IPCS

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

Environmental Health Criteria 242

DERMAL EXPOSURE

IOMC
INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS
A cooperative agreement among FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD

World Health Organization

The **International Programme on Chemical Safety (IPCS)** was established in 1980. The overall objectives of the IPCS are to establish the scientific basis for assessment of the risk to human health and the environment from exposure to chemicals, through international peer review processes, as a prerequisite for the promotion of chemical safety, and to provide technical assistance in strengthening national capacities for the sound management of chemicals.

This publication was developed in the IOMC context. The contents do not necessarily reflect the views or stated policies of individual IOMC Participating Organizations.

The **Inter-Organization Programme for the Sound Management of Chemicals (IOMC)** was established in 1995 following recommendations made by the 1992 UN Conference on Environment and Development to strengthen cooperation and increase international coordination in the field of chemical safety. The Participating Organizations are: FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD. The purpose of the IOMC is to promote coordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

WHO Library Cataloguing-in-Publication Data

Dermal exposure.

(Environmental health criteria ; 242)

1.Hazardous Substances - poisoning. 2.Skin Absorption. 3.Skin - drug effect.
4.Hazardous Substances - analysis. 5.Skin Diseases - chemically induced.
6.Environmental Exposure. 7.Occupational Exposure. 8.Risk Assessment. I.World Health Organization. II.International Programme on Chemical Safety.

ISBN 978 92 4 157242 2 (NLM classification: WR 140)
ISSN 0250-863X

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or policies of the World Health Organization.

The preparation of this report was funded by the European Commission and the Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety of Germany. The views expressed in the report do not necessarily reflect the views of the two organizations.

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ENVIRONMENTAL HEALTH CRITERIA FOR DERMAL EXPOSURE

NOTE TO READERS OF THE CRITERIA MONOGRAPHS

Every effort has been made to present information in the criteria monographs as accurately as possible without unduly delaying their publication. In the interest of all users of the Environmental Health Criteria monographs, readers are requested to communicate any errors that may have occurred to the Director of the Department of Public Health, Environmental and Social Determinants of Health, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda.

ENVIRONMENTAL HEALTH CRITERIA

PREAMBLE

Objectives

In 1973, the WHO Environmental Health Criteria Programme was initiated with the following objectives:

(i) to assess information on the relationship between exposure to environmental pollutants and human health, and to provide guidelines for setting exposure limits;
(ii) to identify new or potential pollutants;
(iii) to identify gaps in knowledge concerning the health effects of pollutants;
(iv) to promote the harmonization of toxicological and epidemiological methods in order to have internationally comparable results.

The first Environmental Health Criteria (EHC) monograph, on mercury, was published in 1976, and since that time an ever-increasing number of assessments of chemicals and of physical effects have been produced. In addition, many EHC monographs have been devoted to evaluating toxicological methodology, such as for genetic, neurotoxic, teratogenic and nephrotoxic effects. Other publications have been concerned with epidemiological guidelines, evaluation of short-term tests for carcinogens, biomarkers, effects on the elderly and so forth.

Since its inauguration, the EHC Programme has widened its scope, and the importance of environmental effects, in addition to health effects, has been increasingly emphasized in the total evaluation of chemicals.

The original impetus for the Programme came from World Health Assembly resolutions and the recommendations of the 1972 UN Conference on the Human Environment. Subsequently, the work became an integral part of the International Programme on Chemical Safety

(IPCS). The EHC monographs have become widely established, used and recognized throughout the world.

The recommendations of the 1992 UN Conference on Environment and Development with the priorities for action in the six programme areas of Chapter 19, Agenda 21, and the outcome document of the United Nations Conference on Sustainable Development "The future we want" all lend further weight to the need for EHC assessments of the risks of chemicals.

Scope

Two different types of EHC documents are available: 1) on specific chemicals or groups of related chemicals; and 2) on risk assessment methodologies. The criteria monographs are intended to provide critical reviews on the effect on human health and the environment of chemicals and of combinations of chemicals and physical and biological agents and risk assessment methodologies. As such, they include and review studies that are of direct relevance for evaluations. However, they do not describe *every* study carried out. Worldwide data are used and are quoted from original studies, not from abstracts or reviews. Both published and unpublished reports are considered, and it is incumbent on the authors to assess all the articles cited in the references. Preference is always given to published data. Unpublished data are used only when relevant published data are absent or when they are pivotal to the risk assessment. A detailed policy statement is available that describes the procedures used for unpublished proprietary data so that this information can be used in the evaluation without compromising its confidential nature (WHO (1990) Revised Guidelines for the Preparation of Environmental Health Criteria Monographs. PCS/90.69, Geneva, World Health Organization).

In the evaluation of human health risks, sound human data, whenever available, are preferred to animal data. Animal and in vitro studies provide support and are used mainly to supply evidence missing from human studies. It is mandatory that research on human subjects is conducted in full accord with ethical principles, including the provisions of the Helsinki Declaration.

The EHC monographs are intended to assist national and international authorities in making risk assessments and subsequent risk management decisions and to update national and international authorities on risk assessment methodology.

Procedures

The following procedures were followed in the development and publication of this EHC. A designated IPCS Staff Member (Kersten Gutschmidt), responsible for the scientific content of the document, served as the Responsible Officer (RO). The IPCS editor was responsible for layout and language.

