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Workplace atmospheres — Measurement of dermal exposure — Principles and methods

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National foreword

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Foreword

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ISO/TR 14294 was prepared by Technical Committee ISO/TC 146, *Air quality*, Subcommittee SC 2, *Workplace atmospheres.*

Introduction

Dermal exposure assessment explores the dynamic interaction between environmental contaminants and the skin. Occupational skin diseases and disorders constitute a significant percentage of workplace illnesses; the number and frequency of work-related adverse health effects involving the skin is considerably greater than health effects involving the respiratory system[1]. Occupational skin diseases affect virtually all industry and business sectors and are estimated to cost the European Union 600 million Euros each year, resulting in around 3 million lost working days[2].

For thousands of chemicals in the workplace, the contribution to total-body exposure by the dermal route has yet to be determined. Historically, the assessment of occupational exposure has focused on inhalation of chemical agents; however, toxicological evidence indicates that dermal contact can serve as the primary route of exposure for many chemical substances and that the contribution to total dose, integrated from all exposure routes, should be considered. As occupational inhalation exposure limits are lowered, the dermal contribution on total dose becomes more critical to assess.

In the decade before publication of this Technical Report, scientific research on dermal exposure continued to be published. An important contribution to this field was the development of a conceptual model for dermal exposure (see Annex A)[3]. The model systematically describes the transport of contaminant mass from exposure sources to the surface of the skin and provides a structure for both qualitatively and quantitatively evaluating dermal exposure.

The purpose of this Technical Report is to provide a framework of methodologies, including guidance on application and consistency regarding the measurement of dermal exposures to agents in the workplace.

Workplace atmospheres — Measurement of dermal exposure — Principles and methods

1 Scope

This Technical Report provides general considerations for the assessment of dermal exposure in workplaces. It offers guidance on dermal exposure assessment and the commonly used approaches for measuring dermal exposure[4][5]. An understanding of the advantages and limitations of each approach assists in the selection of the appropriate method(s) to meet the assessment objective. This Technical Report, however, is not intended to provide expert guidance, such as in the case of exposure scenarios or chemical agents.

This Technical Report is intended to assist occupational hygiene practitioners and researchers in developing a dermal exposure assessment strategy in agreement with its intended purpose. More importantly, it promotes adaptation of a consistent approach to assessing dermal exposure, and provides a framework for the assessment and validation of method performance.

This Technical Report describes the requirements against which sampling methods for determining dermal exposure need to be assessed; methodologies and specifications are proposed for the following procedures (not all requirements may be applicable to all methods):

a) sampling efficiency;

b) recovery efficiency;

c) sample stability;

d) capacity;

e) bias, precision, uncertainty;

f) core information;

g) contextual information.

NOTE 1 Core information is descriptive of measuring procedures, including the purpose of the assessment, sampling strategy, and sampling and analytical methods (see Clause 7). Method-specific core information is further refined within Annexes B to F (e.g. B.4.5 specifies the collection substrate, such as the fabric type, thickness, sizes, and backing materials).

NOTE 2 Contextual information is descriptive of the locations in which samples are collected, the exposure situation, the worker(s), the environment and the exposure agent (see Clause 7).

2 Normative references

The following referenced documents are indispensable for the application 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 3534-1:2006, *Statistics — Vocabulary and symbols — Part 1: General statistical terms and terms used in probability*

ISO 3534-2:2006, *Statistics — Vocabulary and symbols — Part 2: Applied statistics*

ISO 15767:2009, *Workplace atmospheres — Controlling and characterizing uncertainty in weighing collected aerosols*

ISO/IEC Guide 99:2007, *International vocabulary of metrology — Basic and general concepts and associated terms (VIM)*

EN 689:1995, *Workplace atmospheres — Guidance for the assessment of exposure by inhalation to chemical agents for comparison with limit values and measurement strategy*

EN 14902:2005, *Ambient air quality — Standard method for the measurement of Pb, Cd, As, and Ni in the PM10 fraction of suspended particulate matter*

3 Terms and definitions

Definitions of the following terms are obtainable from the references shown in parentheses: bias [ISO/IEC Guide 99:2007]; method detection limit [EN 14902:2005, modified]; precision [ISO 3534-1:2006]; true value [ISO 3534-2:2006]; workplace [EN 689:1995].

Figure 1 illustrates period intervals related to dermal exposure.

For the purposes of this document, the following terms and definitions apply.

3.1
agent
any chemical or biological entity on its own or admixed as it occurs in the natural state or as produced by any work activity, whether or not produced intentionally and whether or not placed on the market

[EN 689:1995]

3.2
dermal contact volume
volume containing the mass of the **agent** (3.1) present on the **dermal exposure surface** (3.7)

NOTE This theoretical term is equivalent to the volume of the **skin contaminant layer compartment** (3.14); however, for practical reasons, it is defined by the mass of all substances present in the skin contaminant layer.

3.3
dermal exposure
process of contact between an **agent** (3.1) and human skin at a **dermal exposure surface** (3.7) over an **exposure period** (3.8)

3.4
dermal exposure concentration
concentration of the **agent** (3.1) contained within the **skin contaminant layer compartment** (3.14)

NOTE 1 The dermal exposure concentration is the **dermal exposure mass** (3.6) divided by the **dermal contact volume** (3.2) or the dermal exposure mass divided by the mass contained in the **skin contaminant layer compartment** (3.14).

NOTE 2 The dermal exposure concentration is a theoretical concept. In reality, only the **dermal exposure mass** (3.6) can be estimated via sampling owing to the fact that the **dermal contact volume** (3.2) is unknown. Dermal exposure concentration can be expressed in milligrams per litre or milligrams per kilogram.

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

NOTE For practical reasons, dermal exposure loading can be expressed as mass of **agent** (3.1) in an exposed part of the **skin contaminant layer compartment** (3.14) divided by the surface area of that part, expressed in grams per centimetre squared.

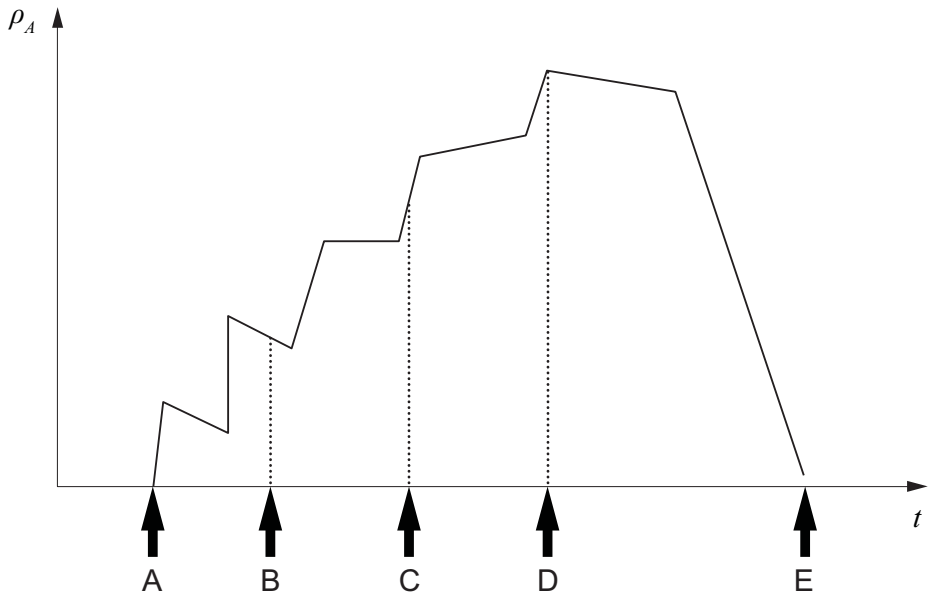
3.6
dermal exposure mass
mass of **agent** (3.1) present in the **dermal contact volume** (3.2)

NOTE For practical reasons, dermal exposure mass is defined by the amount of **agent** (3.1) present in the **skin contaminant layer compartment** (3.14).

3.7
dermal exposure surface
skin surface area where an **agent** (3.1) is present

NOTE For practical reasons, the dermal exposure surface is represented by a two-dimensional representation of the **skin contaminant layer compartment** (3.14), expressed in centimetres squared.

3.8
exposure period
time the **agent** (3.1) is present in the **skin contaminant layer compartment** (3.14)



Key
ρ_A exposure loading
t time

NOTE Figure 1 illustrates relevant period intervals such as sampling period (B-C), **dermal exposure loading** (3.5) or **immission** (3.9) period (A-D), and post-immission period (D-E). Of all these periods, the “sampling period” is arbitrary. Note that these intervals are for illustrative purposes and also that sampling can occur during any interval.

Figure 1 — Illustration of different periods of time, relevant in view of dermal exposure

3.9
immission
flux transport
rate of transport
flux deposition
rate of deposition
transport of an **agent** (3.1) from a defined source to the **dermal exposure surface** (3.7) or outer clothing **contaminant layer compartment** (3.10), resulting in a **dermal exposure loading** (3.5)

NOTE Immission is calculated as mass per time per surface area.

3.10
contaminant layer compartment
layers that contain a contaminant or **agent** (3.1)

NOTE 1 The contaminant layer compartment is characterized by a volume of unknown depth.

NOTE 2 Compartments include source, air, surface, skin, inner and outer clothing contaminant layers (see Figure A.1).

3.11
potential dermal exposure mass
total of mass present in the outer and inner clothing **contaminant layer compartments** (3.10) and **dermal exposure mass** (3.6)

NOTE 1 For practical reasons related to sampling methodology and strategy, the term potential dermal exposure mass refers to the sum of agent mass that has the potential to reach the skin (contaminant layer) from the clothing contaminant layer compartments and the agent mass present in the **dermal contact volume** (3.2). The conceptual model (Annex A) distinguishes between outer and inner clothing contaminant layer compartments, and characterizes the clothing itself as a buffer layer.

NOTE 2 The term actual dermal exposure mass is covered by the definition given for **dermal exposure mass** (3.6).

3.12
recovery efficiency
measure of how well the analytical laboratory can recover the **agent** (3.1) from the collection substrate

NOTE For the recovery efficiency of interception and removal methods, see Annexes B to E. See Annex F for a description of recovery efficiency specific to *in situ* methods.

3.13
sampling efficiency
measure of how well the sampling method can collect the **agent** (3.1) on a collection substrate

NOTE For the sampling efficiency of removal methods, see Annexes C to E. See Annex F for a description of sampling efficiency specific to *in situ* methods.

3.14
skin contaminant layer compartment
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 See Annex A.

NOTE 2 The SCL compartment is characterized by a volume of unknown depth.

3.15
uptake
concentration-driven transport of an **agent** (3.1) from the **skin contaminant layer compartment** (3.14) into the skin, i.e. crossing the interface between the skin contaminant layer (exposure surface) and the stratum corneum (absorption barrier)

NOTE 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 Assessment of dermal exposure

4.1 General

The most important, and often most difficult, part of any effort to assess exposures in the workplace is in designing a strategy to best match the primary objective(s) of the intended work in a manner that is scientifically sound, practical, and cost-efficient. The first consideration is the purpose of the assessment. Purposes may include but are not limited to: a) identifying exposures to chemical hazards; b) evaluating the effectiveness of controls; and c) assessing exposures for epidemiology.

Design of a given assessment strategy should be “fit for purpose”. The most demanding design is often for the study of adverse health effects of skin exposure, because accuracy of exposure estimates is one key input parameter in the overall study outcome. Other research efforts, such as exposure prevention and training, can be satisfied with less accuracy. The particular health effect of skin exposure should also match with the overall study purpose and any sampling efforts. Adverse health effects resulting from systemic uptake (3.15) of a chemical through the skin, such as for some pesticides, requires a different strategy from the study of a local irritant or contact sensitizer. An exposure assessment strategy cannot be successful without proper understanding of the nature of exposure and its variability. The multiple factors that may affect exposure characteristics are well addressed within the conceptual framework discussed in Annex A. Other subtle factors should also be considered including intermittent processes, irregular work schedules, overall health outcome, any of which could also be easily missed.

