21], Stoffenmanager® [22] and DeRmal Exposure Assessment Method (DREAM).[23]

Consideration shall be given to applying the method/tool most suitable for the exposure situation being assessed. See Annex Efor further information on available tools.

6.2.1 Outcome with no effects

If the conclusion of the exposure assessment is no effects, the assessment shall be terminated and documented.

6.2.2 Outcome related to local corrosive/irritation effects

If the exposure assessment has local corrosive or irritant effects as endpoint, appropriate (further) RMMs shall be implemented, after which the assessment for this endpoint is terminated and documented. For example,

when working with corrosive acids, a closed system shall be installed or acid-resistant gloves shall be worn to prevent exposure.

6.2.3 Outcome related to sensitizing effects

If the exposure assessment has sensitizing effects as an endpoint, the assessment continues with a quantitative dermal exposure assessment. When susceptible individuals in the population are exposed to specific sensitizing agents, additional RMMs shall be implemented for these individuals. The assessment continues for local carcinogenic and systemic effects. (see 6.2.4)

6.2.4 Outcome related to local carcinogenic and systemic effects

If the exposure assessment has local carcinogenic or systemic effects as an endpoint, the assessment continues (as in the case of sensitizing effects) with a quantitative dermal exposure assessment (see 6.3). An important consideration is to investigate if there is a DLV available to compare the quantitative results against. When no published DLV exists, it shall be investigated if an own DLV can be established. An example is the derivation of a kickoff value (KOV), defined as the 10th percentile of the DLV distribution of the substances in a hazard category.[24] When no DLV can be derived the assessment is terminated and appropriate RMMs shall be implemented to keep the exposure as low as reasonably achievable.

6.3 Quantitative dermal assessment

6.3.1 Modelling dermal exposure

Exposure models have been developed that can help users to estimate the level of exposure without collecting their own measurements. Most models provide estimates of the extent of (potential) dermal exposure or skin contamination and can be used to provide an initial exposure assessment as part of the risk assessment process. The results may also be applied to help select an appropriate sampling strategy for quantitative exposure assessment, as well as prioritization of RMMs.

If the estimated exposure, based on use of an exposure model, is s below the DLV, it is not necessary to collect exposure measurements as the exposure levels are considered acceptable. The assessment shall be finished and documented.

If the exposure estimation shows that the exposure is equal to or above the DLV, it is advised to first reduce exposure by implementing (further) RMMs before investigating whether there is a suitable and well-documented measurement method available for the substance.

The different types of quantitative dermal exposure models available vary in level of complexity and accuracy and uncertainty in the generated exposure estimates. Users shall select the model most appropriate for their exposure situation, based on e.g. the applicability domain of a particular model, nature of the substance a worker is exposed too and body parts considered. The model shall be applicable for the substance or type of substance being assessed.

The simplest quantitative exposure models consist of compiled exposure levels that have been measured for a specific activity. From these datasets, certain percentiles are used to draw conclusions about the exposure in a comparable situation by analogy. An example is the "TNsG2002 Database Detailed Models"[25] More structured approaches provide semi-quantitative estimates of dermal contamination by using identified or assumed determinants of exposure (or contamination). An example is the DeRmal Exposure Assessment Method (DREAM).[23] ECETOC TRA and MEASE are examples of tools that were designed to provide conservative estimates of exposure (for both inhalation and dermal routes) for a defined exposure scenario. ECTROC TRA is a general chemical exposure assessment tool [26] with the scope of MEASE being more limited to metal and inorganic substances.[27]

If exposures estimated using tools such as those mentioned above exceed the DNEL of a substance, or if the assessor would like to generate exposure estimates with greater accuracy and less uncertainty, it is recommended to use more advanced tools. Examples of such tools are the RISKOFDERM model and the dermal Advanced REACH Tool (dART). The RISKOFDERM model estimates dermal hand and body exposure.[28] dART is a generic exposure model for estimating dermal exposures to the hands to low volatile liquid products and solids in liquid products.[29] In addition to generic dermal exposure models, models have also been developed for specific exposure scenario's, e.g. SprayExpo for spray application of biocidal products [30], and the EFSA Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products.[5]

In Annex Ea non-exhaustive overview of available dermal exposure models and tools is given.

6.3.2 Measuring dermal exposure

The question of whether to measure dermal exposure is an important consideration in the development of any dermal exposure assessment strategy. The modelling approaches described in 6.3.1 generally involve an elevated degree of uncertainty, which is usually compensated by a higher degree of conservatism. This can intentionally lead to some overestimation of exposure and risks. Compared to these approaches, measurements performed at the workplaces using a properly validated method can deliver more reliable data for the assessment, and usually lower exposure levels. As measurements are typically more demanding than modelling in terms of time and costs, they are often used to refine the assessment after previous modelling approaches have failed to demonstrate acceptable exposure levels. After defining the objectives of the assessment, the assessor shall choose the most appropriate sampling and analytical methods. Principles and methods for the assessment of dermal exposures are described in Annex F.

The assessment with measurements, like the approaches described in the previous clauses, is based on the previously identified SEGs. Even at the same workplace, dermal exposure levels are subject to, often quite considerable, fluctuations. These are usually even more pronounced when different workers are observed. It is therefore important to develop an appropriate measurement strategy (for details, see Annex F), including the collection of a sufficient number of measurements. If the SEG includes more than one worker, the measurements shall be performed with different workers.

At least three measurements shall be available per SEG.

Dermal exposure is usually measured separately for hands and the body, and the body can often be subdivided into different sections such as head, torso, arms, legs and feet (for details, see Annex F). For the assessment, generally all body sections have to be considered. However, if the previous assessment steps have indicated that the exposure is predominantly limited to only a part of the body, the measurement of body sections with minor exposure may be omitted. As an example, many activities result in predominant exposure of the hands, e.g. pouring of a liquid on a workbench. In this case, the reasons for omitting the other body sections from the measurements shall be well documented and exposure levels derived for these body sections with quantitative models shall be included in the calculated total dermal exposure.