A first draft working paper, including contributions from several additional authors (see below), was prepared by Ivan Dobrev. This draft was distributed to the Task Group and was available on the WHO/IPCS website for external review and comment; comments received are available on request from the WHO Secretariat. During the Task Group meeting, which was held from 10 to 12 May 2011 and chaired by Inge Mangelsdorf, this revised draft was reviewed, and necessary additional comments were discussed. Subsequently, a final scientific revision of the document was made, and additional points were addressed in supplementary sections for the final draft. The final draft was prepared by Nathalie Costa Pinheiro, including contributions and reviews from the additional authors named below, and reviewed by the Task Group.

The Task Group members serve as individual scientists, not as representatives of any organization, government or industry. All individuals who, as authors, consultants or advisers, participate in the preparation of EHC monographs must, in addition to serving in their personal capacity as scientists, inform the WHO Secretariat if at any time a conflict of interest, whether actual or potential, could be perceived in their work. They are required to sign a declaration of interest statement. The Chairpersons of Task Groups are briefed on their role and responsibility in ensuring that these rules are followed. Such a procedure ensures the transparency and probity of the process. Their function is to evaluate the accuracy, significance and relevance of the information in the document. A summary and recommendations for

further research and improved safety aspects are also required. The composition of the Task Group is dictated by the range of expertise required for the subject of the meeting and, where possible, by the need for a balanced geographical distribution.

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The preparation of this report was funded by the European Commission and the Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety of Germany. The views expressed in the report do not necessarily reflect the views of the two organizations.

WHO TASK GROUP ON ENVIRONMENTAL HEALTH CRITERIA ON DERMAL EXPOSURE

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ABBREVIATIONS

2,4-D	2,4-dichlorophenoxyacetic acid
AC	article category
ACGIH	American Conference of Governmental Industrial Hygienists
ADA	American Dental Association
AHED	Agricultural Handlers Exposure Database
AHETF	Agricultural Handlers Exposure Task Force
a.i.	active ingredient
AISE	Association Internationale de la Savonnerie, de la Détergence et des Produits d'Entretien (International Association for Soaps, Detergents and Maintenance Products)
ANSI	American National Standards Institute
AOEL	acceptable operator exposure level
APVMA	Australian Pesticides and Veterinary Medicines Authority
AQL	acceptable quality level
ARTF	Agricultural Reentry Task Force
a.s.	active substance
ASTM	American Society for Testing and Materials
ATR	attenuated total reflectance
ATR-FTIR	attenuated total reflectance with Fourier transform infrared spectroscopy
BAuA	Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (German Federal Institute for Occupational Safety and Health)
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft (German Federal Biological Research Centre for Agriculture and Forestry)
BDT	breakthrough detection time
BEAT	Bayesian Exposure Assessment Tool

BfR	Bundesinstitut für Risikobewertung (German Federal Institute for Risk Assessment)
BREAM	Bystander and Resident Exposure Assessment Model
BROWSE	Bystanders, Residents, Operators and WorkerS Exposure
bw	body weight
CARES	Cumulative and Aggregate Risk Evaluation System
CE	(originally) Communauté Européenne
CEN	Comité Européen de Normalisation (European Committee for Standardization)
CFR	Code of Federal Regulations (USA)
ConsExpo	Consumer Exposure (tool)
COSHH	Control of Substances Hazardous to Health Regulations (United Kingdom)
CPSC	Consumer Product Safety Commission (USA)
CTB	College voor de toelating van gewasbeschermingsmiddelen en biociden (Dutch Board for the Authorisation of Plant Protection Products and Biocides)
CV	coefficient of variation
DAF	dermal absorption factor
DEO	dermal exposure operation
DERM	Dermal Exposure Ranking Method
DFG-MAK	Deutsche Forschungsgesellschaft – Maximale Arbeitsplatz Kommission (Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area of the German Research Foundation)
DFR	dislodgeable foliar residue
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
DNEL	derived no-effect level
DOEL	dermal occupational exposure limit

DPR	Department of Pesticide Regulation (California, USA)
DR	dislodgeable residue
DREAM	DeRmal Exposure Assessment Method
DTPA	diethylenetriaminepentaacetic acid
EASE	Estimation and Assessment of Substance Exposure
EBRC	Services for the Chemical Industries
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECETOC TRA	ECETOC's Targeted Risk Assessment (tool)
EDTA	ethylenediaminetetraacetic acid
EHC	Environmental Health Criteria (monograph)
EMKG	Einfaches Maßnahmenkonzept Gefahrstoffe (German workplace control scheme by BAuA)
EN	Europäische Norm (European norm)
eteam	Evaluation of Tier 1 Exposure Assessment Models under Reach
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act (USA)
FTIR	Fourier transform infrared (spectroscopy)
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
GSD	geometric standard deviation
HSE	Health and Safety Executive (United Kingdom)
ICPS	International Centre for Pesticides and Health Risk Prevention (Italy)
IgE	immunoglobulin E
INRA	L'Institut National de la Recherche Agronomique (French National Institute for Agricultural Research)
IPCS	International Programme on Chemical Safety
IR	infrared

ISEA	Industrial Safety Equipment Association
ISO	International Organization for Standardization
K_{ow}	octanol–water partition coefficient
LEV	local exhaust ventilation
LOD	limit of detection
LOQ	limit of quantification
MBT	measured breakthrough time
MDL	minimum detectable limit
MEASE	Metals' EASE
MR	migration rate
N	number of samples
NA	not applicable
ND	not detected; non-detectable
NFPA	National Fire Protection Association
n.g.	not given
NIOSH	National Institute for Occupational Safety and Health (USA)
NOAEL	no-observed-adverse-effect level
NR	not recommended
NT	not tested
OECD	Organisation for Economic Co-operation and Development
OEL	occupational exposure limit
OSHA	Occupational Safety and Health Administration (USA)
PAH	polycyclic aromatic hydrocarbon
PBDE	polybrominated diphenyl ether
PC	product category
PCB	polychlorinated biphenyl
PCDF	polychlorinated dibenzofuran
PE	polyethylene
PEG	polyethylene glycol
PEL	permissible exposure limit
PHED	Pesticide Handlers Exposure Database