The question of whether to perform dermal sampling is an important consideration in the development of any dermal exposure assessment strategy. When evaluating the potential for exposure using the conceptual model (see Figure A.1), individual exposure compartments (i.e. exposure mass deposited on skin or clothing, loss of mass from decontamination or redistribution of mass to or from the skin) should each be considered, and a decision made about the best way to estimate exposure potential for a particular compartment. Sampling alone may be sufficient to fully characterize exposure potential, or the results of sampling may be combined with qualitative information, chemical characteristics, or mathematical modelling results to refine exposure estimates. For qualitative or semi-quantitative estimates of dermal contamination, structured approaches are available that use identified or assumed determinants of exposure (or contamination). An example of such an approach is the semi-quantitative DeRmal Exposure Assessment Method (DREAM)[6]. DREAM consists of two components: inventory and an evaluation. The inventory comprises a hierarchically structured questionnaire with six modules: company, department, agent, job, task and exposure; information is obtained by observations and interviews. These modules address general information as well as possible determinants of exposure as identified by the conceptual model and by evaluating literature.

Once it is determined that sampling is to be used as part of the dermal exposure assessment, many important factors need to be considered. The selection of the most appropriate sampling technique and analytical method is often a balance between accuracy of analysis, invasiveness of the sampling protocol, cost, instrumentation, and laboratory availability. Figure 2 summarizes some of these broad groups of factors and is intended to serve as a reminder that basic, but important, questions should be asked at the beginning of the design phase of the study, including those following.

a) What is the purpose of this research?

b) Who should be sampled?

c) How many samples should be collected?

d) When and how should sampling be performed?

e) What is the cost?

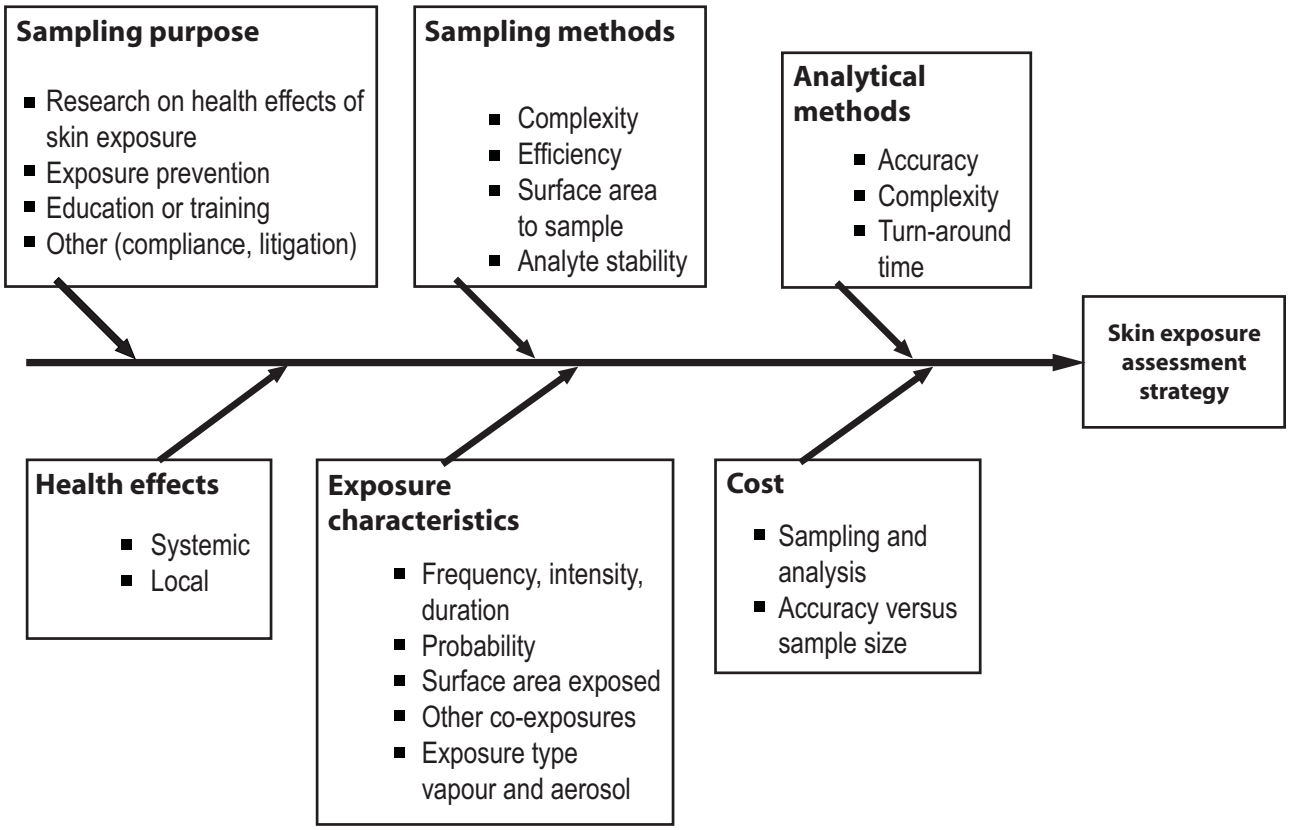


Figure 2 — Multiple factors to consider when designing a skin exposure sampling strategy

This decision process is often complex and requires balancing of competing factors, often between accuracy, access to study population and cost, and is best accomplished in a group effort that involves many disciplines, including exposure science, industrial hygiene, analytical chemistry, and statistics. Thoughtful considerations of these multiple issues at the beginning of the study pay great dividends later. The list of issues to consider is not exhaustive and for the most part self-explanatory. Brief descriptions of most of these issues are offered throughout this Technical Report. The reader is encouraged to add his/her other important considerations.

4.2 Defining study objectives

In general, four objectives (or purposes) for assessing dermal exposure can be distinguished.

a) Research on adverse health effects of chemical exposures, including risk assessment and epidemiological investigations.

   Investigation of possible associations between skin exposure and adverse health effects, development of exposure-response relationships for risk assessment, and estimation of disease burden from skin exposures for prevention purposes or compensation claims requires estimations of skin exposure. Results for risk assessment purposes should be linked to results of hazard assessment. Hazardous agents that show local effects are distinguished from hazardous agents that show systemic health effects after uptake.

b) Evaluation of exposure processes and pathways to assist in the development, implementation, and evaluation of exposure control measures or interventions.

Evaluation of exposure processes and pathways is needed in order to understand the sources and magnitude of exposure, to assist with the development of an adequate sampling strategy, and for effective risk management. Such evaluation is also needed for identification of appropriate control measures and effectiveness after implementation.

c) Education and training.

Skin exposure awareness should become part of the occupational and environmental health (OEH) curriculum, including worker training, field training for occupational hygienists, and training for OEH specialists. Intervention research that includes worker participation and workers' compliance with intervention protocols increases the likelihood that workers recognize the occurrence of skin exposures and understand that good personal hygiene practices are effective in reducing such exposures. Examples might include the evaluation of pesticide exposures using a fluorescence technique and isocyanate (US Patent No. 6,656,737[68]) or lead (US Patent No. 6,248,593[69]) exposures using colorimetric swipes.

d) Compliance, compensation claims or litigation.

Sampling for compliance would be relevant if there were statutory limits for dermal exposure. At the time of publication, however, no such limits have been set by national authorities or other international bodies. On the other hand, action limits may be used as references for compliance. Such limits may be at the level of any parameter of dermal exposure including exposure mass, loading, or surface area. Limits could also be based on determinants of exposure to include surface contamination levels. Contaminated surfaces may represent potential sources of exposure in the case of transfer of contamination to areas of unprotected skin. Disease compensation claims or litigation cases brought to court against business entities may require documentation of skin exposure, especially when inhalation exposure monitoring alone cannot explain the disease.

After deciding first to assess dermal exposures and then defining the objectives of the assessment, the exposure assessor should then choose among the most appropriate sampling methods. Principles and methods of sampling for the assessment of dermal exposures are described in Clause 5.

5 Principles and methods

5.1 Measurements methods and sampling

Figure 3 is a simple diagram of the dermal exposure process, depicting the process of mass transport towards the skin contaminant layer compartment (3.14). The exposure mass as part of the skin contaminant layer results in either a dermal exposure loading (3.5, mass per surface area of the skin contaminant layer) or dermal exposure concentration (3.4, mass per skin contaminant volume). The concentration gradient-driven transport from the skin contaminant layer into the skin (i.e. crossing the exposure surface interface between the skin contaminant layer and stratum corneum as an absorption barrier) is defined as uptake (3.15).

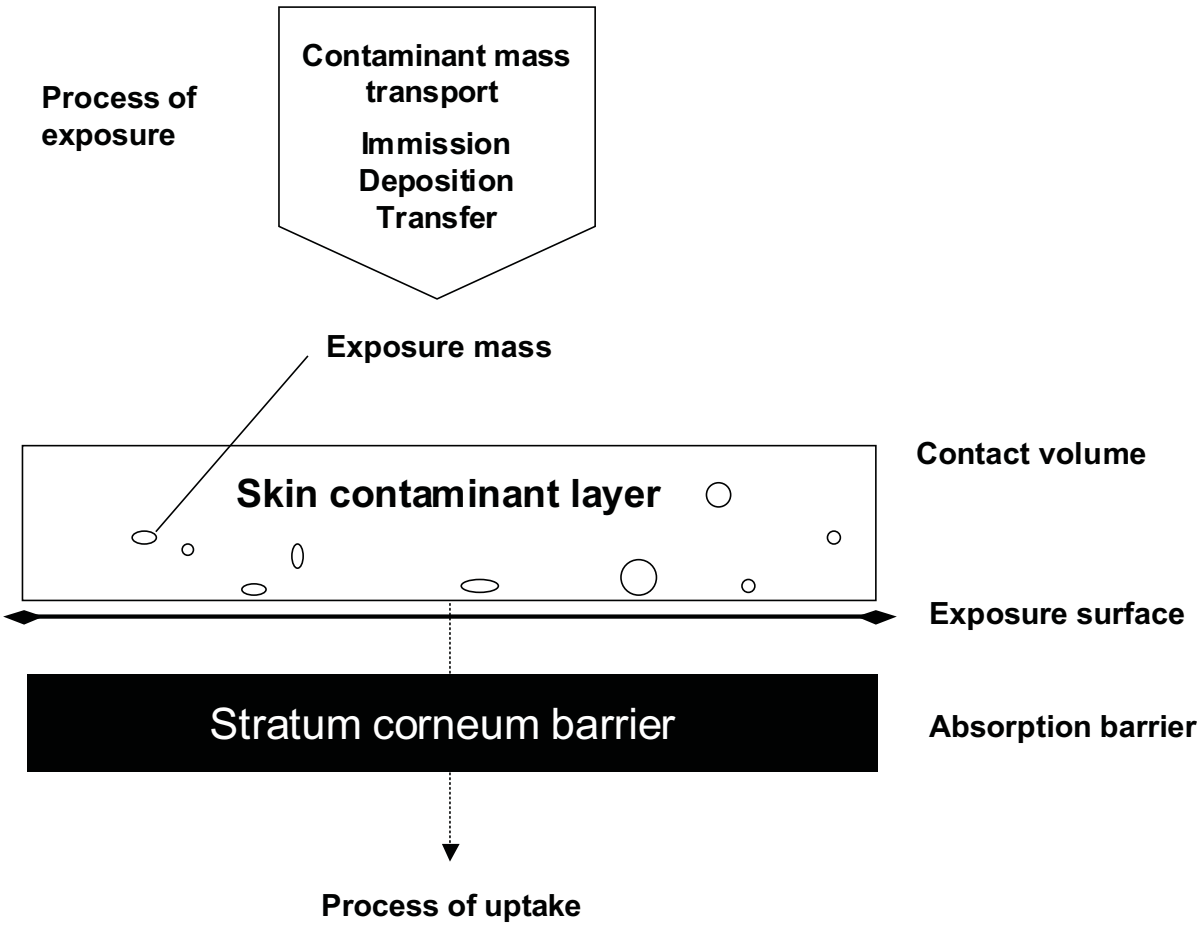


Figure 3 —The processes of dermal exposure, transport, and uptake

Table 1 presents the three major techniques for assessing dermal exposures and an overview of the more frequently used sampling methods for estimating dermal exposure. Agents collected by techniques such as interception and removal can be detected by chemical analysis of extracts from the removal or collection matrices such as wash liquids and wipe fabrics (see Annexes B to F).

Table 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 (Annex B)]	Exposure mass
Removal Removal of the agent mass from the skin surface, the skin contaminant layer, at any given time	Hand wash/rinse (Annex C)	Exposure loading
	Manual wipe (dry or wetted) (Annex D)	
	Tape stripping (Annex E)	
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 rflection (ATR-FTIR); or light probe (Annex F)	Exposure loading

[a] Not an exhaustive list.