Measurement results below the limit of detection (< LOD) on individual samples representing a specific body section can, if possible, be approximated statistically, for example with the method described in EN 689. The advantage of such an approach is that it minimizes distortion of statistical parameters such as the geometric mean or the geometric standard deviation. For the approximation only measurement results obtained for the same sampler location (representing the same body section) may be considered. However, in practice results <LOD often appear repeatedly for the same body sections. Consequently, even with a larger number of repeated measurements, it can not be guaranteed that for the body section in question a sufficient number of measurements >LOD is available to carry out a statistical approximation. If this problem occurs, a value corresponding to the LOD shall be used instead for these samples.

6.3.2.1 Preliminary dermal exposure assessment for 3 to 5 available measurements

For a very limited set of 3 to 5 measurements for a SEG, compliance with DLVs can only be concluded if a ssignificant margin between the measured exposure levels and the DLV is determined. In this regard, the present document follows the approach laid out in EN 689for inhalation exposure.

If all results are below the following values:

1) 0,1 times DLV for three exposure measurements,

2) 0,15 times OELV for four exposure measurements,

3) 0,2 times OELV for five exposure measurements,

it may be assumed that the exposure levels are acceptable.

If at least one measurement is above the limit value, the exposure levels are not acceptable and appropriate RMMs shall be taken.

If all measured values are below the limit value, but at least one is exceeding the applicable criterion from 1 to 3 above, a conclusion is not yet possible, and more measurements are required.

6.3.2.2 Regular dermal exposure assessment for more than 5 available measurements

If more than five measurements are available, a suitable statistical test shall be selected to decide whether exposure levels are acceptable. For the statistical test, it shall be assumed that the measurements are log-normally distributed until there is good reason to believe that this is not the case. A procedure to check for lognormality of exposure measurements is described in EN 689.

The test shall measure, with at least 70% confidence, whether less than 5% of exposures in the SEG exceed the limit value to be kept. A suitable statistical test is described in EN 689. Other tests may be used provided that they have been shown to meet the above confidence specification.

6.3.2.3 Biomonitoring

Biological monitoring is a measurement method for the determination of exposure that accounts for all exposure routes, including dermal exposure. When a substance has significant absorption through the skin it is a useful and important assessment method. It is also possible to isolate dermal exposure from other exposure routes by using respiratory protective equipment (RPE) which can be relevant to the workplace and researchers.[31] It also provides a cost-effective on-going monitoring approach (for details, see Annex F.3). Measured values are given as a concentration of a substance in the sample type, e.g. blood or urine. This can be compared to biological limit values (where available) and exposure above expected levels is an early indication that exposure control is insufficient.

7 Dermal risk assessment report

7.1 General section in the report

The report shall include a general section common to any type of assessment carried out. This general section is aimed to provide essential information relating to the chemical agents concerned and the conditions of exposure.

The general section shall include at least the following information:

a) the purpose and the date of the assessment;

b) name and qualifications of the assessor(s) and institutions undertaking the assessment;

c) name and address of premises;

d) target agent(s) (e.g., particles, liquid, metal (oxide) particles), including identification of hazards;

e) a description of the conditions of exposure:

   1) details on worker history and tasks;

   2) exposure patterns (see Annex A), including frequency of contacts/spills/splashes and indication of relevant body parts;

   3) exposure time;

   4) details on PPE related to dermal exposure,

   5) other relevant information concerning RMMs (eg. local exhaust ventilation andworkplace cleaning).

7.2 Qualitative dermal exposure assessment

The report shall include at least the following additional information regarding the qualitative assessment:

a) the rationale for the choice of qualitative assessment method;

b) the parameters used to perform the qualitative assessment;

c) the criteria used to judge the acceptability of dermal exposures;

d) the conclusion (i.e. acceptable, unacceptable, uncertain);

e) recommendations for the introduction of additional RMMs.

7.3 Quantitative dermal exposure assessment

7.3.1 Modelled dermal exposure assessment

The report shall include at least the following additional information regarding the modelled dermal exposure assessment:

— The rationale for the choice of modelling tool;

— The parameters used to perform the dermal exposure modelling;

— The results from the modelling tool in the appropriate unit(s);

— The criteria used to judge the acceptability of dermal exposures;

— The conclusion (i.e. acceptable, unacceptable, uncertain);

— Recommendations for the introduction of additional RMMs.

7.3.2 Measured dermal exposure assessment

The report shall include at least the following additional information regarding the measured dermal exposure assessment according to ISO 78-2:

a) the rationale for the choice of sampling and analytical method;

b) description of the sampling and analytical method;

c) Unique identifier of the person(s) who sampled and performed the analysis;

d) the date of reception of the samples and the analysis;

e) the sampling strategy used;

f) specific sampling information, with due consideration of the method used:

   1) sampling technique (e.g. wiping, vacuum, etc.);

   2) name and type of the sampling substrate;

   3) sample container to be used for shipment;

   4) sample storage conditions;

   5) surface area of sampling substrate;

   6) surface recovery (transfer efficiency);

   7) maximum capacity;

   8) sampled or measured surface area and body part;

   9) definition of $t = 0$;

   10) sampling interval and history of subject;

g) the analytical method:

   1) details of the sample extraction method used;

   2) the type(s) of instrument(s) used for sample preparation and analysis and unique identifiers(s);

   3) analytical recovery;

   4) results of the measurements with the appropriate units;

   5) the analytical variables used to calculate the result, including:

      i) the concentrations of each determined chemical agent in the blank and sample test solutions;

      ii) the volumes of the blank and sample test solutions and the dilution factor, if applicable;

   6) the estimated instrumental detection limits, method detection limits and quantification limits under the working analytical conditions;

7) the measurement uncertainty determined in accordance with [32];

8) quality control data if requested by the client;

9) any inadvertent deviations, unusual occurrences, or other notable observations;

8 Evaluation and periodic reassessment

The outcome of the dermal exposure assessment shall be evaluated. This evaluation includes:

— prioritization of the dermal exposure risks;

— formulating an action plan for risk mitigation;

— documenting the findings and the action plan (if relevant);

— informing the workers involved about the outcome and actions.

The risk assessment shall be periodically reviewed and updated as necessary to ensure that it is current. In case of significant changes in workplace factors, like introduction of new equipment, RMMs, substances/products or procedures, or if the assessor becomes aware of any new or additional health complaints, the assessment shall be updated as soon as possible.