PMRA	Pest Management Regulatory Agency (Health Canada)
POEM	Predictive Operator Exposure Model (United Kingdom)
PPE	personal protective equipment
ppm	parts per million
PROC	process category
PSD	Pesticides Safety Directorate
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
REACT	Reach Exposure Assessment Consumer Tool
RIVM	Rijksinstituut voor Volksgesondheid en milieu (Dutch National Institute for Public Health and the Environment)
RMM	risk management measure
rpm	revolutions per minutre
SD	standard deviation
SHEDS	Stochastic Human Exposure and Dose Simulation
SIN	Substitute It Now
SPP	skin protective product
SWIMODEL	Swimmer Exposure Assessment Model
TC	transfer coefficient
TCDD	2,3,7,8-tetrachlorodibenzo-*p*-dioxin
t_{exp}	duration of exposure
t_{lag}	lag time for chemical penetration through the stratum corneum
t_{TS}	time needed to completely remove the stratum corneum by tape stripping
TF	transfer factor
t.g.	technical grade
TLV	threshold limit value
TNO	Nederlandse Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek (Dutch Organization for Applied Scientific Research)

TNsG	Technical Notes for Guidance
TPGDA	tripropylene glycol diacrylate
TR	transferable residue
TRA	Targeted Risk Assessment
TRGS	Technische Regeln für Gefahrstoffe (German Technical Rules for Hazardous Substances)
TS	tape strip
TSCA	Toxic Substances Control Act (USA)
TTR	turf transferable residue
UF	uncertainty factor
USA	United States of America
USEPA	United States Environmental Protection Agency
USFDA	United States Food and Drug Administration
UV	ultraviolet
UV-A	ultraviolet A

1. SUMMARY

Dermal exposure has been identified as an important exposure route, as people are exposed to a variety of substances and products either directly or indirectly while at work, in the home or in public facilities. Dermal exposure is a complex process of contact between a relevant substance and the skin over a period of time. Diseases resulting from dermal exposure (and consequently absorption) may have a significant impact on human health. The best approach to manage the risks associated with dermal exposure is to identify relevant hazards (chemicals and products), sources and pathways of exposure, quantitatively assess the exposure (by either measuring or modelling it) for further risk assessment and eventually eliminate or at least reduce and control the exposure.

1.1 Sources and pathways

In the occupational environment, hazardous exposures are generally governed by either the work activity or the toxic profile of a product. Dermal exposure occurs predominantly as a result of splashes, spills or drifts (principally during mixing and loading), during the application itself or from contaminated surfaces, such as machinery or foliage. Accordingly, as such conditions of the general exposure scenario are influenced by national safety regulations and work standards, the main determinants leading to dermal exposure may be different for developed and developing countries (e.g. direct use of the hands as working tools, use of leaking equipment and working under less regulated occupational safety requirements in developing countries). Pesticides, organic solvents and metalworking fluids are considered to be important contributors to occupational ill-health. Prolonged and/or repeated contact with water (wet work) can be harmful for the skin as well, and this effect can be enhanced by the presence of other irritants (e.g. in occupations such as hairdressing or metalworking).

Although direct handling and application to the skin can be considered the most direct sources of dermal exposure, studies have

identified that other pathways or work processes can often be the most relevant. Hence, indirect pathways of dermal exposure (e.g. contact with substances being deposited on or adsorbed onto surfaces) have to be considered as well. Examples are the re-entering of a field after pesticide application, contact with contaminated materials or contact with other residues, such as lead from paints in house dusts or soils. Moreover, workers may live close to their occupational facilities and in addition (unintentionally or intentionally) carry hazardous substances to or store them in their homes. Thus, the workers or operators themselves as well as their families are supplementarily exposed inside their residences, and exposure inside homes may particularly affect young children and the elderly, who may be more sensitive. Contributing factors to such types of exposure are the lack of adequate training and knowledge on specific products and methods (e.g. for pest control), as well as easy access to cheap and highly toxic products.

In non-occupational settings, people can be dermally exposed to chemicals in a variety of chemical classes through use of a diverse range of consumer products. Most relevant types of products include personal care products and cosmetics, textiles (including shoes) and household products, due to either their conditions of use or their inherent toxicological profiles. For instance, the use of personal care products and textiles results in direct skin contact, often involving exposure of a large body surface area, as well as a prolonged duration of contact, which may occur repeatedly (daily use). If for such products critical substances in relation to the dermal pathway (e.g. new or unusual allergens) are used, negative effects such as allergic contact reactions may occur.

Fragrances and preservatives are the most frequent allergens that may be used in personal care products, cosmetics and household products, as well as in textiles, children's toys and air fresheners. Product ingredients are changed frequently, and national safety regulations and definitions vary, depending on the country. Moreover, the international variety of marketed products differs, and some may be used for a long time (e.g. for cultural reasons). For instance, some traditional cosmetics have been found to result in dermal exposure to heavy metals (e.g. the use of summa/kohl as eye preparations) or to cause severe allergies (e.g. the use of black henna for temporary skin tattoos).