These measurement methods do not attempt to evaluate dermal uptake (3.15), but rather are intended to evaluate dermal exposure concentration (3.4) or dermal exposure loading (3.5). Choice of measurement methods in cases where dermal uptake is an issue is described in CEN/TR 15278:2006[74].

The techniques and measurement methods specified in the preceding have the following limitations:

a) retention characteristics of interception substrates differ from real skin or clothing;

b) removal techniques (e.g. tape stripping, solvent washing, and use of surfactants) may influence, or be influenced by, the characteristics of the skin and may also be of limited use for repeated sampling;

c) some removal techniques (e.g. skin washing) may not be appropriate for all body parts;

d) extrapolation from small areas sampled (e.g. patches or skin strips) to the whole exposed area can introduce substantial errors;

e) the behaviour of a tracer (e.g. fluorescent) introduced in the mass transport when using *in situ* techniques may differ from the behaviour of the substances of interest.

5.2 Selection of sampling methods

Selection of the appropriate sampling method is part of the sampling 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. Selection of sampling methods should be part of a coherent and documented sampling strategy (see Figure 2). Principles behind various approaches, methods, materials, specific procedures and limitations are described in Annexes B to F.

Objectives for assessing dermal exposure (see 4.2) should take into consideration the following:

a) research on health effects:

   1) for risk assessment, it would be relevant to measure the concentration and time period profile in the skin contaminant layer compartment (3.14),

   2) for epidemiological investigations, the mechanisms of the health effect or other considerations determine the relevant parameters of exposure;

b) for evaluating exposure processes and pathways and in view of the conceptual model (Annex A), it is relevant to know mass transport rates from different compartments to the skin contaminant layer compartment (3.14) and how the different transport pathways contribute to total contamination;

c) to evaluate exposure control measures, it would be appropriate to measure compartment agent (contaminant) mass;

d) for compliance measurements, the definition of the exposure limit would prescribe the measurement range required for the analytical method.

Developing an appropriate sampling strategy related to the sampling objectives should include the selection of the relevant:

— agent (3.1);

— population/jobs/tasks;

— time of sampling (i.e. time of day);

— sampling period (i.e. duration of the sampling event);

— frequency of sampling;

— body locations;

— sampling method(s);

— sample size;

— selection of relevant analytical method(s).

Since the results obtained by different sampling techniques reflect different mass transport processes, additional method-specific core information, such as type of substrate, fabric, thickness, and size (see Annexes B to F) should be specified in the test report for proper interpretation of measurement results (see Clause 7). Quality control issues should also be included (see Clause 6):

— for interception methods: sampling medium, mass recovered from sampling medium, surface area of sampling medium, and sampling interval;

— for removal techniques: wipe/wash medium, mass recovered from wash/wipe medium, sampled surface area and body part, definition of $t = 0$, sampling interval, and history of subject;

— for direct techniques: total area measured, surface area exposed, definition of $t = 0$, pre-exposure screening, and sampling interval.

5.3 Temporal and spatial variations of exposure

Analyses of data on dermal exposure[7][8][9] indicate a generally higher within-worker variability than between-worker variability in levels of dermal contamination; therefore, it is important to include repeated sampling over relatively ‘long’ periods of observation (more than one week) to accurately characterize exposure conditions. While this approach is ideal, it may not always be possible. As a result, adjustments based on professional judgement or other factors may be necessary. Reliability of the estimate is determined more by the numbers of samples than by the accuracy of the individual sample. As a rule of thumb, collect three samples per individual per task at minimum.

An appropriate start time for target sampling or the duration of the sampling period is also determined by the rate of transport from the skin contaminant layer compartment (3.14). Transport processes can be divided into two pathways: a) from the skin contaminant layer into the skin by uptake (3.15); b) from the skin contaminant layer to other compartments by removal, resuspension or evaporation. The predominant pathway affects the selection of the sampling method depending on the sampling objective. If both transport rates are low, any of the sampling principles or methods for evaluating the mass transport processes (as described in Table 2) are applicable, but in case of high rates of one or both pathways, the removal technique might underestimate the level of contamination substantially. The importance of rates of uptake or evaporation for specific substances cannot be overemphasized when selecting the most appropriate method.

Table 2 — Process or pathway analysis

Removal, resuspension and/or evaporation rates	**Uptake rate**	
	High[a]	Low[a]
High[b]	Interception or *in situ* (direct) methods	Interception or *in situ* (direct) methods
Low[b]	Interception or *in situ* (direct) methods	Interception, removal or *in situ* (direct) methods

[a] High and low uptake rates are derived from kinetics data.

[b] High and low evaporation rates are derived from physicochemical data.

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 and *in situ* detection 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 3).

Table 3 — Proposed sampling methods for risk assessment purposes

Removal, resuspension and/or evaporation rates	**Uptake rate**	
	High	Low
High	Biomonitoring	Biomonitoring
Low	Interception and *in situ* (direct) methods	Removal and *in situ* (direct) methods

6 Quality issues

6.1 General

Quality measures are important components for each of the methods. Generic quality parameters are outlined in 6.2 to 6.6 and in more detail in the Annexes B to F.

6.2 Sampling efficiency

Methods for determining sampling efficiencies are given in Annexes B to F. In practice, sampling efficiency may only be approximated due to methodological limitations.

6.3 Recovery efficiency

Recovery efficiency is determined by spiked quality control samples (generated by dispersing a known and relevant quantity of the agent under investigation on to the sampling substrate). Spiked quality control samples should be collected, handled, transported and stored in conjunction with the experimental samples. Ideally, a separate set of quality control samples should be included at each site on each day of monitoring for each relevant sampling substrate. The same approach may be used in laboratory experiments to determine recovery efficiency.

OECD guidance[10] states that recovery efficiencies between 70 % and 120 % with coefficients of variation of 20 % generally demonstrate the capability of an analytical laboratory to perform accurate and precise measurements. Recovery results $>$95 % to 100 % should be noted, but should not be used to correct the data; however, results $<$95 % should be used to correct the data.

6.4 Background and contamination

Blank quality control samples are used to determine the upper limit of the agent in question present in the sampling substrate or skin not arising from direct sampling but due to background contamination and/or contamination due to sample handling, transport and storage. The blank quality control samples should be handled, transported and stored in conjunction with the experimental samples. Ideally, a separate set of quality control samples should be included at each site on each day of monitoring for each relevant sampling substrate.

6.5 Sample stability

The sample stability varies by agent (3.1), transport method, and storage and should be assessed as part of the field recovery investigation (especially relevant for agent-specific methods).

6.6 Analytical method

The analytical method should be validated according to standard laboratory analysis quality control protocols. Details, specific for the various sampling methods are given in Annexes B to F.

7 Test report

7.1 Description of the measuring procedure

The test report should give a description of the measuring procedure or give reference to guideline(s) according to which the measurements have been conducted and should contain all necessary information (core information) to carry out the measurements:

a) the purpose of the assessment;

b) the sampling strategy used;

c) the sampling method;

Descriptions of each procedure should contain all necessary information to carry out the sampling procedure, information about the attainable uncertainty[11], specified measuring range, averaging time, interferences and information on environmental or any other conditions which can influence the performance of the procedure. Where appropriate, the description for a specific method should include:

1) sampling medium, including information on constituents;

2) surface area of sampling medium;

3) sampled or measured surface area and body part;

4) definition of $t = 0$, (i.e. the point at which time is equal to zero, such as the beginning of a work shift or task);

5) sampling interval and history of subject;

6) sampling efficiency;

7) recovery efficiency;

8) sample stability.

d) the analytical method.

Results obtained with appropriate statistical analysis:

— bias;

— precision;

— uncertainty;

— method detection limit;

— method quantification limit.

Detailed specification for the core information is given in Annexes B to F. Other contextual information should also be collected and reported including information about:

— location;

— exposure situation;

— worker;

— environment;

— agent(s).

7.2 Core information

Annexes B to F should consider as “core information” that information about the purpose of the assessment, the sampling strategy, and the sampling method, including analytical laboratory requirements regarding capabilities and desired units of measure. Preliminary information may, in some cases, include some guidance about whether the agent is expected to be present in nanogram, microgram, or milligram quantities. This information may influence selection of the analytical technique, including the possible need for solvent extraction, solid-phase extraction, etc.

Annex A
(informative)

The conceptual model

The conceptual model[3] was developed to identify and describe mass transport processes resulting in dermal exposure assessment. The model is illustrated in Figure A.1. Explanations of abbreviations and their use are given in the following.

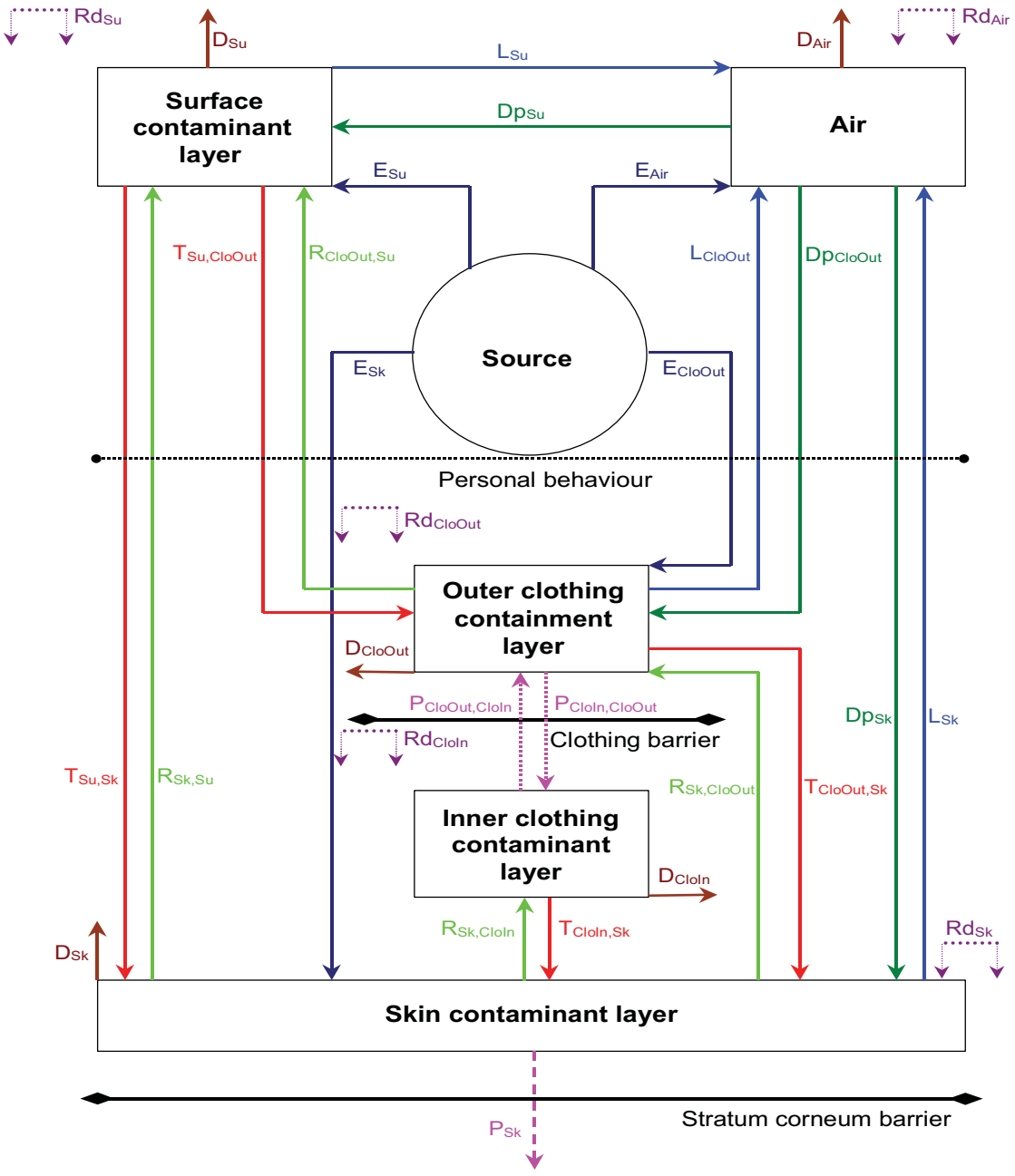


Figure A.1 — The conceptual model

The multi-compartment conceptual model begins with the exposure source, a process or activity from which mass is introduced into any remaining compartment, including the surface contaminant layer (Su), the inner and outer clothing contaminant layers (CloIn, CloOut), and 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: emission, deposition, resuspension, transfer, removal, redistribution, decontamination, and penetration and permeation. The horizontal dotted line in Figure A.1 indicates that personal behaviour is likely to influence mass transport processes.