In general, an annual review is recommended to determine whether reassessment is required. The review shall include changes affecting exposure, such as maintenance status, gradual deterioration of equipment or subtle changes in ways of working. When reassessment is required, the same methods as used previously shall be used in the reassessment to allow direct comparison with previous assessments, unless there are other reasons to adopt new approaches (e.g., undertaking a quantitative assessment following the outcomes of a qualitative assessment etc).

When reassessment is conducted with exposure measurements, periodic intervals for measurements should be considered. For periodic reassessments with measurements, the assessor shall decide upon the number of periodic measurements per group.

Annex A
(informative)

Conceptual model

Schneider and a group of other European researchers devised a conceptual model of dermal exposure[2][33], which was a major milestone for assessing dermal exposure. This describes the processes and "compartments" involved in dermal exposure, from the source of the hazardous chemical through to permeation of the chemical through the outer skin layers, i.e., uptake. The model is illustrated in Figure A.1. Explanations of abbreviations and their use are described below.

In the conceptual model, six compartments were identified: 1) the source of contaminant, 2) the air, 3) the surface contaminant layer (Su), 4) the outer clothing contaminant layers (CloOut), 5) the inner clothing contaminant layer (CloIn, 6) the skin contaminant layer (Sk). The outer and inner contaminant layers include a buffer that represents the mass retained by the clothing which does not come into contact with surfaces or skin.

Within the model, mass transport of contaminants can be divided into eight different processes:

1) Emission (E): transport of substances into the air, onto surfaces, outer clothing and the skin contaminant layer from all primary sources. The air compartment contains vapours and dispersed particles (aerosols) which have been emitted by a source (E_{Air}). Emission from sources to work surfaces (E_{Su}), clothing (E_{CloOut}), or skin (E_{Sk}), can arise from splashing, spilling, immersion, and impaction.

2) Deposition (Dp): the transport of substances from the air to surfaces (Dp_{Su}), outer clothing (Dp_{CloOut}) or the skin contaminant layer (Dp_{Sk}).

3) Resuspension and evaporation (L), also called loss: the transport of substances from surfaces (L_{Su}), outer clothing (L_{CloOut}), and the skin contaminant layer (E_{Air}) to the air while evaporation is a continuous process driven by diffusion or evaporation.

4) Transfer (T): the transport of substances by direct contact between surface, skin, clothing in a direction toward the workers. Pathways include from surfaces to skin ($T_{Su,Sk}$), surfaces to outer clothing ($T_{Su,CloOut}$), and outer or inner clothing to skin ($T_{CloOut,SK}$, $T_{CloIn,Sk}$).

5) Removal (R): transport of substances by direct contact between skin, inner and outer clothing, and surface contaminant layer in a direction away from a worker. Pathways include skin to inner or outer clothing ($R_{Sk,CloIn}$, $R_{Sk,CloOut}$) and skin to surfaces ($R_{Sk,Su}$).

6) Redistribution (Rd): the transport of substances from a subcompartment to another (i.e. touching the face with contaminated fingers (Rd_{Sk}) or touching the outer clothing of a shirt with contaminated gloves (Rd_{CloOut})). Other redistribution subcompartment pathways include air (Rd_{Air}), surfaces (Rd_{Su}), and the inner clothing contaminant layer (Rd_{CloIn}).

7) Decontamination (D): the deliberate transport of contamination from the system (e.g. ventilation (D_{Air}); cleaning of contaminated surfaces (D_{Su}), outer clothing (D_{CloOut}), and inner clothing (D_{CloIn}); or removing material from the skin (D_{Sk})).

8) Penetration and Permeation (P): both involve transport of substances through a rate-limiting barrier, such as clothing or the stratum corneum. Pathways include transport of substances from outer to inner clothing ($P_{CloOut,CloIn}$) or from inner to outer clothing ($P_{CloOut,CloIn}$) and through skin (P_{Sk}). Penetration is transport from external to internal compartments. Permeation always involves diffusion.

The top horizontal dotted line in Figure A.1indicates that personal behaviour is likely to influence mass transport processes.