Special attention is paid to the dermal exposure of children because of their specific activity patterns (spending the day lying, crawling, touching and mouthing) and their higher surface area to body weight ratio compared with adults. Moreover, children's toys and other products of their home environments may include various substances relevant for the dermal exposure pathway (e.g. flame retardants, polycyclic aromatic hydrocarbons, phthalates, plasticizers).

1.2 Analytical approaches to estimate dermal exposure

Different approaches are used to estimate dermal exposure. They can be roughly categorized as direct and indirect methods. The direct methods are further subdivided into three groups: interception, removal and in situ techniques. The interception techniques involve the use of whole-body dosimeters or patches, which serve as surrogates for the skin for collecting deposited substances or products. Removal techniques include frequently used sampling methods—wiping, handwashing and tape stripping—and the seldom applied suction and immersion methods. The most important in situ technique is video imaging.

All three sampling approaches are based on different technical designs, which result in special features or limitations of these methods. For example, for the interception techniques, the potential absorption process is usually prevented by interception material. The removal techniques sample only the substance available on the skin surface; the substance absorbed during exposure cannot be assessed. For video imaging, a tracer is used, and the similarity of the tracer to the substance determines the accuracy of the measurement. Additional differences in the analytical results may be caused by the pathway of exposure. Some gaps were identified with respect to analytical validation of the sampling procedures, lack of comparison studies and lack of internationally harmonized procedures.

The indirect methods either investigate the processes before dermal exposure occurs (migration and transfer approaches) or measure the concentrations of the substance in body fluids or tissues after absorption (biomonitoring). Migration measurements determine the amount of the substance that can migrate into an artificial fluid (e.g. sweat)

per product surface area. The migration rate depends mainly on the substance–matrix combination. In the transfer approach, transfer parameters (coefficients or rates) describe the process of transfer to the skin and depend on the activity that is considered as well as on the substance–matrix combination.

Biological monitoring is a very useful tool for risk assessment, especially when exposures from several routes are to be considered. For assessing dermal exposure, biomonitoring requires knowledge of toxicokinetics in order to extrapolate to the original amount of dermal exposure. Additionally, the other exposure routes, inhalation and oral, should be negligible in order for dermal exposure to be assessed.

Currently, study designs used to estimate dermal exposure are mainly oriented to practical issues. There is no method applicable for all circumstances, nor can a guide be provided to aid in the selection of a proper method for specific circumstances. To overcome the current gaps in knowledge, comparative studies are needed. These should help to compare the usefulness of the methods, to derive harmonized protocols and, finally, to improve our understanding of the underlying processes and determinants of dermal exposure.

1.3 Models and tools to estimate dermal exposure

In the absence of measured values or when measurements are not feasible, modelling is seen as a valuable approach in assessing dermal exposure. Dermal exposure modelling is used for a variety of purposes, often driven by regulatory needs, such as estimating exposure in a particular population, assessing the efficiency of risk-reducing measures or identifying necessary limits for substances in products. Models describing physical processes as well as empirical models have been developed, and one or more models may be implemented in computer-based software or other tools (e.g. a spreadsheet) to simplify the use of the models.

Several models and tools that were developed for different objectives are presented. The semiquantitative concept DREAM is meant to evaluate exposure determinants and supply additional activity-related information for analytical measurement strategies. DERM is

intended to be a practical "easy-to-use" tool (e.g. for educational programmes in developing countries). RISKOFDERM is based on the concept of establishing models from task-based clusters using available measurement data. BEAT provides the option to search for similar exposure scenarios with measured exposure data that can be combined with a hierarchical Bayesian model for probabilistic predictions. ECETOC TRA is developed as a screening tool for risk assessment, MEASE is designed for workers' exposure to metals and other inorganic substances, ConsExpo covers several consumer-related activities and SprayExpo focuses on a variety of spray applications. Although both focus on pesticide application, the European Union modelling approaches (German and Dutch models, POEM and EUROPOEM) differ from the receptor-oriented models in the United States of America (USA) (Calendex, CARES, LifeLine, PHED, SHEDS), as these account for the accumulation of dermal exposure due to multiple pathways.

It is not possible to state which models or tools are most accurate in what circumstances, whether the models or tools provide comparable results or which models or tools should be recommended for use, as their scope, features and limitations vary. For very similar exposure assessment situations, different organizations may use different models and tools. Thus, the evaluation and description of the applicability of models and tools are influenced by various factors, such as the initial purpose of their development (often in a regulatory context), their task descriptions, their data basis and the appropriate use of provided default values and extrapolation steps. A first attempt to provide a comparative overview of the different applicability, features and limitations of the various models and tools is provided in this document. In addition, the underlying algorithms of the presented models and tools are provided in an appendix in a synchronized and condensed form to facilitate a comparison of the underlying principles and exposure determinants used in the different models.

1.4 Skin diseases associated with dermal exposure

Dermal exposure can lead to local damage to the skin and/or systemic effects after crossing the skin barrier, and there is an emerging risk of developing skin diseases that can have a critical impact on the

health and economy for both working people and the general public. The most common skin diseases are described, including typical circumstances causing these diseases. The most important skin disease is contact dermatitis (localized inflammation), caused by direct skin contact with external irritants and/or allergens. There are two types of contact dermatitis: irritant contact dermatitis and allergic contact dermatitis. The most important occupational skin disease is irritant contact dermatitis, with 50–90% of all skin diseases due to contact with chemicals or wet work. Occupational skin disease represents about 10% of all occupational diseases in Europe and the USA, with a prevalence (a measure of the spread of a disease) of up to 65% for workers in occupations such as hairdressing, printing or cleaning. In contrast, the most relevant skin disease in relation to the general population is allergic contact dermatitis, with a prevalence of 21.2% (for contact dermatitis from exposure to at least one allergen) for the North American and western European populations. Additional skin diseases as well as direct effects (e.g. irritation, urticaria, acne, cancers and phototoxicity) are also presented.