Emission (E) is the transport of substances into the air, on to 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.

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

Resuspension or evaporation (L) is the transport of substances from surfaces (L_{Su}), outer clothing (L_{CloOut}), and the skin contaminant layer (E_{Sk}) to the air.

Transfer (T) is the transport of substances by direct contact between surface, skin, and outer and inner clothing contaminant layers in a direction towards the worker. Pathways include from surfaces to skin ($T_{Su,Sk}$), surfaces to outer clothing ($T_{Su,CloOut}$), and outer or inner clothing to skin ($T_{CloOut,Sk}$, $T_{CloIn,Sk}$).

Removal (R) is the transport of substances by direct contact between skin, inner and outer clothing, and surface contaminant layers 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 ($R_{Sk,Su}$).

Redistribution (Rd) is the transport of substances from a subcompartment to another subcompartment of the same type [e.g. touching the face with contaminated hands (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}).

Decontamination (D) is 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})].

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}). The skin contaminant layer compartment (3.14) is separated from perfused tissue by the stratum corneum, which acts as a rate-limiting barrier having a certain buffer capacity. Hazardous substances in the skin contaminant layer are taken up continuously into the body, driven by the concentration gradient between the skin surface and the perfused tissue. The risk arising from dermal exposure is thus firstly related to the time-dependent concentration of a substance on the skin surface rather than the mass of material on that surface at any given time.

Annex B
(informative)

Interception methods

B.1 Description of approach

B.1.1 Sampling principle

The principle of sampling is interception and consecutive retention of the mass transported towards the skin contaminant layer compartment (3.14) (i.e. immission, 3.9) by a collection substrate attached to the skin or clothing. Mass recovered from the collection substrate is a surrogate of the dermal exposure mass (3.6):

a) in the case where the collection substrate is attached to the outside of the outermost layer of clothing, the mass recovered from the collection substrate is a surrogate of the potential dermal exposure mass (3.11, see CEN/TR 15278:2006[74]);

b) in the case where the collection substrate is attached to the covered (protected) skin contaminant layer, the mass recovered from the collection substrate is a surrogate of the dermal exposure mass;

c) in the case where the collection substrate is attached to the uncovered (unprotected) skin contaminant layer, the mass recovered from the collection substrate is a surrogate of both the potential dermal exposure mass and the dermal exposure mass.

The main types of interception methods are patch, whole suit, and glove. These methods are conceptually simple. In interception sampling, absorbent or retentive dosimeters (e.g. patches, whole suits, and gloves), are attached to an operator's clothing or skin at various locations on the body prior to exposure. Following exposure, the dosimeters are removed and the amount of an agent retained by each patch is determined by an appropriate analytical method.

B.1.2 Sampling materials

Physical properties (e.g. roughness and porosity, absorbance capacity of the collection material), determine both capture/collection and retention properties (i.e. sampling and recovery efficiency, respectively). A wide range of collection materials are used in the construction of patches including cotton, rayon/polyester, polyester/cotton, flannel, filter paper, filter paper impregnated with lanolin, aluminium foil, surgical gauze, polypropylene and 6 mm polyurethane foam pads[5]. The World Health Organization (WHO) method[12], US Environmental Protection Agency (EPA) method[13] and Organisation for Economic Co-operation and Development (OECD) guidelines[10] all recommend the use of α-cellulose paper when measuring exposure to pesticides. The OECD guidelines also suggest that 100 % cotton or polyester cotton material can be used as alternatives. The use of charcoal cloth for monitoring dermal exposure to volatile compounds has been suggested.

In general, when assessing exposure to liquids, the sampling material should be absorbent enough to retain all liquids that contact it. Sampling for particles presents unique challenges, but current recommendations (e.g. OECD)[10] are that the material used should be porous enough to retain all particles landing on it.

The principle of complete retention of all challenge material is generically known as "infinite sink." The WHO and OECD methods specify when a sampler becomes saturated that it should be replaced with a fresh one, although no guidance is given on how to determine whether or not a sampler is saturated, and no guidance is given whether the entire sampler or only a portion should be saturated prior to replacement (e.g. the fingertip of a glove). The description of the patch method in Annex I of the OECD document[10] is ambiguous here; it also states that "The patch material should be absorbent enough to retain all liquid residues anticipated to be

in contact during an actual field study, as if it were the clothing *or the skin*, depending on the location of the patches" (italics added).

The principle of retention of only that fraction of challenge material that would be retained on the skin is generically known as "skin-equivalent." The OECD guidelines do not differentiate between the infinite sink and the skin-equivalent principles, but suggests that skin-equivalent is preferred.

Patches are generally backed with an impermeable material such as aluminium foil or polyethylene to ensure that collected contaminants do not escape from the patch into the skin or clothing beneath it, and also that the reverse does not occur. Additionally, the backing generally adds a degree of robustness to the patch. Alternatively the patch may be placed in a protective envelope.

The object of whole-body sampling is to measure the amount of a particular agent transported to the clothing or skin or penetrating the outer clothing layers. Typically, lightweight overalls are used to estimate exposure to covered areas of the body. Exposure of the head is measured either by a hood attached to the overalls or a separate hat. Exposure of the hands and feet can be measured by using gloves and socks respectively. Exposure of various body regions can be determined by sectioning of the suit, with analysis of the relevant region. The whole-body undersuit method can also be used to estimate exposure mass, by sampling next to the skin contaminant layer and intercepting the contamination that would otherwise reach the skin. Exposure mass has been measured next to the skin using close fitting long-sleeved vests and "long-johns".

Unlike patch sampling, a relatively limited range of materials has been used for suit sampling. Most typically, 100 % cotton or cotton-polyester mix is used, though the use of disposable overalls and coveralls has also been reported. Worn immediately underneath protective clothing, the method has been used to provide some indication of the effectiveness of protective clothing.

B.1.3 Sampling procedures

For patch sampling, "generic" protocols that prescribe sizes, numbers and location and method of attachment of patches are provided by WHO[12], US EPA[13], OECD[10]. Tailor-made study designs and protocols may deviate from these protocols. These protocols provide estimates of the body area represented by each patch, which vary slightly from one another. Some patch methods are chemical specific, including those of the US National Institute for Occupational Safety and Health (NIOSH)[14], specifically Methods 3600 (maneb), 9201 (chlorinated organonitrogen herbicides), and 9205 (captan and thiophanate-methyl).

OECD[10] also provides a procedure for standard and refined whole-body suit sampling. Basically, the procedure prescribes covering the body, including the arms to the wrists and the legs to the ankles, with pre-extracted and laundered dosimeters. Exposure to the head, neck and face should be determined by measuring transport to a hood as part of the suit (coverall) or to a hat or cap. Exposure to the feet should be estimated from measuring transport to socks. Following sampling, the suits are removed and usually sectioned according to the body parts of interest in terms of distribution of exposure mass, (e.g. forearms, upper arms, upper legs, lower legs, chest/torso, and back/torso). Each section should be stored separately and the agent being monitored extracted and analysed.

Dosimeters should represent as closely as possible normal work clothing. To avoid interference of the outer dosimeters with the transport process to the skin contaminant layer, sometimes only undergarments (T-shirt and briefs) are used to estimate exposure mass.

Specific procedures for the use of absorbent gloves have been identified in the literature for carbon nanotube material[15] and beryllium[16].

B.2 Use or applications of methods and interpretation of results

Interception sampling using patches, absorbent gloves and whole-suit dosimeters is appropriate for estimating the mass of an agent (3.1) that has potential for reaching the skin contaminant layer compartment (3.14). In addition to estimating the mass of the agent, interception sampling also allows estimation of the mass of exposure (i.e. the hazardous agent in the skin contaminant layer). Metrics are mass (e.g. in milligrams) or mass per surface area sampled (e.g. milligrams per body part or milligrams per anatomical region).

Extrapolation is needed to clarify assumptions (i.e. standardized body surface areas, homogeneous distribution of contaminations, etc.).

Results can also be used to estimate different rates of mass transport, (e.g. mass of agent transferred from the surface contaminant layer to the skin contaminant layer, the inner clothing contaminant layer to the skin contaminant layer, and the outer clothing contaminant layer to the skin contaminant layer). Furthermore, results may be used to estimate the mass of agent in the air compartment that is deposited on the skin contaminant layer.

If the collection substrate is not placed directly at the skin surface but is outside an underlayer of clothing, results only indicate potential dermal exposure mass (3.11) or potential mass transport rates to that clothing layer.

B.3 Limitations

Some limitations of interception methods are listed in a) to d).

a) Different collection materials and different “weights” (surface densities) of the same type of cloth obviously have different absorption, retention, and repellence characteristics affecting estimated exposure. It has also been shown that there can be substantial differences in characteristics between unwashed and washed overalls of the same fabric. In case of wet work or exposure to liquids, absorbent materials may tend to get overloaded.

b) The material from which dosimeters are made, used to measure potential dermal exposure mass, may be very different from that of the normal or protective clothing worn underneath. As a result, it is likely that the repellency, retention, and absorption characteristics of the sampling substrates differ from the worker's typical clothing which, in turn, influence measured exposure levels. Hence, estimated exposure mass as measured by dosimeters can be very different to the exposure actually experienced.

c) The major disadvantage of patch sampling is that estimates represent only the amount of an agent deposited on a particular area. The implicit assumption is that contamination is uniformly distributed over the area represented by both inner and outer patches. However, the patch represents only a relatively small proportion of a particular region and extrapolation could lead to underestimation, should droplets miss the patch when spraying, or overestimation, should a splash land on the patch. This methodology has been derived for agricultural exposure situations[10][13] where wide dispersive application methods such as fogging and spraying can (but not always) give rise to uniform deposition over body areas. The use of the same methodology in other industrial application or exposure situations where distribution may be non-uniform could result in less reliable estimations of exposure.

d) For suit sampling, large volumes of solvent are required to extract the contaminant from the substrate during analysis. Additionally, when the concentration of the contaminant is low, concentration of the solvent may be required, making the technique both time-consuming and costly. Also, using an extra layer of clothing to measure exposure can be uncomfortable, particularly with respect to the temperature, and restrict the movements of the wearer, leading to further problems. Where close-fitting suits are used as undergarments, the surface area of the sampler may be approximated by the equivalent body areas. Where (larger) oversuits are used as an outer layer, the increase in surface area may cause oversampling compared to an equivalent body skin area. However, the calculation of clothing surface area for the outer clothing contaminant layer has not generally been addressed in the literature: the surface area of a worker’s clothing may also be much higher than that of the skin underneath.

B.4 Quality issues

B.4.1 Number of patches

Different protocols recommend the use of different numbers of outer patches, ranging from 6 (WHO)[12], to 10 (US EPA)[13], to 13 (OECD)[10]. The UK Health and Safety Executive (HSE) uses another method, based on the WHO protocol, that suggests the use of a full set of patches (11) or a reduced set of patches (6)[17]. In contrast, generally only one or two inner patches are used and these should be placed on areas of the body where it is perceived that contamination is significant (US EPA, UK HSE)[13][17]. Inner patches should not be occluded by outer patches. In non-pesticide situations, fewer patches have been used, typically placed on the skin surface. Extrapolation of results should be justified and should only pertain to relevant anatomical region(s) of the body where exposure is expected to be significant. Consideration should be given to results less than the limit of detection.

B.4.2 Sampling efficiency

Sampling efficiency of interception substrates should be assessed, including well-defined characterization of the immission of an agent originating from a source and collection and retention by the sampling substrate. In general, data result from elaborated studies that involve combinations of substrates and immission types (e.g. patches and spraying).

B.4.3 Recovery efficiency

Recovery efficiency is equal to mass (quantified) divided by immission. The laboratory approach to verify recovery efficiency is based on spiking followed by extraction of the sampling substrate with known quantities of the agent. The method of spiking should be realistic, and should reflect the contamination pathways in the survey. A spike whereby the entire quantity is placed on one small central region of a patch would not reflect the average surface loading of the whole patch. See OECD guidance in 6.3; additional guidance can be obtained from organizations such as the European Commission (EC), US Occupational Safety and Health Administration (OSHA), US NIOSH, UK HSE, and other national health and safety organizations.

B.4.4 Sample stability

Stability over time should also be investigated by preparing sampling substrates with spiked quantities of the agent and analysing them immediately and at suitable time intervals thereafter, until the maximum anticipated storage period has been reached. It is important that both laboratory samples and exposed field samples are stored under the same conditions throughout this time.