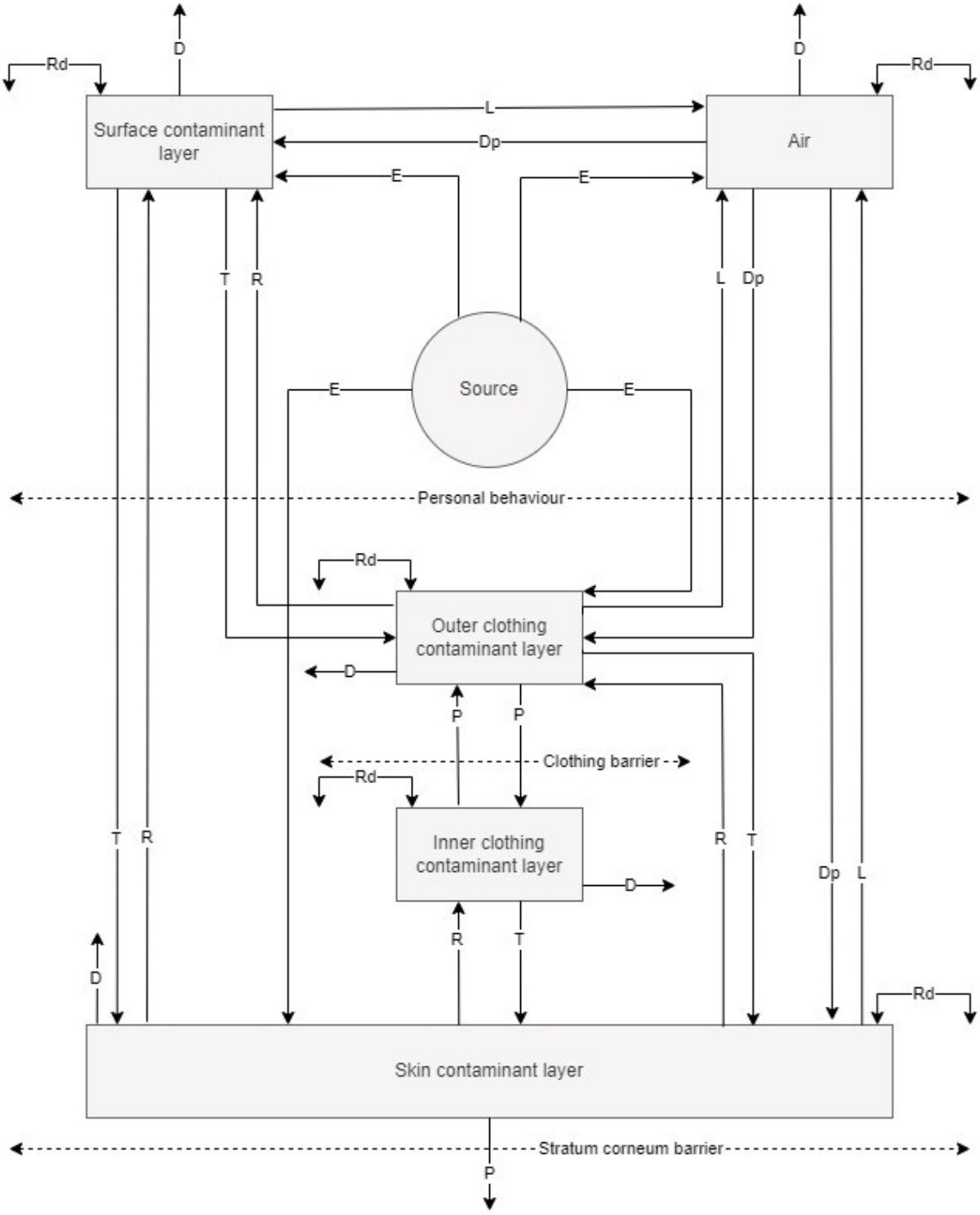


Figure A.1 — Conceptual model for assessment of dermal exposure

Annex B
(informative)

Local and systemic effects related to dermal exposure

A substance that comes in contact with the skin can cause local or systemic effects which are determined by the substances characteristics and penetration and permeation properties.[34]

B.1 Local dermal effect

B.1.1 Irritation

Mild irritants can cause disruption of the stratum corneum, inflammation and the onset of irritant contact dermatitis, characterized by erythema, oedema, fissures, sometimes papulae and vescicles in the area of contact. Strong irritants and corrosive substances can cause chemical burns, also with necrosis of the tissue.[34]

B.1.2 Allergic sensitization

Sensitizing substances can cause mainly allergic contact dermatitis. These substances induce a cell-mediated late reaction characterized by erythema, oedema, papulae and vescicles, not only in the site of contact but also in the surrounding area of the skin. This is a two-step process, in brief:[35][11]

1) the induction phase is the result of initial exposure(s) to a sensitizing substance (allergen) inducing a cell-mediated immune response;

2) the elicitation phase is in response to a subsequent exposure and results in an allergic reaction.

In case of sensitization exposure to a very low amount of the substance, could trigger an allergic reaction with delayed response depending on its potency (e.g., 12-24 hours after the contact). Typical examples are metals such as nickel, chromium and cobalt[36], p-phenylendiamine[37], epoxy resin[38], rubber additives[39] causing allergic contact dermatitis.

Some substances can cause an immediate immunoglobulin E (IgE) mediated reaction, causing local and systemic urticaria and also asthma (e.g. latex).[40][41]

B.1.3 Skin cancer

Some substances can cause skin cancer after contact with the skin (e.g. polycyclic aromatic hydrocarbons or arsenic)[42]

B.2 Systemic dermal effect

Systemic absorption can cause effects related to the substance characteristics. Acute and chronic systemic effects are described in the literature in relation to the amount of substance that has penetrated through the skin. This is affected by parameters such as duration of contact, surface involved, vehicles , skin condition (integrity of the skin barrier), physiochemical characteristics of the substance, potency of the substance for the specific effect, occlusion, anatomic site, metabolism, sweating, etc.[43]

B.2.1 Acute systemic effect

Acute poisoning is possible after contact with toxic substances that can easily permeate the skin. Some examples such as organophosphate pesticides[44], diquat and paraquat[45][46], chlorinated hydrocarbons[47], hexavalent chromium[48], which depending on the substance can cause cardiovascular, kidney, lung and/or neurological toxicity, or possibly death.

Arsenic trioxide poisoning can cause damage to the nervous system, heart, liver, kidney and other organs.[49]

Chemical warfare agents (nerve medicine such as tabun, sarin, soman, etc.) cause lethal effects.[50] Lewisite is a strong vesicating and chemical warfare agent. Moreover, due to the rapid transdermal absorption, cutaneous exposure to lewisite can also elicit severe systemic injury involving lungs.[51]

Nitrobenzene skin absorption can cause hypermethemoglobinemia, hemolytic anemia, liver and kidney dysfunction, cardiogenic pulmonary edema, and toxic encephalopathy.[52]

Solvents that can easily permeate the skin, such as dimethylformalmide, can cause acute or chronic hepatic failure.[53]

B.2.2 Chronic systemic effect and cancer

Chronic intoxication is reported after repeated exposure of the skin to substances causing different effects according to their toxicity. Some examples are provided below.

Skin exposure to glycol monomethyl ether caused hematological problems in women working in the eyeglasses industry.[54] Exposure to isopropyl alcohol caused poisoning with neurological effects.[55] Exposure to boric acid has proven fatal in some cases, with abdominal pain and local effects on the skin also being reported.[56]

Mercury can cause kidney diseases and neuropathy (dizziness, fatigue, hand tremor, and limb pain) after repeated skin contact.[57][58][59]

Arsenic absorbed through the skin cam cause local effect and skin cancer, but systemic absorption can cause cancer in other organs, such as the liver kidneys, etc.[59]

Aromatic amines can be absorbed through the skin and can cause bladder cancer and have been classified as a Group 1 (carcinogen for human) by International Agency for Research on Cancer (IARC).[60]

Contact with terpenes (e.g., pulegone, menthofuran, camphor, and limonene), and sesquiterpenes (e.g., zederone, germacrone), widely used in essential oils and cosmetics, can cause liver diseases and increased concentration of reactive oxygen species with impairment of antioxidant defense.[61] While the application of a salycilates cream caused illness and multi-organ failure.[62]

Annex C
(informative)

Checklist for visiting workplaces

The following checklist of Table C.1 Table C.2 and Table C.3 can be used to investigate dermal exposure in the workplace. This checklist can be revised as necessary to reflect company specific operations. Suggested responses to the questions are also provided.