1.5 Methods for exposure prevention and reduction

A brief overview of legislative measures to protect workers and consumers and general methods of hazard identification is presented. Methods used to reduce exposure and their hierarchy are then explained.

Legislation in many different countries deals with the safe handling of substances at the workplace. Legislation directed to the consumer frequently deals with labelling and packaging. Hazard and precautionary statements according to the Globally Harmonized System of Classification and Labelling of Chemicals warn workers and consumers about hazards and advise on proper use. In addition, several institutions that derive occupational exposure limits also provide skin notations, which indicate the potential for dermal uptake of a chemical. Finally, dermal occupational exposure limits are intended as quantitative measures of maximum acceptable exposure.

Elimination or substitution is the preferred approach for the prevention of dermal exposure. Other measures to reduce exposure at

workplaces are engineering controls, organizational measures and, finally, personal protective equipment. Engineering controls include separation approaches (e.g. enclosing, containing or isolating) and product or process changes (e.g. less concentrated products, liquids or granules instead of powders, packaging in smaller containers). Organizational measures define work practices and procedures and address the education of occupational personnel and the consequences of non-compliance. Personal protective equipment must be considered as a "last resort" if other measures are not practical. Selection criteria for using personal protective equipment are summarized, and the factors influencing the overall efficiency of personal protective equipment (e.g. material characteristics, use and working conditions, and the acceptance, correct use and maintenance by the user) are described in more detail.

In non-occupational settings, exposure prevention and reduction can be achieved by product-related changes, instruction or communication on safe use or administrative measures. Product changes (e.g. allowing a maximum concentration or changing the product's form, such as pellets or granules instead of powder) are considered to be the most effective measure. Administrative measures (e.g. setting of limit values, marketing restrictions, prohibition) and the need for better labelling of hazardous substances to improve public awareness of potential risk are also expounded.

Finally, differences in the effectiveness of several regulations are presented.

2. INTRODUCTION AND SCOPE

Human skin is a highly complex organ, and one of its main functions is to protect the body from noxious agents or substances such as toxic chemicals, ultraviolet (UV) radiation and prolonged exposure to water. The skin can be exposed to a variety of environmental and occupational substances in different ways. Depending on their physicochemical properties, these substances either can be absorbed by the skin or can remain on the skin surface; in both cases, they can damage the skin's function and eventually contribute to the risk of ill-health. Thus, dermal exposure is an important component that needs to be considered when conducting human health risk assessments.

We still know very little about the circumstances under which dermal exposure arises, the relationship between dermal and inhalation exposures, the best approaches to express and estimate the magnitude of dermal exposure and the effectiveness of control measures. Hence, the purpose of this report is to provide an overview of general aspects and current methodologies relating to the assessment of dermal exposure to chemicals in a broad sense. Dermal exposure to biological agents (e.g. pathogens, animal hair, spices) is not covered in this document.

A key step in improving the science of dermal exposure assessment was the work of Schneider et al. (1999), who developed a conceptual model that describes dermal exposure as a complex process combining transfer processes (pathways) and possible compartments or sources (both environmental and personal). Pathways contributing to dermal exposure occur simultaneously with pathways that reduce dermal exposure, and the final estimate of dermal exposure is influenced by several determinants. As a result of this complex process and the different approaches for its description and assessment, it is important to choose the most appropriate metric of dermal exposure and use terminology correctly. Therefore, chapter 3 describes the processes involved in dermal exposure, presents definitions of terms and explains the relationship between the different estimation approaches (measuring and modelling).

Chapter 4 briefly addresses the importance of the dermal route of exposure and presents some of the major sources of exposure and the different types of exposed populations. In relation to occupational exposure, the use of pesticides, the use of organic solvents and wet work are identified as significant sources of dermal exposure. This is due to the toxicological profile of these common product types as well as the specific exposure situations and work activities they imply. As the general population is exposed to a variety of products containing a diversity of different substances, dermal exposure of consumers is discussed in broad categories. On the one hand, exposure in relation to typical exposure situations by the use of specific product types (e.g. personal care and household products) is discussed; on the other hand, the most relevant substance classes (e.g. fragrances) that may occur in various products are presented. In addition, indirect exposure (e.g. by dust) and the need for special awareness in relation to exposure of children are addressed.

Reliable and valid methods for estimating dermal exposure are required in order to identify risks and subsequently initiate preventive or mitigative measures; they can be used, for example, to monitor the effectiveness of control measures or to measure compliance with regulatory safety standards. Thus, chapter 5 provides an overview of the general principles of analytical measurement approaches that are currently in use, including their special features and limitations. As measurement approaches depend on numerous factors that are difficult and time consuming to quantify simultaneously, modelling approaches are frequently used, offering an efficient way of identifying either when risk management measures are needed or where monitoring would be useful to refine risk estimates. Hence, chapter 6 presents an overview of the models and tools that are available for estimating dermal exposure.