Quality control (QC) samples should also be used during the exposure measurements, including blanks and spiked samples in which the amount of agent added should reflect the levels expected during the study. These QC samples are then exposed to the same conditions under which samples are collected, handled, transported, and stored. QC samples should also be analysed alongside the exposure samples. This approach allows determination of sample losses, if any, and hence allows for correction of field results. Recovery results >95 % to 100 % should be noted, but should not be used to correct the data; however, results <95 % should be used to correct the data.

B.4.5 Core information

In addition to general core information (7.2), sampling results should be accompanied by a clear description of materials and methods, including:

a) specification of the type of collection substrate: material type, fabric, specific density, thickness;

b) specification of size(s) of collection substrate;

c) specification of backing material (if appropriate);

d) description of numbers and locations of collection substrates;

e) description of surface area of collection substrates.

Metric(s) of exposure parameter: (potential) exposure mass per body part.

NOTE For patch sampling, this estimate is obtained from the product of the mass collected by the patch and the ratio of the body part area to the patch area.

B.5 Strategic considerations

Interception methods are appropriate for evaluating mass transport processes. Professional judgement should be used when applying interception methods to risk assessment, particularly in situations involving high transport rates from the skin contaminant layer (e.g. removal, resuspension or evaporation). Interception methods may be appropriate for estimating exposure mass when high rates of uptake are combined with low removal rates. Sampling can be repeated several times per work shift (i.e. prior to start of the work shift, before breakfast, before lunch, and prior to the end of the work shift) to obtain information about variation of dermal exposure during the work shift. However, the aim of the sampling may also be to assess exposure during specific tasks to evaluate consistency or variability by consecutive replicate sampling of the same workers, which demands end-of-task or periodic sampling.

Annex C
(informative)

Hand wash methods

C.1 Description of approach

C.1.1 Sampling principle

The principle of sampling is the removal of contaminants from the skin contaminant layer compartment (3.14) by providing an external force that equals or exceeds the force of adhesion. Three categories of external forces can be distinguished: mechanical action, hydrodynamic drag, and wet chemical action.

Generally, two basic methods can be identified:

a) (hand) washing can be defined as scrubbing the skin by mechanical agitation exercised by movements and pressure of both hands in liquid in a routine washing fashion — the contaminant is detached from the skin by a combination of mechanical forces and wet chemical action (dissolution);

b) (hand) rinsing or pouring can be defined as liquid-skin contact, where the contaminant is removed by a combination of hydrodynamic drag, and wet chemical action (dissolution).

Clearly, the basic distinction between both methods is the presence or absence of mechanical forces in the process of detachment. Within both methods, subcategories can be distinguished using either flowing or containerized liquids (which influences hydrodynamic drag), and the kinds of liquid (which influences solubility). Often detergents are introduced in the process to enhance the detachment of insoluble particles.

C.1.2 Sampling materials

Wash liquids may vary among tap, distilled, or de-ionized water, possibly in combination with commercially available surfactants, consumer product mild liquid hand soaps, and organic solvents. Organic solvents with mild irritative effects on skin such as neat alcohols [e.g. ethanol, 2-propanol (isopropanol)], may be used pure or as a solution (at mass fractions of 10 % or 40 % in water)[18].

Collection bags should be sturdy enough to hold 250 ml or 500 ml of solvent [e.g. commercially available polyethylene bags (0,025 mm thick)][13][19]. Wide-neck 5 l polyethylene containers filled with 1,5 l to 2,0 l tap water and detergent have also been used in washing procedures. No information is available on other types of bowls or containers.

A specially developed hand-washing device has been designed for hand washing with tap water flow[20]. This device consists of a tube attached to a water supply, an adjustable flow control set at a flow rate of approximately 3 l/min, a timer, a tap, a funnel, and a 5 l polyethylene bottle to collect the rinse water.

C.1.3 Sampling procedures

During bag rinsing, one approach is to immerse one hand in solvent while a technician holds the bag tightly just above the wrist to prevent leakage. Alternatively, the bag may be tightly sealed above the wrist with a rubber band. The hand should be shaken vigorously, either by the person being sampled or by the technician during a fixed period of time (e.g. 30 s)[7][19][20], a fixed number of shakes (e.g. 50 times)[13], or a fixed number of shakes (60) during a fixed period of time (30 s)[21][22] or (60 s)[22]. The person should cup the hand slightly and hold the fingers a short distance apart during agitation, and occasionally rub the thumb and fingers together and against the palm.

During hand washes, the subject is asked to wash his/her hands thoroughly in a routine fashion or according a six-step procedure[23]. Other references[7][19] report a procedure for solvent-based routine fashion hand washing in a bag, where workers were asked to wash their hands during 30 s. After removal from the solvent, the hands were allowed to dry above the solvent for 10 s before removal from the bag, and the procedure was repeated a second time in a fresh hand wash solution. Other chemical-specific procedures are described by the US NIOSH in Methods 3601 (maneb) and 9202 (captan and thiophanate-methyl)[14].

Another reference[20] uses a tap water and soap-based method for routine hand washing. After transferring approximately 1,5 ml of hypoallergenic soap from a dispenser on to the palm, the worker moistened his/her hands using a small volume of water. The worker then washed his/her hands in a routine fashion for a period of 15 s. The procedure was repeated for 30 s during which time the hands were kept in a stream of running water at a flow rate of approximately 3 l/min and allowed to drain into a funnel held above a container for 10 s. After rinsing the funnel with de-ionized water, the procedure was repeated again for 30 s.

Table C.1 summarizes the materials and procedures associated with hand washing and rinsing techniques.

Table C.1 — Example of materials and procedures

Washing	Solvent	Device	Fashion
Rinsing (one hand)	250 ml solvent	bag	vigourous shaking
Washing (two hands)	500 ml solvent	bag or bowl	routine[22]
Washing	1 500 ml to 2 000 ml water + detergent	5 000 ml container	routine
Washing (soap)	1 500 ml tap water	special device	routine
Washing (soap)	all	all	protocol[22]

C.2 Use or applications of methods and interpretation of results

The results of hand washing or rinsing could be interpreted as estimates of the exposure mass present in the skin contaminant layer compartment (3.14) that covers the hands at the time of washing. The metric would be mass per hand(s).

Assuming homogeneous distribution of exposure mass over the skin contaminant layer, the results could also be expressed as rough estimates of the mean dermal exposure loading (3.5) of the hands (mass per centimetre squared) (e.g. in the case of direct contact or immersion and a known surface area of the hands). Note that the mass collected may differ considerably among anatomical regions of the body.

Since all mass transport processes towards and from the skin contaminant layer of the hands are included, the results are highly relevant in view of risk assessment.

C.3 Limitations

A major limitation of hand wash methods is that practical use is limited to a single body location (i.e. hands, wrists, and parts of the forearms). Another limitation is that the barrier function of the skin may be disrupted during sampling; therefore, potentially minimizing the numbers of hand washes per day.

Associations between exposure mass (recovered from the wash liquid) and work activities can only be made when the hands have been decontaminated prior to initiation of work activities.

C.4 Quality issues

C.4.1 Removal efficiency

Removal efficiency is the mass of agent recovered from the wash liquid divided by the dermal exposure loading multiplied by the sampled area.

Hand wash removal efficiency tests are recommended[10][17][18], but a standard approach has not been adopted. Two different approaches have been identified.

a) Mass balance approach[24][25]. The contaminant is transferred from a surface with a known amount of contaminants to the hands of human volunteers. The amount of the contaminant that has been transferred is estimated from the difference between the amount of the contaminant which was not removed from the surface and the amount initially spiked.

b) Direct spiking[7][19][22]. For diluted metalworking fluids, 1 ml was spiked on the hands of a human volunteer[22] in portions of 0,5 ml. This procedure mimics exposure resulting from liquid exposure (spills, aerosol deposition).

C.4.2 Recovery efficiency

Recovery of the contaminant from the hand wash sample should be determined, which is usually linked to sample stability testing. See OECD guidance in 6.3; additional guidance can be obtained from organizations such a the European Commission, US OSHA, US NIOSH, UK HSE, and other national health and safety organizations.

C.4.3 Sample stability

Stability of hand wash samples over time should also be investigated by preparing spiked hand wash samples (QC samples) with known quantities of contamination and analysing them immediately and at suitable time intervals thereafter, until the maximum anticipated storage period (after completion of sampling) has been reached. QC samples should also be used during the exposure measurements, including blanks and spiked samples in which the amount of agent added should reflect the levels expected during the study. These QC samples are then exposed to the same conditions under which samples are collected, handled, transported, and stored. QC samples should also be analysed alongside the exposure samples. Also, caution is advised on correction of field results using (spiked) QC samples, as results can be altered by skin or transport. This approach allows determination of sample losses, if any, and hence allows for correction of field results. Recovery results $>$95 % to 100 % should be noted, but should not be used to correct the data; however, results $<$95 % should be used to correct the data.

C.4.4 Core information

In addition to general core information (7.2), sampling results should be accompanied by a clear description of materials and methods including:

a) wash liquid/solvent, wash volume, detergent (if any);

b) wash procedures and duration.

Metric(s) of exposure parameter: exposure mass, in milligrams, per body part.

C.5 Strategic considerations

For general considerations see Clause 5. In general, removal techniques are inappropriate in cases of high transport rates from the skin contaminant layer (e.g. removal, resuspension, or evaporation) and in cases of high uptake rates. When no indications can be obtained of either transport or uptake rates, the sampling interval or time window should be kept as small as practically achievable.

OECD[10] recommends performing hand wash sampling whenever the worker normally washes his/her hands (i.e. every 2 h to 3 h, before breaks, and at the end of the working day). However, the aim of the sampling may also be to assess hand exposure during specific tasks to evaluate consistency or variability by consecutive replicate sampling of the same workers, which demands end-of-task or periodic sampling.

Both OECD[10] and US EPA[13] recommend a (solvent) prewashing prior to the start of the task to remove background contaminants.

Annex D
(informative)

Wipe methods

D.1 Description of approach

D.1.1 Sampling principle

The principle of sampling involves the removal of contaminants from the skin contaminant layer compartment (3.14) by providing an external force that equals or exceeds the force of adhesion. Three categories of external forces can be distinguished: mechanical action, hydrodynamic drag, and wet chemical action.

Skin wiping can be defined as the removal of contaminants from (parts of) the skin by manually providing an external force to a (normally wetted) collection medium that equals or exceeds the force of adhesion over a defined surface area. Similar to hand washing, the contaminant is detached from the skin by a combination of mechanical forces and wet chemical action (dissolution).

D.1.2 Sampling materials

For skin wipe sampling, a cotton fabric-based sampling medium has been used most typically; however, cellulose smear tabs have also been used to collect PCBs from hands of transformer repair workers[26]. For skin sampling, wetted or soaked sampling media are used. In most cases, the sampling medium is soaked in de-ionized water or neat alcohols (e.g. ethanol and isopropanol), owing to the fact that these solvents enhance the solubility of most compounds and are not overly irritating to the skin. However, skin irritation may not be excluded with repeated exposure, which may be indicated by a remarkable increase (twofold) of sampling efficiency over a period of three consecutive days of sampling, also reported in the literature[27]. In a study to compare four solvents for their ability to remove selected agricultural pesticides from an *in vitro* porcine model[28], polyethylene glycol, soap and water, and a commercial decontamination product, in addition to 1-propanol, were used to demonstrate that repeat wipe sampling appeared to affect subsequent recovery.

With the exception of sampling hand skin surface, mostly templates are used to delineate the surface area to be wiped. The surface area depends on the body part. Circular, rectangular or squared templates have been used[28][29][30][31].

D.1.3 Sampling procedures

One study[29] used two different methods to wipe tracer particles from the forearms of volunteers. In one experiment, cotton fabric wipes, measuring approximately 10 cm^2 in surface area, were used as the sampling medium. The procedure included first soaking the wipes in distilled water. A rigid steel template with a circular hole in the centre (4 cm in diameter) was placed directly on to the forearm of the volunteer (exposed person). An operator (unexposed person) held the template in place, blotted excess moisture from the wipe and, using forceps, conveyed it to the gloved hand of the volunteer who wiped his/her own arm. The wipe was then transferred to a clean, labelled plastic bag. The procedure was repeated five times. In a similar experiment, a filter paper measuring approximately 8 cm^2 in area was used as wipe medium. A flexible aluminium template with rectangular hole in the centre (8 cm^2 in area) was placed directly on to the forearm of the volunteer and held in place by the operator. After blotting excess moisture from the wipe, the operator then rigorously wiped the arm of the volunteer and transferred the sample to a clean, labelled plastic bag. This procedure was repeated three times.