Table C.1 — Workplace design – Engineering controls

Question	Circle response	Why is this important?
1. Is remote handling used?	Yes / No	This contributes to reduce the potential of exposure
2. Is the process designed to minimize handling operations?	Yes / No	This contributes to reduce the potential of exposure
3. Are clean and dirty areas segregated?	Yes / No	This is good practice for controlling spread of contamination
4. Is there a barrier between clean and dirty areas?	Yes / No	This is good practice for controlling spread of contamination
5. Are there easy to clean smooth, impermeable surfaces?	Yes / No	This facilitates cleaning and contributes to surfaces contamination

Table C.2 — Work practices – Potential dermal exposure

Question	Circle or record response	Why is this important?
1. Do work practices differ between workers?	Yes / No	If “yes “try to identify the reason why and promote best practices
2. Is splashing a risk?	Yes / No	Splashing might lead to increase dermal contact and can be critical with corrosive substances
3. Do workers have direct contact with dermal hazards via bare skin or gloved hands?	Yes / No	Risk of dermal contamination is higher in case of contact of surfaces which can be touch either by a bare skin or by gloved hands
4. Are tools shared in the workplace?	Yes / No	Sharing contaminated tools increase the potential of dermal exposure
5. Are tools cleaned/disinfected after use?	Yes / No	Cleaning shared tools after use decreases the potential of dermal exposure
6. Which parts of the body can be exposed (indicate all that apply)?	Head Chest Back Hands Lower arms Upper arms Lower legs	The body parts which might be exposed shall be correctly protected

Question	Circle or record response	Why is this important?
	Upper legs	
7. How frequently is the skin exposed (e.g. daily, weekly)? Enter free text		The higher the frequency, the higher the exposure
8. How long is the duration of dermal exposure in an average shift (hours)? Enter as a numeric value		The higher the duration, the higher the exposure
9. Frequency of hand washing (e.g. several during the task, after the task) during an average shift. Enter as a numeric value.		Even if efficacy of hand washing as a control measure is unknown, this measure contributes to a reduction of exposure
10. Do some employees have skin problems?	Yes / No	This might be an alert of dermal exposure at the workplace

Table C.3 — Protective gloves

Question	Circle or record response	Why is this important?
1. Are protective gloves used?	Yes / No	If no protective gloves are used, move to last item in Table C.3 (number 17).
2. Primary type of glove material used (e.g., nitrile, latex, PVC)? (Record as free text)		Not all glove materials are suitable to protect against the hazardous substances being handled. Natural rubber latex proteins have the potential to cause asthma, urticaria and also possibly anaphylaxis.
3. Are gloves single-use (disposable)?	Yes / No	
4. Number of pairs of gloves used by worker per shift. Enter as a numeric value.		The should be adjusted on the basis of the intensity of glove contamination
5. Have the gloves been carefully selected?	Yes / No	Selection should be based on the chemicals handled in the workplace. Comfort, fit and duration of use should also be taken into account when selecting personal protective equipment (PPE). Glove manufacturers usually produce charts to show how well their gloves perform against different substances. Manufacturers use three key terms, breakthrough time, permeation rate and degradation. It is helpful to review this information.
6. Do the gloves limit workers dexterity for carrying out their tasks?	Yes / No	If gloves are uncomfortable for workers, they are less likely to be worn. They can also potentially lead to accidents / incidents due to loss of manual dexterity.
7. Are gloves being used beyond their performance limits?	Yes / No	This should never occur. Gloves should be inspected prior to use.

Question	Circle or record response	Why is this important?
8. Is there a possibility of cross-contamination from glove to skin?	Yes / No	This may occur for example, during glove removal.
9. Are the gloves correctly donned and removed?	Yes / No	Training should be provided to instruct workers on the proper use, storage, and maintenance of gloves.
10. Is it possible to wipe / wash gloves clean before taking them off?	Yes / No	This is a good practice
11. Are 'single use' gloves only used once?	Yes / No	Single use gloves shall not be reused
12. Do workers systematically wash their hands after removing protective gloves?	Yes / No	This is a hygiene measure
13. Is it a designated area for putting on and taking off gloves?	Yes / No	Ideally such an area should be close to the work area, equipped with a sink and storage for gloves
14. Are clean gloves stored in a place free from contamination?	Yes / No	This helps prevent cross contamination from occurring prior to use.
15. Are contaminated gloves disposed safely as hazardous waste?	Yes / No	Contaminated gloves must be considered as hazardous waste
16. What other PPE are used for carrying out the task? (Indicate all that apply)	Arm sleeves Protective suit Eye protection Face shield Respiratory protective equipment Hearing protection Other (specify)	Consider all PPE requested for the task and check for possibilities of interfering interactions
17. What specific additional PPE is being worn to protect against dermal exposure (e.g., arm sleeves, protective suits etc) (Indicate all that apply)	Arm sleeves Protective suit Face shield Other (specify)	

Annex D
(informative)

Kinney and Fine risk assessment method

Kinney and Fine risk assessment method[17], can be easily performed in a spreadsheet. The principle is according to probability, frequency, and severity (risk factors). For severity scores the sum for each classification shall be taken. The product of the risk factors gives the dermal exposure risk score, which can be used to prioritize the dermal exposure risk in a specific situation. An example of probability scores based on the level of workers protection are given in Table D.1.

Table D.1 — Example of probability scores

Situation	Score
Closed system	0,2
Adapted collective RMMs	0,5
Adapted collective RMMs and PPE	1
No collective RMMs but adapted PPE	3
Non-adapted collective RMMs and PPE	6
No collective RMMs or PPE	10

An example of frequency scores based on the exposure frequency are given in Table D.2.