Dermal exposure to harmful agents can result in either local or systemic (after crossing the skin barrier) effects. As skin diseases make up a significant proportion of all occupational diseases and as several consumer products have been identified as being relevant for the development of, for example, contact dermatitis, chapter 7 gives a brief overview of the spectrum of possible diseases resulting from dermal exposure. Direct skin effects, such as irritation, burning and urticaria, are presented, as well as diseases caused by immunological reactions

after systemic delivery (i.e. after absorption), such as contact urticaria, acne, cancer, leukoderma (vitiligo) and phototoxicity.

The best approach for the prevention of dermal exposure to chemicals that may result in work-related skin diseases is the early recognition, evaluation and identification of potential hazards prior to the implementation of control measures or treatment of disease symptoms. Consequently, chapter 8 presents a brief overview of legislative measures intended for occupational and consumer protection, followed by general means of hazard identification. In addition, exposure prevention and reduction methods, including personal protective equipment (PPE), are presented, and aspects concerning their protection efficiency, proper use and principles for adequate selection are discussed.

3. GENERAL BACKGROUND

Dermal exposure is the process of contact between an agent and human skin over an exposure period (ISO/TR 14294:2011[1]). This dynamic process is triggered or determined by the preceding (skin loading) and subsequent processes (e.g. evaporation, decontamination or absorption). Whereas dermal "exposure" ends on the skin, dermal "absorption" describes the uptake through the skin (see also Appendix 1). The terms exposure and absorption are, however, often used interchangeably. This Environmental Health Criteria (EHC) monograph deals only with dermal exposure. Dermal absorption was addressed in a separate EHC monograph (see IPCS, 2006).

This chapter explains the processes involved in dermal exposure and briefly introduces the concepts of models and tools as well as metrics of dermal exposure.

3.1 Processes involved in dermal exposure

3.1.1 The source–receptor model of Schneider et al. (1999)

A conceptual source–receptor model (Fig. 1) for dermal exposure was proposed by Schneider et al. (1999, 2000) for occupational scenarios, but it may be applied, with some small adjustments, to consumer uses and environmental contamination. The model provides the compartments and pathways involved in the process of dermal exposure.

Mass transport processes according to the Schneider et al. (1999, 2000) dermal exposure model (Fig. 1) are as follows:

- emission of an agent from its source (e.g. by splashing, spilling or ejection of particles) into air or onto surfaces, clothing and the skin;
- deposition of an agent from air onto surfaces, clothing or the skin (independent of its aggregate state);

[1] A list of standards, test methods, guidelines and technical specifications cited in this monograph may be found at the end of the references.

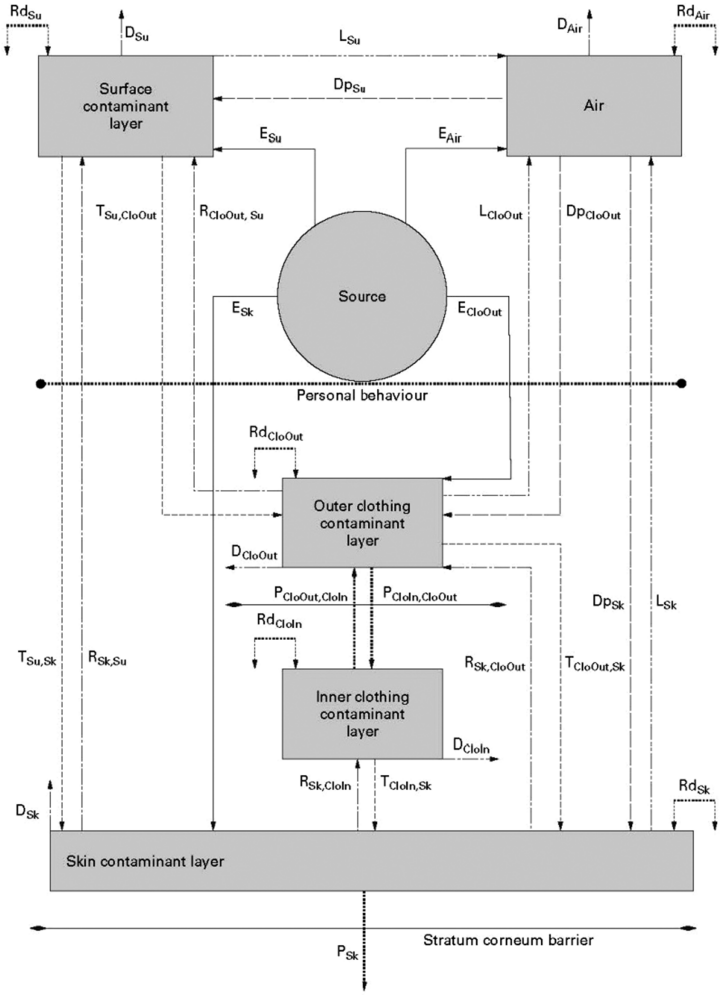

Fig. 1. Conceptual source–receptor model for dermal exposure (Schneider et al., 1999). Abbreviations: CloIn, inner clothing; CloOut, outer clothing; D, decontamination; Dp, deposition; E, emission; L, resuspension or evaporation; P, penetration and permeation; R, removal; Rd, redistribution; Sk, surface contaminant layer; Su, source; T, transfer.

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- resuspension or evaporation of an agent from a surface as a result of its high volatility or activities such as brushing, wiping and cleaning, followed by transfer to the skin;
- transfer of an agent by direct contact between surface, skin and clothing contaminant layers in a direction towards the worker[1];
- redistribution of an agent from a subcompartment to another subcompartment of the same type, if not homogeneously distributed in one compartment (air, surface, clothing or skin), such as redistribution from one subcompartment to another subcompartment of the compartment "skin" by touching the face with contaminated fingers;
- removal by direct contact between skin, clothing and surface in a direction away from the worker (event-based transport in the opposite direction of transfer), such as by washing off, abrasions and evaporation;
- decontamination of compartments or zones along the various pathways, such as by cleaning or washing of contaminated surfaces or by installing exhaust ventilation systems (in contrast to resuspension, a permanent loss of mass from the system);
- penetration and permeation[2], which refer to the transport through a rate-limiting barrier (clothing or the stratum corneum) involving diffusion.