A second study[30] used a cotton ball as a wipe medium with a surface area of approximately 4,8 cm^2. Prior to exposure, a flexible 20 cm × 5 cm template was used to mark a surface area at a flat skin surface (e.g. the forearm). Cotton roll plugs were soaked in ethanol and wiped over the skin surface by the operator in one stroke. The operator wore vinyl gloves and, after wiping, transferred the plug to a labelled disposable polyethylene tube. Wiping was repeated 10 times.

A third study[31] used prepackaged, wetted polyvinyl alcohol wipes to collect nickel from the index fingers and palms of the dominant hands of workers before, during, and at end of shift; wipes were collected from workers' necks and foreheads before and at end of shift. Surface areas of index fingers were calculated using paper tracings; 4 cm × 2,5 cm acetate templates were used for palm, neck, and forehead samples. A fourth study[16] used prepackaged, wetted polyvinyl alcohol substrates to wipe beryllium from the necks and faces of workers following the performance of routine work activities. The procedure involved instructing each worker to first put on a pair of clean nitrile gloves and then to wipe their neck sequentially with each of two substrates in the area delimited from the top of the Adam's apple to the base of the chin and from ear to ear for a period not to exceed one minute. After placing the second wipe into a plastic bag, each worker put on another clean pair of nitrile gloves and wiped their peri-nasal area sequentially with each of two substrates for a period not to exceed 1 min. The same group[32] used pre-packaged, wetted cellulosic substrates to collect wipe samples from the hands and necks of workers before and during the performance of routine work activities.

For wiping hands, a fifth study[27] used commercial sponges wetted with 10 ml 2-propanol. The subject was instructed to perform a general wipe of the hands and then to place the sponge into a glass jar. A second sponge was wetted and the subject was instructed to thoroughly wipe each digit and the palm of the hand.

A sixth study[21] used 12 ply-cotton surgical pads wetted with water containing 1 % surfactant. For assessment of hand exposure, three separate wipes were used: one for the palm, one for the back of the hand, and one for the fingers and the thumb.

Table D.1 — Examples of materials and procedures

Materials		Procedures		
Sampling medium	**Wetting liquid**	**Template**	**No. passes**	**Operated by**
Cotton	neat alcohols	circular	2	operator
Filter	decontamination product	rectangle	6	volunteer
Wetting sponge	—	none	10	—
Smear tab	—	—	>10	—

D.2 Use or applications of methods and interpretation of results

The results of skin wipes may be interpreted as estimates of exposure mass present in the skin contaminant layer at a particular anatomical region of the body at the time of sampling. The metric is mass per body part. In most cases, body parts are not entirely sampled, but over a limited (and known) surface area. Therefore, results may also be expressed as rough estimates of mean exposure loading (mass per centimetre squared).

D.3 Limitations

A major limitation of wipe methods is that practical use is limited to a single body location (i.e. fingers, hands, wrists, forearms, foreheads, and necks). Another limitation is that the barrier function of the skin may be disrupted during sampling; therefore, potentially minimizing the numbers of wipes per day. Additionally, not all contaminant may be removed from the surface of the skin. One group[33] observed experimentally that serial wipe sampling was insufficient to remove all lead-containing dust from the hands of study subjects. Finally, another limitation is uncertainty regarding the representativeness of sample results.

Associations between exposure mass (recovered from the substrate) and work activities can only be made when the skin has been decontaminated prior to initiation of work activities.

D.4 Quality issues

D.4.1 Removal efficiency

Removal efficiency is the mass of agent on the collection substrate divided by the dermal exposure loading multiplied by the sampled area.

Removal efficiency is a key factor using wipe sampling results for assessing dermal exposure. In general, similar approaches are needed as used for the determination of hand wash removal efficiency (i.e. mass-balancing and direct spiking). A mass-balance approach was used[27] to determine removal efficiency for two pesticides. A solution of pesticides was spiked on a 15 mm × 15 mm square aluminium foil. After drying, volunteers pressed the foil using their hands and the residue remaining on the foil was analysed. The difference between applied and recovered mass to the foil was considered the mass transferred to the hands.

As part of a dermal penetration study[30], 0,3 ml of a pesticide solution (50 % volume fraction water + methanol) was directly spiked on to the forearms (area 100 cm^2) of 15 volunteers. The pesticide was allowed to reside on the surface of the skin for a period of 4 h prior to collecting wipe samples. A single operator used commercial swabs soaked in a water +ethanol mixture as the wiping substrate.

Wipe removal efficiency has been assessed[28] using four different solvents for four different radio-labelled pesticides. Each pesticide was directly spiked on to porcine skin at three different levels. Two drops (40 µl each) of a formulation were spread over a 6,45 cm^2 area of the skin. Each solvent, pesticide, and skin-loading combination was repeated three times. The time of residence (interval between application and wiping) was 90 min.

D.4.2 Recovery efficiency

Recovery of the contaminant from the skin wipe should be determined, which is usually linked to sample stability testing. See OECD guidance in 6.3; additional guidance can be obtained from organizations such as the European Commission, US OSHA, US NIOSH, UK HSE, and other national health and safety organizations.

D.4.3 Sample stability

Stability of wipe samples over time should also be investigated by preparing spiked wipe samples (QC samples) with known quantities of contamination and analysing them immediately and at suitable time intervals thereafter, until the maximum anticipated storage period has been reached. QC samples should also be used during exposure measurements, including blanks and spiked samples in which the amount of agent added should reflect the levels during the survey. These QC samples are then exposed to the same conditions under which samples are collected and are subsequently handled, transported, and stored. QC samples should also be analysed alongside the exposure samples. This approach allows determination of sample losses, if any, and hence allows for correction of field results. Recovery results >95 % to 100 % should be noted, but should not be used to correct the data; however, results <95 % should be used to correct the data (see 6.3).

D.4.4 Core information

In addition to general core information (7.2), sampling results should be accompanied by a clear description materials and methods, including:

a) wipe medium, wetting liquid, surfactants;

b) use of template, template dimensions, wiping pattern and number of passes;

c) other relevant information on procedures (e.g. operational details including time expended during sample collection).

Metric(s) of exposure parameter: exposure loading (milligrams per centimetre squared).

D.5 Strategic considerations

For general considerations see Clause 5. In general, removal techniques are inappropriate in cases of high transport rates from the skin contaminant layer compartment (3.14) (e.g. removal, resuspension or evaporation) and in cases of high uptake rates. When no indications can be obtained of either transport or uptake rates, the sampling interval or time window should be kept as small as practically achievable.

Timing and frequency of skin wipe sampling and selection of sampling locations depend on the sampling objectives. Skin wipe samples are generally collected post-exposure due to the fact that exposure assessment is often the major objective. Removal efficiency tests should be conducted, taking into consideration times of residence that are relevant for realistic durations of exposure (e.g. 90 min or 240 min). Note that spatial distribution of skin contamination is difficult to assess when entire body parts are wiped (e.g. hands, forearms, necks, foreheads); therefore, every effort should be made to use templates to delineate the surface areas of the skin when collecting samples from the various body parts. Spatial variability of exposure distribution then becomes more relevant. Even so, under- or overestimation of specific body parts is possible when extrapolating results from the area sampled.

Annex E
(informative)

Tape-stripping method

E.1 Description of approach

E.1.1 Sampling principle — Overview

Dermal exposure (3.3) to an agent (3.1) can be estimated by measuring the dermal exposure loading (3.5) of an agent removed from the skin with adhesive tape[34][35]. Tape sampling one or more times from the same area is called tape stripping. The method applies both for particulates and viscous compounds that remain on the skin for significant periods of time, thus enabling sampling. The method is non-invasive and offers the potential to recover or measure agents in the stratum corneum, distinguishing tape stripping from other skin sampling techniques that only recover superficial residues.

The principle of sampling is the removal of agent with an adhesive tape by providing an external force (peeling of the tape) that exceeds the force of adhesion of the agent on the skin[36][37]. Other types of sticky surface samplers are available, developed mainly for measuring surface contamination.

Adhesives in tapes are high molecular mass organic substances that flow under applied pressure so as to form an intimate mechanical bond with a substrate, in this case the skin contaminant layer compartment (3.14) and/or stratum corneum. As long as the adhesion of this interface, the internal cohesion of the adhesive material, and the adhesion to its support surface are all higher than the internal cohesiveness of the skin contaminant layer compartment, some portion of skin contaminant layer compartment (and also stratum corneum) is separated when the support surface is peeled away from the skin.

Removal efficiency is a key parameter for this method, dependent on the properties of the tape (adhesive and supportive backing), properties of the agent and amount on the skin contaminant layer compartment, and properties of the skin. The surface area of the tape defines the area sampled. Removal efficiency may be improved by increasing the number of tape strippings performed. Analytical recovery is also a key parameter. When the analysis is a visual technique (e.g. microscopy for asbestos, glass fibres and microorganisms), analytical recovery may not be a significant issue; however, when the tape has to be dissolved to perform the analysis, the technique shall be particularly robust for complete dissolution of adhesives.

Tape stripping can be employed for measuring dermal exposure on body areas[38] with high risk of dermal exposure during work tasks (e.g. hands and palms, lower arms, neck and forehead).

In occupational hygiene, tape stripping has been employed for sampling acrylates[39][40][41], asbestos, corticosteroid particles, diisocyanates, epoxy, glass fibres, jet-fuel, terpenic resin, acids, toxic metals, and microorganisms from the skin and contaminated surfaces.

Tape stripping is a well-established method in dermatology[42][43] used for sampling the stratum corneum. This method has been applied to study skin morphology, properties or function of the skin after exposure to different substances, and to determine the uptake and clearance of volatile and non-volatile solvents on the stratum corneum[44][45][46][47][48].

E.1.2 Sampling materials

The types of adhesive tapes commonly used for tape stripping have not been scientifically evaluated for use in dermal exposure assessment. A number of adhesive tapes, each with different properties, are available for dermatological, medical, and technical purposes. One tape was scientifically tested and verified and was used for measuring dermal exposure and surface contamination to acrylates[39].

Adhesive tapes should be absorbent enough to retain viscous compounds. Removal efficiency can be increased by repeated tape stripping. For particulates, the tape should be adherent, transparent to enable visual analysis by microscopy, and free of the agent of interest (i.e. background).

E.1.3 Sample preparation

The procedure for sampling, for handling samples, and analyses are all affected by tape selection. Tapes with removable backing are recommended, simplifying the whole procedure. Tape on a roll is hard to prepare in advance and the adhesive surface may lose part of its properties during preparation.

The size of the sampling tape depends on the study aim(s). The size of the sampling tape also influences the practical aspects of sampling and handling of samples. Size is usually limited to 10 cm^2. Some tapes enable flexibility of the area to be sampled.

The sampling tape should be cut into the desired size in a clean environment with a clean cutting tool (e.g. a scalpel). Uniform-sized pieces of tape should be transported in clean containers.

QC samples shall be prepared at the same time and stored in the same manner as sampling tapes.

E.1.4 Handling of samples

The risk of contamination in all phases of preparation, sampling, and sample handling shall be minimized.

Disposable, powder-free gloves should be used during sampling and changed immediately if contaminated, or at least after collecting each series of tape-stripping samples from a study participant.

Special care should be taken to protect samples in the field. The samples should be transported to the laboratory in sealed, individually marked containers. The containers should be handled to minimize residue losses in transit and storage. Caution should be taken to avoid cross contamination; ideally, gloves should be changed between samples.

E.1.5 Sampling procedure

The following is an example of a sampling procedure, which may vary depending on sampling aims, properties of the agent to be sampled, and the type of tape.

Sampling of the skin is performed according to a strategy planned in advance (see Annex A).

a) Apply a predefined size of tape on to the skin site. Press gently with either tweezers or a finger covered by a clean disposable glove to improve adhesion. Avoid risk of contamination by holding the tape at the perimeter.

b) The sampling duration is defined *a priori*. In occupational settings, this duration is often limited to up to 2 min for practical reasons.