Table D.2 — Example of frequency scores

Situation	Score
<5 min /week	0,5
5 –15 min /week	1
2 hours /week	1,5
2 –5 hours /week	2
5 –10 hours /week	3
10 –20 hours /week	6

The severity score depends on the classification as provided in 5.2 and is provided in Table D.3.

Table D.3 — Severity scores

Situation	Score
no H or EUH phrases	1
H313; H316	3
H312; H315	7
H311; H340; H350; H360 series; H362; H371; H373	15
H310; H314; H317; H341; H351; H361 series; H370; H372	40

Multiplying all scores provides the dermal exposure risk score used for prioritization, see Table D.4.

Table D.4 — Dermal exposure risk scores divided into exposure risk classes

Score	Exposure risk category	Description exposure risk category	Proposed action
< 20	1	very limited, acceptable	no further action required
20 – 70	2	attention is required	Frequent follow up
70 – 200	3	RMMs are required	Quantitative assessment is recommended
200-400	4	take immediate action	immediately consider to introduce RMMs Quantitative assessment is required
> 400	5	stop activity	consider substitution measures or closed system

Annex E
(informative)

Models and tools

In Table E.1 an overview of exposure models and tools is given that can be used to assess dermal exposure. Before using a tool, the information provided should be verified by the user who should satisfy themselves that it fulfils their required purposes.

The list provided is to the best of knowledge at the time of writing this document. Assessors should also check if other models have been developed or models have been updated since the publication of this document.

Table E.1 — Overview of exposure models and tools

Model	Output	Body parts	Reference	Website (if applicable)
Qualitative models				
DeRmal Exposure Assessment Method (DREAM)	Dream estimate (score) divided into seven DREAM categories	nine body parts: head, upper arms, lower arms, hands, torso front, torso back, lower body part, lower legs and feet	[23][63]	http://www.isa.una.ac.cr/index.php/es/publicaciones-y-materiales/dream
SEIRICH	Prioritization (1-3)	skin based on classification	[64]	https://www.seirich.fr/seirich-web/index.xhtml
Stoffenmanager ®	6 exposure categories + 2 times 3 prioritizations (dermal uptake and direct skin effect)	9 categories (can be combined) Small surface One hand or less Both hands Lower arms Upper arms Head Chest Back Legs and feet	[65][66]	https://stoffenmanager.com/
Dermal Risk Assessment Model (DRAM)	Deterministic model – Dermal exposure rating Monte Carlo model – Dermal assessment category probabilities	Hands, forearms, skin	[21]	https://www.aiha.org/public-resources/consumer-resources/apps-and-tools-resource-center/aiha-risk-assessment-tools/dermal-risk-assessment-model
Easy-to-use Workplace Control Scheme for	Hazard group (3 levels)	skin	[20]	https://www.baua.de/EN/Topics/Work-design/Hazardous-

Model	Output	Body parts	Reference	Website (if applicable)
Hazardous Substances (EMKG)	Exposure group (3 levels)			substances/EMKG/Easy-to-use-workplace-control-scheme-EMKG_node.html
Control of Substances Hazardous to Health (COSHH) Essentials .	Hazard group (5 levels), least to special) Skin Hazard (Y/N)Recommendations for control	Skin	[67]	https://www.hse.gov.uk/coshh/essentials/index.htm
'Italian model'	Hazard group (4 levels: green/yellow/orange/red Recommendations for control	Skin	[68]	/
Simple models				
Metals EASE (MEASE) v 2	Exposure estimate in µg/cm^2/day Provide the exposed skin surface and total dermal loading in mg/day is provided.	Any as exposed skin surface	[27]	https://www.ebrc.de/tools/downloads.php
ECETOC-TRA v 3	mg/kg/day	hands, forearms	[26]	http://www.ecetoc.org/tra
More advanced models				
RiskOfDerm model [1]	Exposure rate in µL/min (liquids) or mg/min (solids) or exposure loading in µL (liquids) or mg (solids)	hands, body (not for each of the six Dermal Exposure Operation units (DEO units) body exposure is estimated)	[28]	https://echa.europa.eu/documents/10162/19680902/calculator_riskofderm_enl.xls/9e0c3fa8-4764-4a18-95f9-8fbccf3acf2a
Dermal Advanced REACH Tool (dART) [1]	mg/min	hands	[29][69][70]	https://diamonds.tno.nl/ (When registered, one has to sign up separately for dART with an email to support.diamonds@tno.nl to gain access)
Models for dermal exposure for specific groups of products				
ConsExpo	Dermal load mg/cm^2	Skin	[71]	http://www.consexpo.nl
EFSA Guidance (Online Calculator)	mg/kg bw/day &	Total dermal exposure (Hands & Body); both	[5]	Calculator: https://r4eu.efsa.europa.eu/app/opex

Model	Output	Body parts	Reference	Website (if applicable)
	% of AOEL/AAOEL	potential/external and the absorbed amount		Guidance: https://r4eu.efsa.europa.eu/app/opex
SeedTropex	mg/kg bw/day	Total dermal exposure (Hands & Body); both potential/external and the absorbed amount		

Annex F
(informative)

Measurement of dermal exposure

When measuring dermal exposure, the classification of measuring procedures according to their purposes and the requirements that have to be fulfilled by measuring procedures as stated in ISO 20581should be followed. The classifications of measuring procedures according to their purposes are based upon the measurement strategy in EN 689.

F.1 Measurement principles

Dermal exposure is usually reported separately for the hands and the body. For measurement of dermal exposure three basic principles exist, these being interception (also known as surrogate skin), removal and in-situ. Each sampling principle includes a diversity of methods, each with degrees of freedom for selection of agent, collection media, extraction media, body location, etc. Each measurement principle results in different measurement results, representing in either potential or actual exposure values.

Table F.1 — Sampling techniques and methods for estimating dermal exposure

Technique	Method[a]	Estimates
Interception Interception of agent mass transport by the use of collection media placed at the skin surface or covering work clothing during the sampling period	Media [substrates include patches, gloves, and coveralls]	Exposure mass
Removal Removal of the agent mass from the skin surface, the skin contaminant layer, at any given time	Hand wash/rinse Manual wipe (dry or wetted) Tape stripping	Exposure loading
In situ Direct assessment of the agent or a tracer at the skin surface, e.g. by image acquisition and processing systems at a given time. No actual sample removal takes place	Detection of UV/fluorescence of agent or added tracer as a surrogate by video imaging: attenuated total reflection (ATR-FTIR); or light probe	Exposure loading
[a] Not an exhaustive list.		