3.1.2 Contamination pathways (dermal exposure loading)

As described by Schneider et al. (1999), dermal exposure is the result of a complex combination of transfer processes (pathways). The contamination pathways (dermal loading) can be categorized as follows (adapted from Sithamparanadarajah, 2008):

- **Direct skin contact** with the compound or product
  - immersing the hands (and sometimes the forearms)

[1] It should be noted that the term "worker" is used differently in different regulations, such as Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (EC, 2009a) and the European Union (EU) agricultural pesticide regulation (EC, 2009b). In this document, the term is used as a synonym for "occupational user".

[2] Definition is according to Schneider et al. (1999). The reader should refer to Appendix 1, as the terms are to be differentiated.

  - using hands for handling or to manipulate chemical-containing materials (including products, tools, equipment, surfaces) or using hands directly as working tools
- **Indirect skin contact** with the compound or product
  - splashing of chemicals: inappropriate handling may lead to accidental splashes onto the skin or contamination of clothing or surfaces
  - deposition from air: airborne contaminants in the form of vapours, dust, fumes or mists can be deposited on the skin
  - contact with contaminated surfaces: skin contact may occur from contact with contaminated surfaces (accidental as well as intentionally treated), such as workbenches, cleaning equipment, work tools, contaminated hands, clothes and protective equipment (e.g. gloves)

"Direct exposure" is considered if direct skin contact predominantly determines the resulting magnitude of exposure. For "indirect (secondary) exposure", the substance or product of interest is not intentionally touched. However, the term often leads to confusion, as even if the tool is intentionally touched, the contact with the contaminants on the tool is usually not intended.

These pathway categories are frequently used when modelling dermal exposure. For instance, the consumer exposure estimation tool ConsExpo contains a model "instant application", which relates to the above pathway category of direct skin contact, and a model for transfer of a substance from a material due to dermal contact (termed "migration"[1] in ConsExpo), which corresponds to "contact with contaminated surfaces".

Similarly, the extent of exposure also depends on the performed (work) activity, such as the dermal exposure operation (DEO) approach used in BEAT and RISKOFDERM (see Table 30 in

[1] "Transfer" (= transfer to skin) is differentiated from "migration" (= possible amount on surface that is available for transfer, such as due to leaching out of a product); see section 5.2.

section 6.2.6). Activities are always related to specific pathways (e.g. mixing and loading tasks may relate to the splashing pathway).

3.1.3 Pathways reducing dermal exposure

In addition to the processes that contribute to dermal loading, the source–receptor model also addresses diverse subsequent exposure-reducing processes (see Fig. 1 above). The continuous and dynamic interaction of loading and exposure-reducing processes may simultaneously occur throughout the whole exposure period. Therefore, exposure-reducing processes should be included in the exposure assessment to more realistically reflect the exposure situation.

3.2 Exposure scenario (description)

An exposure scenario describes the circumstances of an exposure situation and contains the relevant determinants. The development of the exposure scenario accompanied by adequate documentation is fundamental. The documented exposure scenario serves as the basis for the exposure estimation itself, but it is also necessary to provide adequate transparency or traceability and/or refinement.

Moreover, the exposure scenario determines the selection of approaches to estimate the dermal exposure—that is, the applicability of measurement and/or modelling approaches. For instance, the chosen duration of an exposure scenario can affect the method and setting design of the measurement, which in turn limits the usability of this measurement for different models. In addition, if a relevant determinant is identified in the exposure scenario, yet information about it is not available or obtainable in an objective manner, it is not feasible to include it in modelling approaches (Marquart et al., 2003).

An exposure scenario should include the following information:

- amount of the substance and/or product used
- concentration/mass weight fraction of substance in product
- physicochemical characteristics of the substance or product
- process or activity description (including release rates)
- population exposed

- skin contact area
- use behaviour:
  - frequency of events
  - duration of contact
  - intensity of contact

3.3 Determinants influencing the pathway and extent of exposure

The exposure assessor has to identify the predominant contamination pathway and the relevant determinants of dermal exposure. However, this task is difficult because of the complex interrelationships among all the transport processes and determinants involved.

Influencing factors may result in a shift of the predominance of a pathway, which consequently may change the resulting magnitude of dermal exposure. Particularly in relation to consumers, personal habits may determine the resulting extent of dermal exposure. Indeed, these habits are further influenced by, for example, cultural background and traditions or lifestyle, the array of products that are used and available, environmental circumstances or economic conditions. For instance, contact with surfaces being treated with insecticides will occur more often in regions that need to intensively control vector-borne diseases such as dengue, chagas or malaria. As a matter of fact, factors that are initially intended to reduce a pathway and protect the skin may actually enhance dermal exposure—for example, PPE, due to its ingredients, contamination on the PPE, unsuitable PPE material or inappropriate use of PPE (see section 8.5.4). Further examples are provided in Table 1.