   The amount of agent removed from the skin at each stripping is substance specific; therefore, the adhesive tape employed for sampling should be verified for each specific subject to verify optimal removal efficiency as well as suitability for analysis.

c) Remove the tape carefully using tweezers. Use steady constant speed and an angle of 45° from the skin to optimize the effect of adhesion force. Handle the tape sample at the perimeters to avoid contamination.

d) Place the sample in an individually marked container.

e) Repeat steps a) to d) according to the sampling strategy defined in advance. One to three strippings per skin site is considered sufficient in occupational settings.

NOTE This approach is valid when sampling compounds with low vapour pressure (non-volatile or weakly volatile) as well as for compounds that penetrate slowly on to or through the skin. Basically, the number of strippings depends on the objective of the sampling (e.g. properties of the agent, recovery of the agent from the skin contaminant layer, and available resources).

f) Add a volume of a solvent (defined a priori and optimal for the analysis) to the container, spiked with internal standard. Seal the container and place into a transportation container for laboratory analysis.

According to the literature, the amount of stratum corneum removed by stripping is not linearly proportional to the number of strips removed. Removal of stratum corneum is seldom studied when dermal exposure to chemicals is measured.

Although some investigators have reported preliminary results from laboratory-based studies that suggest the potential utility of this method for assessing environmental purposes, at the time of publication there were few larger-scale applications for assessing dermal exposure to harmful chemicals such as acrylates.

E.2 Use or applications of methods and interpretation of results

The result (mass removed by tape stripping) of the contaminated skin area estimates the exposure loading or the concentration present in the skin contaminant layer covering the skin area at the time of sampling. The metric is milligrams per centimetre squared and the area of the adhesive tape defines the surface area sampled. The result represents only the sampled skin surface area. Homogeneous distribution of the exposure mass over the skin contaminant layer is seldom assumed.

If repeated tape stripping is employed for sampling contamination from the skin, the total mass removed (pooled sampling) is the sum of all partial masses analysed from each tape.

If the removal efficiency of the selected adhesive tape is verified for the agent in the laboratory, then results from field measurements can be corrected to accurately estimate the amount of agent initially applied. By fitting a mixed-effects linear regression model to the tape stripping data, it is possible to estimate accurately the amount of initially applied agent.

Since mass transport processes towards and from the skin contaminant layer are accounted for, the results from tape stripping are highly relevant in view of risk assessment and preventive measures.

E.3 Limitations

A major limitation of the tape-stripping method is related to sampling area and body locations covered by hair, but the latter is also a problem for other dermal exposure measuring techniques. The number of samples per day may be limited in some occupations, but is seldom a concern. Another limitation of tape stripping is when sampling chemicals from the skin that have high transport rates from the skin contaminant layer (e.g. removal, resuspension or evaporation, and in case of high uptake rates).

There are several factors that should be considered before adhesive tape can be employed to measure dermal exposure, including removal efficiency of the agent from the skin. Although the choice of the tape is of crucial importance for the results, selection criteria and verification are dominantly absent in the literature (i.e. poor documentation and standardization). Selection of the optimum tape medium depends on characteristics of the agent, interaction between the agent and the skin, and the objectives of the user. Tape stripping can address multiple questions, but like other methods requires an informed understanding of multiple factors that may influence the results.

It is important to understand the difference between tape stripping from clean, dry skin (typical of controlled laboratory studies) and from dirty, contaminated, and/or wet skin (typical of the work environment). These conditions influence the amount of stratum corneum removed from the first few tape strips. Removal is also influenced by the properties of the agent and the amount of agent on the skin.

The application of the tape-stripping method for field evaluation of dermal exposure may be limited by the analytical limit of detection; however, pooled analysis of repeated tape stripping may overcome this problem.

The limited surface area of the tapes (typically up to 10 cm^2), compared to larger surface areas of the skin that may become contaminated, might result in strategic sampling problems also encountered with interception and other removal techniques (e.g. skin wiping). These issues, such as minimizing the sampling interval, might be enhanced for tape stripping because lateral diffusion of components in the stratum corneum may also influence the sampling result.

Limited data are available to enable evaluation of precision, within- and between-operator variability, and influence of physical sampling parameters including applied pressure, adhesion time, removal speed, and angle. Data from one study[39] indicate moderate variation in removal efficiencies from tape strips collected from different exposure sites and different volunteers.

It has been hypothesized that normalizing the amount of analyte removed from the mass of stratum corneum could alleviate some of this sampling variability. Approaches for measuring the amount of stratum corneum removed are available; however, practical application is limited due to the inherent high degree of biological variation.

E.4 Quality issues

E.4.1 Removal efficiency

Removal efficiency can be confirmed in laboratory studies and is defined as:

$$\frac{x_0 - x_1}{x_0} \times 100$$

where

x_0 is the initial mass or concentration of agent applied to the skin, which can also be considered to be the total amount of agent transported to the skin contaminant layer compartment;

x_1 is final mass or concentration of agent remaining on the skin.

Removal efficiency testing for adhesive tape is recommended[39], but has not yet gained attention in the literature. The laboratory approach is based on direct spiking of a known volume of an agent on to selected areas of the skin of human volunteers. The agent is removed after a defined period of time by tape stripping. This approach provides additional information about the behaviour of the agent on the skin. This procedure mimics exposure resulting from liquids (e.g. spills, aerosol deposition, and direct skin contact with contaminated surfaces).

E.4.2 Analytical recovery (from the aliquot)

Recovery of the agent from the aliquot should also be determined, which is usually linked to sample stability testing. See OECD guidance in 6.3; additional guidance can be obtained from organizations such as the European Commission, US OSHA, US NIOSH, UK HSE, and other national health and safety organizations.

E.4.3 Sample stability

Stability of tape-stripping samples over time should be investigated by preparing spiked samples (QC samples) with known quantities of contamination and analysing them immediately and at suitable time intervals thereafter, until the maximum anticipated storage period has been reached. A statistically relevant number of blanks shall be prepared and analysed to verify that the sampling matrix (tape) does not affect results at increasing sampling times.

QC samples should also be used during exposure measurements, including blanks and spiked samples in which the amount of agent added should reflect the levels during the survey. These QC samples are then exposed to the same conditions under which samples are collected and are subsequently handled, transported and stored. QC samples should also be analysed alongside the exposure samples. This approach allows determination of sample losses, if any, and hence allows for correction of field results. Recovery results >95 % to 100 % should be noted, but should not be used to correct the data; however, results <95 % should be used to correct the data (see 6.3).

E.4.4 Core information

In addition to general core information (7.2), sampling results should be presented accompanied by a clear description of materials and methods, including:

a) specifics of the collection substrate(s): material type, fabric, specific density, thickness;

b) specific size(s) of collection substrate(s);

c) location(s) on the skin and body part(s);

d) surface areas and numbers of tape-stripping samples per anatomical region of the body;

e) additional specifics of the tape (e.g. manufacturer and lot number);

f) specifics of the extraction solvent and volume used during analysis.

Metric(s) of exposure parameter: exposure mass (mg) per sampled area of the skin.

E.5 Strategic considerations

For general considerations see Clause 5. In general, removal techniques are inappropriate in cases of high transport rates from the skin contaminant layer (e.g. removal, resuspension or evaporation) and in case of high uptake rates. When no indications can be obtained of either transport or uptake rates, the sampling interval or time window should be kept as small as practically achievable. In field measurement, the sampling of the selected skin sites can be repeated several times per work shift to get better information about the variation of dermal exposure during work shift.

Sampling can be performed prior to start of the work shift, before breakfast, before lunch and prior to the end of the work shift. However, the aim of the sampling may also be to assess exposure during specific tasks or consistency or variability through consecutive replicate sampling of the same workers, which demands end-of-task or periodic sampling.

Improving extrapolation from single point sampling results to larger surfaces has been explored in dermal exposure studies using geostatistical approaches such as Dirichlet tessellation[49][50]. The Dirichlet tessellation is a geometric construction that divides a space populated by n points into n regions, each corresponding to all locations closer to a particular point than any other. If the space is convex, then these regions are connected and commonly referred to as tiles. Such an approach could also be applicable for the extrapolation of the results of tape strips from limited surface areas to larger surfaces.

Annex F
(informative)

In situ methods

F.1 Description of approach

F.1.1 Sampling principle — Overview

Dermal exposure (3.3) to an agent (3.1) can be quantified by measuring the quantity of the agent or an added tracer chemical, such as a fluorescent material or visible dye, directly on the clothing or skin. The sampling principle is "*in situ* detection of a surrogate tracer present at the skin or clothing surface". An important advantage of this method is that the skin or clothing serves as the collection medium, rather than dosimeter patches of different materials.

Three methods may be used as appropriate:

a) video imaging of the agent itself or an added tracer as a surrogate for the agent;

b) detection of the agent or a surrogate at the surface using attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectroscopy;

c) detection of the agent or a surrogate at the surface using a light probe.

The first method may be used over large surface areas. The second and third methods are restricted to small areas under a sensor.

F.1.2 Use of a tracer

If an agent itself cannot be detected directly on the skin by the methods above, a fluorescent or coloured dye or an infrared absorbing chemical may be incorporated into the challenge formulation at a known (absolute) concentration, or at a known concentration relative to the agent of interest. The subject uses the formulation to carry out normal work duties that give rise to dermal exposures.

If an investigator chooses to use a tracer compound or visible dye, he/she should check its suitability for use on the skin[51], and validate its performance and suitability as a surrogate for the intended measurement prior to the field study. Apart from the usual criteria of QC acceptability that are as applicable to tracers as to all agents, including pesticides, the surrogate compound should not significantly alter the physical properties of the formulation or spray mixture. The key question regarding the utility of a tracer or dye is whether it impacts, is retained by, or penetrates clothing in fixed proportion to the agent of interest. The relative transfer of the tracer and agent can be assessed by conducting ancillary studies to determine whether there are any differences. The tracer can sometimes be extracted from passive dosimeters or clothing and analysed in parallel with, or instead of, the agent, usually a pesticide.

F.2 Video imaging

The fluorescent tracer/video imaging method[52][53] reveals non-uniform patterns of exposure over large surface areas that might escape detection by other methods limited to small selected areas.

After carrying out work tasks using the agent or tracer, the subject stands in front of a bank of longwave ultraviolet (UVA) or filtered, visible lights. The exposed areas are photographed using a filtered video camera

to record the visible light emitted by the fluorescence or natural colour of the dye. The intensity of each pixel of the image is used to calculate the equivalent mass of dye present by reference to a calibration curve.

A second-generation imaging system with improved exposure quantification is now available[54]. Variations of the technique have been developed in several establishments:

a) using modified versions of Fenske's software[55][56][57];

b) using different software altogether in a similar physical set-up[58];

c) using different software and a different physical set-up[59][60];

d) using a small version for hands only, with illumination in the visible region of the spectrum rather than the ultraviolet[61].

The method is particularly useful for training operators by demonstrating the extent of their contamination, thus allowing them to modify their working practices to reduce exposure, although a non-quantitative system can also achieve this.

Reversing the concept, extinction of a pre-existing fluorescent brightness through the masking effects of a non-fluorescent contaminant (e.g. paint) may also be used to measure the area or concentration on the skin or clothing[62][63].

F.2.1 Sampling principle — Video imaging — Mass measurements on skin

The appropriate calibration may depend on the natural fluorescence and hue of the uncontaminated skin, so a set of photographs of the skin is usually necessary before starting work.

Mass measurements also require surface area measurements to be made. If a fixed focal length lens is used, each rectangular pixel corresponds to a fixed surface area. In-picture calibration of a known length can also be used for fixed and variable focal length lenses.

The mass calibration is non-linear. Whereas fluorescent dyes in solution follow the Beer-Lambert law resulting in linear increase in fluorescent intensity with concentration at low concentrations, fluorescent dyes on surfaces follow the Kubelka-Monk law, which is log-linear at low concentrations. However, the useful range of the method extends above the log-linear range, and a variety of linear or polynomial calibrations may be appropriate. Different software packages calculate the results in different ways.

A "sumpixels" approach has been used[52][55][57], in which the sum of all the pixel intensities in a body region is calibrated against total mass of dye in that region, the appropriate calibration being selected from a set of up to 11, as specified by the natural fluorescence. This method assumes that a linear profile exists such that each increment in the pixel or the sum of the pixels gives the same incremental increase in (logarithm of) mass. Another approach[58] also uses a sumpixel approach, but rather than select from a set of calibrations, the natural fluorescence is included as a variable in the linear calibration equation.

A non-linear calibration of intensity against surface loading for each pixel , which is then corrected for natural fluorescence, has also been used[59][60]. The surface area of each pixel is used to sum the loadings into masses. If the intensity calibration is linear, this process is effectively the same as the sumpixel approach, but can avoid the need for the assumption of linearity. A reference length in each image avoids the need to maintain a fixed focal length after calibration.