Sampling techniques and methods for estimating dermal exposure

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F.1.1 Interception methods

Interception methods are also known as surrogate skin methods, these methods rely on intercepting the agent of interest on the way to the body with collection media (samplers). Common samplers are patches and clothing in a broader sense, such as gloves, underwear, or coveralls. Exposure of feet and the head can also be

sampled with socks and a hat, hood or headband, respectively. The collection media are worn or, in case of patches, attached to the working clothes during the investigated task(s) or shift. After finishing the task(s) or shift, the collection media are removed and extracted with a suitable solvent. The extracts are subjected to chemical analysis in order to determine the amount of the agent of interest. Spatial and temporal resolution depends on the number of (sub)samples taken from 1) a surface and 2) in time. Key elements are the collection efficiency and the ability to retain the agent over the sampling period. Retention characteristics of interception substrates often differ from real skin or clothing.

F.1.2 Removal methods

The agent of interest deposited on the skin is collected by removal from the skin. Removal is commonly performed by washing or rinsing with a solvent, by wiping with a medium, or by using tape strips. If removal is performed by wiping or with tape strips, the agent of interest is extracted from these media afterwards. The washing or rinsing solution, or the extract in case of wipes or tape strips is then subjected to chemical analysis. Usually, these types of methods are used for those body parts that are not covered by normal (work) clothing, e.g., hands, wrist, forehead or the neck. The spatial and temporal resolution depends on the number of (sub)samples taken from 1) a body surface and 2) in time; however, the barrier function of the skin can be disrupted by (frequent) sampling. A Critical issue is the removal efficiency in relation to the time of residence (interval between contamination and removal), where properties of the contaminant are important parameters, e.g. volatility, permeation/penetration and adherence to skin layers. Removal techniques may influence, or be influenced by, the characteristics of the skin and may also be of limited use for repeated sampling. Some removal techniques (e.g. skin washing) may not be appropriate for all body parts.

F.1.3 In situ methods

A requirement for *in situ* methods is that the contamination of the skin or clothing can be visualized. Particularly sensitive signals can be generated by fluorescence when irradiated by UV light, but strongly coloured substances (e.g. dyes) can be detected as well. If the substance of interest is not coloured or fluorescent by itself, a suitable dye or fluorescent tracer may be added to the substance or product that is used. The agent of interest deposited on the skin or clothing is detected directly by visualization. This can be performed by photographic methods. Visualization with UV light is advantageous, but requires a fluorescent agent of interest or addition of a fluorescent tracer. The resulting photographs are then evaluated, for example by using computer software. In principle, detection by Fourier-transform infrared (FTIR) spectroscopy or using (UV) light probes is possible as well, but in practice limited to very small areas that fit under the sensor that is used.

F.1.4 Lack of suitability for quantification of in situ methods

In general, quantitative measurements employing interception or removal methods are well established and reliable. In contrast, quantification of dermal exposure based on *in situ* methods is error prone and less reliable at the current stage of development. *In situ* methods show their advantages rather in the possibility of visualizing exposure patterns, which may enable optimisation of the measurement strategy (e.g. identification of affected parts of the body, allowing exclusion of rather unaffected body sections for quantitative exposure risk assessment (see 6.3), identification of favorable positions for attaching patches), assist selection of RMMs (including PPE), and open up training opportunities on exposure reducing working methods.[73][74] For this reason, *in situ* methods are not recommended for quantitative measurements in this document.

Interception and removal measurement methods are intended to evaluate dermal exposure mass or dermal exposure loading. It should be taken into account that extrapolation from small areas sampled (e.g. patches or skin strips) to the whole exposed area can introduce substantial errors.

F.1.5 Potential and actual exposure

Measurements of dermal exposure mostly aim to determine the potential exposure, i.e., the exposure expected to occur on the unprotected skin or clothes. In-situ methods can be very helpful to evaluate the exposure

pattern and to decide which body parts are likely to be exposed. In some cases, determination of the actual exposure, i.e., exposure expected to occur under PPE such as coveralls or gloves is desired. This can be achieved with interception methods by placing the collection media under the protective equipment, or with removal methods by taking the samples from skin that was covered by the PPE during the investigated work task(s) or shift. In this respect, removal methods are typically used for the hands and forearms that may be covered by PPE and also for the chest region in some instances. If actual exposure is sampled, it must be ensured that the sampled areas are not covered by other patches or samplers that influence the possible penetration through the work clothing.

F.2 Selection of methods

Selection of the appropriate measurement method is part of the measurement strategy and depends on a range of factors, including the sampling objectives, the compartment, transport process of interest, nature of the agent, and use of analytical methods.

As is described above, the predominant transport processes affect the selection of the sampling method depending on the sampling objective. If both transport from the skin contaminant layer into the skin by uptake and transport from the skin contaminant layer to other compartments (by removal, resuspension and/or evaporation) are low, any of the sampling principles or methods for evaluating the mass transport processes are applicable, but in case of high rates of one or both pathways, the removal technique might underestimate the level of contamination substantially(see Table F.2).

For risk assessment purposes, the impact of high or low transport rates on the selection of sampling methods is slightly different. Low transport rates allow use of removal techniques applied immediately before decontamination to adequately estimate the level of contamination of the skin contaminant layer relevant for uptake. If the removal, resuspension and/or evaporation rates are low, but uptake rate is high, an interception or in situ (direct) technique would give a good measure of dermal uptake. If the removal, resuspension and/or evaporation rates are high and uptake rate is low, an interception sampler (assumed to have a better retention performance compared to skin) would greatly overestimate uptake. In this case, biological monitoring, being a non-route-specific method for uptake, would be preferable, and also in the cases that both transport rates are high (see Table F.3).

