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Workplace atmospheres — Measurement of dermal exposure — Principles and methods

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Foreword

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The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

In exceptional circumstances, when a technical committee has collected data of a different kind from that which is normally published as an International Standard ("state of the art", for example), it may decide by a simple majority vote of its participating members to publish a Technical Report. A Technical Report is entirely informative in nature and does not have to be reviewed until the data it provides are considered to be no longer valid or useful.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

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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.

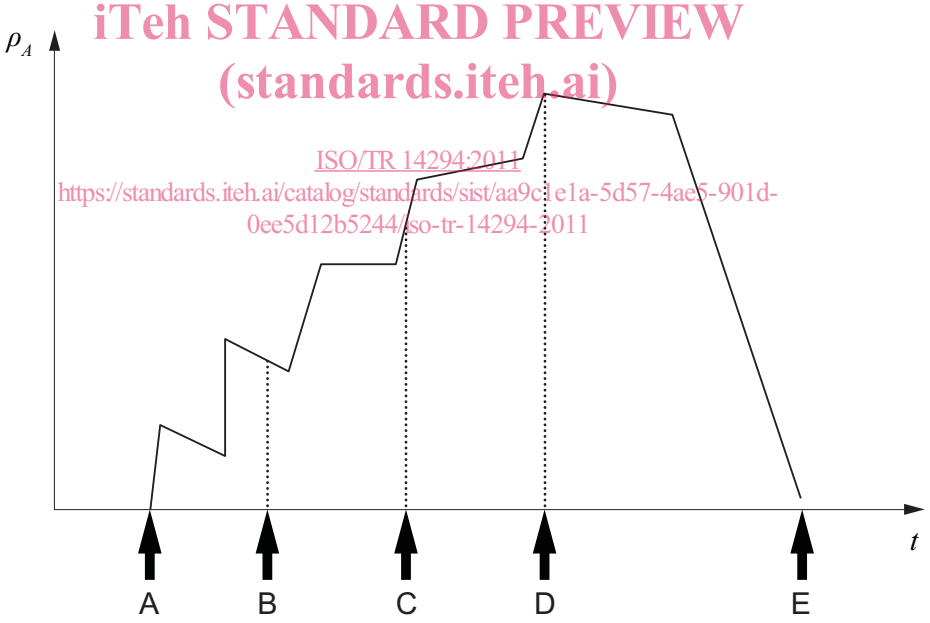
3.6
dermal exposure mass
mass of **agent** (3.1) present in the **dermal contact volume** (3.2)

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?