In addition, a non-linear calibration, but without the need for correction for natural fluorescence, has been reported[61].

F.2.2 Sampling principle — Video imaging — Area measurements on skin

A simplified analysis system can be used to measure just the contaminated surface area from its fluorescence in the apparently flat two-dimensional video image. This measurement may be done on flattened clothing as well as flat areas of skin. Visible food dyes are an alternative to fluorescent dyes on clothing for this purpose. There is no need for calibration as identification of contaminated areas is achieved by manual outlining, or by thresholding the image.

Where simultaneous mass and surface area measurements are required, more sophisticated area measurements may be needed when photographing curved surfaces as an apparently flat two-dimensional video image. Angled surfaces at more than 20° to the normal are foreshortened in the camera image and appear smaller. They also receive less light from a planar array, so their fluorescence is reduced. More photographs have to be taken to ensure that all surfaces are photographed at less than 20°. However, no method exists to delineate those areas less than 20° in each image. Fenske's software[52] included an algorithm of unknown origin to compensate for non-normal body surfaces. As it was unable to be validated, other users[57], removed it. Another study[58] has no compensation. A spherical lighting system has been used to eliminate variation in illumination at angles, and a correction algorithm introduced for foreshortening based on successive photographs[59][60]. This lighting system has been adopted directly into planar (Fenske-type) systems to reduce variation in illumination due to angles, but without need to adapt the planar software. Another contribution[61] restricts use of the method to flattened hands that do not need compensation on the palms and fronts of the fingers, although fingers remain problematic if contamination has spread around to the sides.

F.2.3 Sampling principle — Video imaging — Mass measurements on clothing

The dye can soak into absorbent fabrics and the dermal exposure mass (3.6) of dye can be drastically underestimated. Surface area measurements are not affected.

F.2.4 Sampling methods — Video imaging

Pre- and post-exposure photographs are taken of each limb in a set series of poses to record the location of any contamination from a variety of angles. Reference intensities (standard surfaces) may be included in each image to relate back to calibration images. The image size is calibrated for length and area beforehand for use with fixed focal length lenses, or a standard length is also included in each image.

F.2.5 Sampling materials — Video imaging

Usually, the fluorescent materials should fluoresce reliably in the dry state on the skin. Alternatively, measures should be taken to rewet the skin in a standard fashion[61].

Tracer materials have included:

a) oil- or water-soluble UV fluorescent dyes;

b) fluorescent dusts;

c) impregnated silica microspheres;

d) food dyes, vitamin B_2 (riboflavin);

e) titanium dioxide-containing paint (to absorb UV light and mask underlying fluorescence).

Light, non-fluorescent clothing materials shall be used where measurements on clothing are undertaken.

F.2.6 Use or applications — Video imaging

The amount of the fluorescence detected represents the amount of the fluorescent tracer material that is present in the skin contaminant layer (3.14) at the time of sampling. If it has been added at a known concentration relative to the agent of interest, the amount of the agent may be inferred. In rare cases, the agent itself fluoresces sufficiently to quantify. Additionally, the surface area exposed is quantified; therefore, the results can be used both as estimates of exposure mass and exposure loading.

F.3 Reflectance

ATR-FTIR spectroscopy may be used for skin surface analysis of optically dense materials such as lubricants and food products and can also be used for identification purposes. This method is limited to small selected areas using a crystal probe, which may be a large ZnSe crystal up to 10 cm × 1 cm (but which is toxic if swallowed and a skin irritant), or a diamond crystal of much smaller contact area ($<$1 cm^2).

Three pesticides have been measured[64], dosed on to the skin at up to 5 µg/cm^2, either placing contaminated fingertips on to a ZnSe crystal (n = 2) and measuring the mass, or dosing the crystal itself with pesticide then placing clean skin on top to measure surface loading. Another study[65] measured isocyanates on guineapig skin with a diamond crystal, but showed that it was possible to measure using ATR-FTIR on humans, bearing in mind the ethical issues of calibrating on human skin with sensitizing substances. Soap residues on the skin have been examined[66] after washing and rinsing with hard and soft water using a ZnSe crystal to detect absorption by the calcium carboxylate bond in soap. The residues were not quantified as absolute masses of soap, but the relative effects on the signal for the different treatments were examined.

F.3.1 Sampling principle — Reflectance

The key element of the method is an infrared-transparent crystal with a uniform refractive index. When infrared light is internally reflected off the crystal surface from beneath, an evanescent wave is produced extending out of the crystal surface and penetrating into any surface (such as the skin) in direct contact with it. The depth of penetration of less than 1 µm depends on the wavelength, angle, and refractive indices of the crystal and contact material. The infrared absorption of this evanescent wave by the surface can be measured and qualitatively and quantitatively analysed. A wide range of chemical bond structures may be detected over several wavebands by the wavelength-specific attenuation of the spectrum compared to the untouched crystal. Any agents with a suitable infrared spectrum would be suitable for the method. Compounds with large ring structures and halogen substitutions have relatively strong and specific absorption spectra.

F.3.2 Use or applications — Reflectance

The amount detected represents the amount of the agent or tracer material that is present in the skin contaminant layer at the time of sampling. If it has been added at a known concentration relative to the agent of interest, the amount of the agent may be inferred. The surface area exposed is not quantified unless the contact area on the crystal is defined; therefore, the results can only be used as estimates of local exposure loading.

F.4 Light probes

Amounts on small areas of the skin have been quantified[67] by fluorescence using a small probe and a light fibre. This method is limited to small selected areas of up to 1 cm^2. So far it has been limited to measurement of polyaromatic hydrocarbons on skin, but could also be used for surfaces.

A similar device (SMF2) has recently been produced commercially, with a UVA and UVB flashgun source but with spectroscopic capability for surfaces up to 5 cm^2. UVB should not be used on skin without careful consideration of exposure levels; however, the very short duration of a flash contributes no significant dose to the skin.

F.4.1 Sampling principle — Light probes

A light source irradiates the skin or surface (excluding stray light) to produce fluorescence. The Vo Dinh lightpipe[67] uses an optic fibre to transport the UVA light to the surface and the fluoresced visible light back to the detector. The SMF2 device produces broad spectrum light ranging from the visible to UVB, from a flashgun source close to the skin or surface and transports the fluoresced light back to a spectrometer via the optic fibre. The wide range of emission spectra includes visible, UVA, and UVB to allow a range of fluorescing dyes to be used.

F.4.2 Sampling methods — Light probes

As for video imaging.

F.4.3 Sampling materials — Light probes

As for video imaging.

F.4.4 Use or applications — Light probes

As for reflectance.

F.5 Interpretation of results

Where the tracer is not absorbed into the skin, it may be used as a surrogate agent where the agent itself diffuses into the skin with a high uptake rate. The data represent the amount of agent that came into contact with the skin and was available for uptake.

When the agent or tracer may be absorbed into the skin (e.g. polyaromatic hydrocarbons), it may be used to represent the amount of agent remaining at the skin surface.

However, the data recorded are a snapshot of the contamination on the skin at that moment of time. If the dye stains the skin and cannot be washed off with subsequent wettings, the data represent the accumulation of all agent on the skin up to that moment, even if the agent *could* be washed and is no longer there. If the dye is soluble and can be washed off again, the data represent the amount of agent remaining on the skin at that moment. The choice of dye is critical to the intended use for the data.

F.6 Limitations

The main limitations of *in situ* methods are the assumptions that the relative transfer of the tracer and the agent to and from the skin in the field, and their permeation and penetration of the clothing, are all equivalent. However, these assumptions are analogous to those involving generic exposure data (i.e. the exposure to an agent measured under a given set of conditions is assumed to represent that associated with a second agent under the same conditions). Possible differences in the relative transfer of the tracer and the agent can be assessed by conducting ancillary studies.

Among the other limitations of the video method are:

a) saturation of the non-linear calibration curve at high surface loadings;

b) fading of the tracer dye in sunlight during the work task or fading in the time interval between task and measurement;

c) fading in storage (clothing or calibration standard solutions);

d) difficulty achieving even coatings for calibration;

e) state of dryness of skin/surface;

f) absorbance into clothing (masking);

g) existence of fluorescent or coloured skin blemishes;

h) measurements of uncontaminated surface areas are less accurate than those of more contaminated areas because the edges are better defined.

Limitations of the infrared method have yet to be fully realized because the technique has had limited use up to now:

— applicability to surfaces other than skin, such as clothing;

— variability of refractive index of the skin between locations and subjects;

— difficulty obtaining good contact with the skin over the entire sensor area;

— contamination of the sensor through successive skin contacts;

— difficulty achieving even coatings for calibration;

— absorbance into clothing (masking).

F.7 Quality issues

F.7.1 Sampling efficiency

Sampling efficiency when the agent or tracer is detected does not apply because no recovery or removal is required.

Detection efficiency of a tracer is defined as the total amount of tracer remaining on the skin surface divided by the total amount of contaminant remaining on the skin at the termination of the sampling period, which is essentially the same as the relative transfer of the tracer and the agent to and from the skin. However, coloured contaminants such as soil (other than those in the calibration solutions) could mask or quench the fluorescence or absorb infrared at the same wavelengths.

F.7.2 Recovery efficiency

Regarding fluorescent tracers, recovery efficiency may be determined using calibrations of measurement intensity against surface concentration of the tracer. Measurement intensity may be influenced by the natural fluorescence and colour of the skin. Tracers have been calibrated on volunteers' skin[60], demonstrating that a simple multiplicative correction procedure aligned all responses to one calibration curve. The calibration data were best fitted by log-log polynomials, although linear polynomials were acceptable.

F.7.3 Sample stability

The stock solution may deteriorate in storage. Fluorescent dyes should be stored in a cool, dark place. A check should be made that the addition of the dye has not disturbed the stability of the formulation (e.g. as a result of sedimentation due to precipition from an emulsion).

F.7.4 Capacity

The capacity for retention of the formulation containing the agent or surrogate is the same as for the skin; however, the instrument may have lower capacity limits.

Video imaging: nonlinearity of the fluorescence calibration curve leads to a saturation plateau. The maximum calibration of the image processor shall not be exceeded.

Reflectance: the linear region of the infrared absorption characteristic should be investigated.

F.7.5 Core information

Core information includes:

a) clear description of materials used;

b) sampling period, i.e. interval of collection;

c) location on the skin;

d) presence of interfering marks/blemishes/damage on the skin;

e) presence of interfering contaminants such as soil;

f) range of applicability of the calibration curve;

g) limit of detection, especially to distinguish dye from natural skin fluorescence;

h) exclusion criteria (video imaging), used to reject pixels (e.g. thresholding pixels below limit of detection).

F.7.6 Metrics of exposure parameter — Video imaging

Data are recorded as pixel intensity which relates to mass per area for each pixel, equivalent to a surface loading. However, it is usually summed into mass of dye (agent) and exposed surface area for each photograph. These, in turn, are summed for each body area, limb or for the whole body.

F.7.7 Metrics of exposure parameter — Reflectance and light probes

Data are recorded in units of signal strength which relate to average mass per area at each local area measurement. For reflectance, the measured area is defined as the area of the crystal. For the light probe, the measured area is the “field of view.” However, the contaminated skin area may only cover part of the crystal, especially for the larger ZnSe crystal. Where the contaminated skin area is less than the detection (sensor) area, local mass measurements can be made but surface-loading measurements can only be averaged over the entire area of the sensor. Where the contaminated area is greater than the detection (sensor) area, surface-loading measurements can be made but local mass measurements cannot.

F.7.8 Strategic considerations

In situ techniques using added tracers are suitable where an agent is quickly absorbed into the SCL, because the tracer is left behind as a record. Where the tracer binds to and stains the skin, only immission (3.9) is measured rather than net exposure (immission minus losses), even if the agent itself is washed off or absorbed. Repeat measurements may be made during the work shift to monitor immission rates over time.

Where the tracer is lost through removal or absorption processes to the same extent as the agent, net exposure remaining on the SCL is measured (immission minus losses). Repeat measurements may be made during the work shift to monitor net exposures over time because the measurement process does not remove the agent or the tracer.

Added tracers are not carried with vapour phase of a volatile liquid agent, so may be used to detect exposures caused by splashing or aerosol deposition, but not exposures caused by vapours.

Reflectance measurements may be used to detect the presence of volatile agents in the SCL (e.g. from vapours).

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