The following considerations are largely based on the study on comparison of different measurement methods.[73] [75][76] The study investigated one agent (Tinopal SWN) in 10 exposure situations sampled with two sets of methods and 12 repeats each, resulting in a total of 160 experiments for each method set and 4000 individual samples. There it was found that both interception and removal methods are in general similarly suitable for measuring dermal exposure, whereas in situ methods suffer from the problems outlined above.

If a measurement of dermal exposure is necessary, it should first be considered which parts of the body are exposed to what extent. There are many activities in which exposure is restricted predominantly or even exclusively to the hands and possibly the forearms or lower legs. In these cases, it might be useful to limit the measurements to these body parts. Head exposure, on the other hand, might only be relevant for some specific situations, e.g., large-scale or overhead spraying. In any case, if body parts are omitted from the measurement strategy, the reasons shall be justified in the study report.

For hand exposure, sampling with cotton gloves tends to measure higher exposure levels than washing or wiping of hands. In the above mentioned study, the ratio between values measured with cotton gloves and by handwashing was between 0.9 and 5.7, based on median values measured for different activities, for liquids of different viscosity and for powders. The observed differences might be attributable to the nature of the contaminant (e.g., liquids with different viscosity or powders), the source of the exposure and its resulting pattern (e.g., liquids running over the hand, splashes or transfer due to contact with contaminated surfaces or tools). However, a systematic approach that would allow to make a prediction in this regard could not be identified so far. On this background, a more conservative approach using the interception method with cotton gloves is recommended to measure hand exposure.

For measuring body exposure, using patches or coveralls are by far the most common methods. Both methods measure similar exposure levels, but there is a tendency for patches to generate slightly higher exposure levels if extrapolation to the same body surfaces is performed with either method. Apart from this, both methods seem to be equally suitable for measuring body exposure from a scientific point of view. This applies also to very different exposure patterns, including evenly distributed exposure as occurring towards (e.g. spray aerosols), and, on the other hand, scattered, splash dominated patterns (that occur during e.g. painting or pouring), to name two extremes. The experiments thus have disconfirmed a popular belief according to which patches were inappropriate to measure splash dominated exposure patterns, because splashes could completely miss or hit a patch, which would lead to under- or overdetermination. However, it was observed that the different exposure patterns influence the variation of values determined during a series of individual measurements. For both methods, the variation is higher for splash dominated patterns, which should be considered when designing measurement campaigns. For instance, scattered, splash dominated exposure patterns may require a higher number of measurements than homogenous patterns to allow drawing robust conclusions.

An advantage of using coveralls is that in total higher substance amounts are collected, which might allow reaching lower limits of quantification (LOQ), which may be relevant in cases where this parameter is crucial. On the other hand, using coveralls is usually more labor and cost intensive. During field trials, coveralls require to be taken on and off carefully with the assistance of one or two technicians, and in addition they are usually cut up according to a given pattern of body sections. The extraction of the coverall sections also requires more solvent than for the smaller patches, which increases the method LOQ and may make the method inapplicable. Thus, for a given budget, a higher number of measurements may be feasible when using patches. In summary, this document recommends both methods equally, considering the aspects discussed here individually for a given exposure situation.

Table F.2 — Process/Pathway analysis in relation to selection of measurement methods

Removal, resuspension and/or evaporation rates[a]	**Uptake rate**[b]	
	High	Low
High	Interception	Interception
Low	Interception	Interception Removal

[a] Evaporation rates are derived from physicochemical data

[b] Uptake rates are derived from kinetics data

Table F.3 — Proposed sampling methods for risk assessment purposes

Removal, resuspension and/or evaporation rates	Uptake rate	
	High	Low
High	Biomonitoring	Biomonitoring
Low	Interception (In situ)	Removal (In situ)

F.3 Biomonitoring

Biological monitoring, or biomonitoring, is a tool for use in assessing good exposure control. It is the measurement and assessment of elements, chemical compounds, or their metabolites in biological samples from exposed workers. This can determine the total uptake by an individual accounting for all exposure routes,

these primarily being dermal, inhalation, ingestion, and, potentially, injection. It can be used as a complementary occupational risk assessment to workplace air monitoring.

Biological monitoring is especially useful when there is likely to be significant absorption through the skin and/or the control of exposure depends on PPE and/or the substance of interest is highly volatile and may not remain on dermal samplers. It combines all routes of exposure and any combination of them, but this does make it difficult to identify the source of any exposure (occupational or non-occupational). It is not applicable for acute or local toxic effects.

Samples taken are typically urine, blood or exhaled breath, or any combination of these. Other potential samples include hair and saliva. Quantitative analysis of the samples allows for the determination of the overall systemic exposure or internal dose for the target chemical(s).

It is important to understand that using dermal dosimeters that cover all or most of the worker's skin may prevent the deposition and absorption of a substance expected to be measured with biological monitoring. The simultaneous use of biological monitoring and dermal dosimeters should be a considered decision.

Measured values are given as a concentration of a substance in the sample type e.g., blood or urine. In urine this may be corrected for the level of creatinine. These concentrations can be compared to limit values such as Biological Monitoring Guidance Values (BMGV), Biological Tolerance Values (BAT), Biological Limit Values (BLV), Threshold Limit Values (TLV) and Biological Exposure Indices (BEI). Exposure above expected levels (as previously discussed in 6.3) is an early indication that exposure control is insufficient, and action is required before irreversible health consequences might begin to appear in workers.

Biological effect monitoring is the quantification of an early, reversible, indicator of toxic effect. It normally involves measuring biochemical responses (for example, measuring plasma and erythrocyte cholinesterase activity in workers exposed to organophosphorus pesticides). These responses may have potential health implications for the individual and may arise from causes other than occupational exposure. Consequently, biological effect monitoring should always be carried out with the close involvement of an occupational health physician.

Ethical considerations must be regarded during the entire process of the study. Individual biomonitoring results are personal data and should be handled accordingly. The two significant ethical issues are the confidentiality of results and the right of the workers to know results related to their samples. It is essential to obtain written consent from workers and it should be remembered that employees are not obliged to participate in a biological monitoring programme, and they are free to withdraw at any time without explanation or consequences.

There are several sources of further information [77][78][79]and the OECD (Organisation for Economic Cooperation and Development) have developed an Occupational Biomonitoring Guidance document.[81]

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