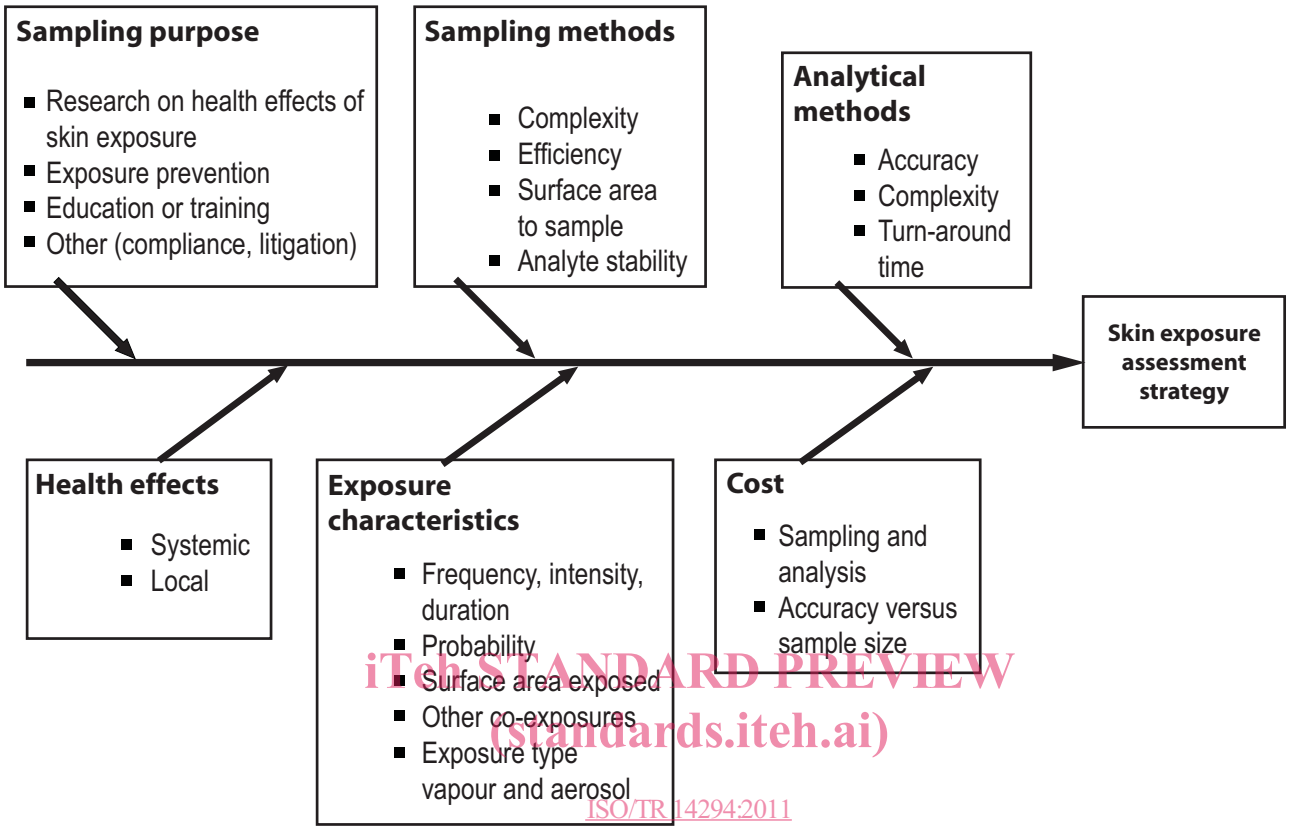


Figure 2 — Multiple factors to consider when designing a skin exposure sampling strategy

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).

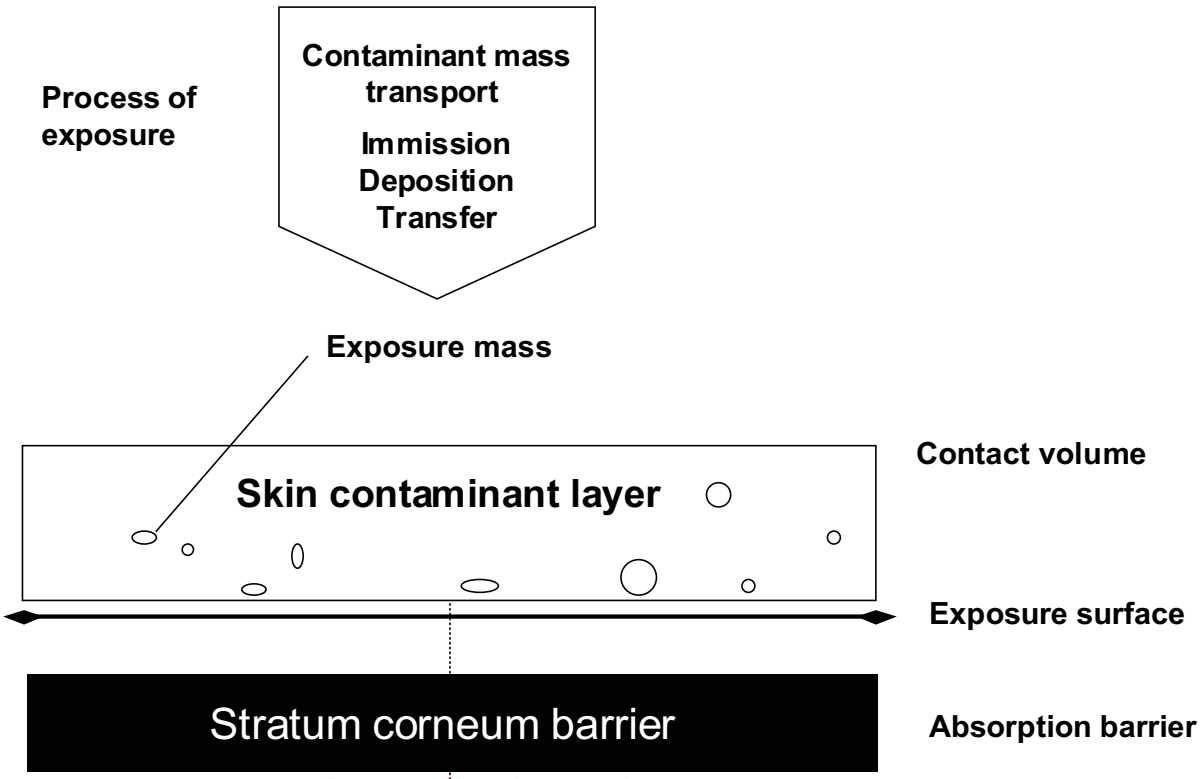


Figure 3 —The processes of dermal exposure, transport, and uptake

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);