These influencing factors are often reflected by the determinants of exposure. However, the determinants are also not independent of each other. For instance, if the mass fraction of the active substance in the working solution is low (highly diluted), more product will be used accordingly to achieve the same efficiency, which consequently may result in a higher exposure duration and/or mass/volume of handled product. This is especially relevant for the selection of a suitable exposure model and the determinants in the model (see chapter 6; Marquart et al., 2003).

Table 1. Examples of dependencies and interrelationships among pathways, determinants and resulting extent of exposure

Influencing factor	Consequence
Environmental conditions	
Contaminated water used for bathing	Direct skin contact increases
Living close to or in regions of high pesticide use	Indirect skin contact increases (relating to indirect pathway "contact with contaminated/treated surfaces")
Working environment	
Well-designed ventilation systems, enclosures, closed systems used	Direct skin contact and indirect skin contact decrease (relating to indirect pathway "deposition from air")
Substance characteristics	
Substance is not volatile or vaporized or sprayed	Indirect skin contact decreases (relating to indirect pathway "deposition from air")
Working equipment	
Using hands as working tools	Direct skin contact becomes relevant and/or increases
Using appropriate equipment	Direct skin contact decreases
Personal protective equipment	
Using suitable PPE in an appropriate manner	Direct skin contact and indirect skin contact decrease
Personal habits	
Occupational user is well trained and uses appropriate equipment/PPE	Direct skin contact and indirect skin contact decrease (relating to indirect pathway "splashing of chemicals")
Extensive use of cosmetics (personal care products)	Direct skin contact increases
Using appropriate gloves during household cleaning	Direct skin contact decreases
Handwashing after task/application	Dermal exposure loading decreases

3.4 Measuring and modelling

Depending on the need, both measuring and modelling have their advantages. On one hand, direct measurements are considered to reflect the best "truth" available, as the setting of the measurement can be specifically designed and thus fitted to the exposure situation in question. On the other hand, modelling approaches that involve extrapolation from other data, including measurements, existing monitoring data or questionnaires, can cover a huge range of variations (exposure scenarios). Modelling is considered to be an attractive, cheap and less extensive method, because it does not involve the workload and costs of a well-designed measurement study. Both approaches have their limitations: while analytical methods can be unsuitable for certain exposure scenarios, models can be insufficiently precise.

However, exposure assessments often rely to some extent on exposure models that combine measurements and assumptions in order to produce an estimate of exposure (IPCS, 2005), and thus measuring and modelling approaches can supplement each other and do not compete with each other.

3.5 Models and tools

A "model" is based on assumptions, approximations and a mathematical abstraction of complex reality (see Appendix 1). Models can range from simple mass balance equations to complex algorithms in order to include various influencing factors. Thus, an exposure model is a conceptual or mathematical representation or a computational framework designed to reflect real-world exposure scenarios and processes defining the physical, chemical and behavioural information and exposure algorithms.

In contrast, the term "tool" is used when referring to computer-based software or other product (e.g. a spreadsheet) that is intended to simplify the estimation procedure (see Appendix 1). Consequently, a tool may implement one or more modelling approaches (mathematical models or algorithms) in order to simulate different or complex realistic situations. Different tools may even implement the same model or include different variations of it.

In conclusion, the differentiation of the terms model and tool may be difficult to accomplish, and frequently the terms are not used correctly.

3.6 Metric (dimension/unit) of dermal exposure

A rather complex issue is the most appropriate metric of dermal exposure (Marquart et al., 2003). As different terminology is used, the following sections describe and discuss the most relevant terms in relation to possible metrics for dermal exposure.

3.6.1 Dermal exposure mass, loading and dose

Whereas the term "dermal exposure loading" addresses the mass (amount) of an agent in contact with a specific region of the skin (i.e. mass per exposure surface), the term "dermal exposure mass" is favoured when referring to the mass of an agent in contact with an undefined exposure surface (i.e. the amount of agent present on the entire skin).

In addition, variations of the term "dose" are often in use. The "administered/applied dose" relates to the amount of the agent that is directly in contact with the body's surface barrier (skin) and thus available for absorption. Some model or tool outputs are expressed in "exposure dose" (normalized to the body weight), which can therefore be easily compared with reference values or with other exposure estimates.

In this document, "exposure mass" is the preferred term, to avoid confusion. The term "exposure loading" is used when referring to a specifically defined skin area, and the term "dose" (including all described variations) is used solely when referring to an agent crossing the skin as an absorption barrier.

3.6.2 Dermal exposure mass per unit of time (rate) and normalization

In addition to the dermal exposure "mass" and "loading", another proposed metric is "mass per unit of time", which is usually related

to sampling duration. However, before using this value for extrapolations or interpolations, the dependency of dermal exposure on duration should be provided as a function (linear, sigmoidal, etc.), as there is no clear evidence that longer duration will lead to higher exposure, although this is generally assumed. Moreover, although a term for the frequency or duration of dermal exposure is often included in the final output, details about this information is seldom presented transparently (see section A3.2.4 in Appendix 3).

Furthermore, normalization of outputs (mass per unit "x") may be used to enable comparison between exposure estimates—for example, by adjusting to the unit of product handled, the dermal surface area, the event or body weight (see section 6.4.3).

4. SOURCES OF DERMAL EXPOSURE

In order to address the importance of dermal exposure in overall human health risk assessment, sources of exposure at the workplace (occupational sources) as well as for consumers (non-occupational sources) are presented in this chapter. Important sources of dermal exposure are identified first by the incidence of skin diseases associated with each source (further information on skin diseases is provided in chapter 7). In addition, potential for absorption, or frequency, duration and intensity of contact, is considered.

4.1 Occupational sources

The European Agency for Safety and Health at Work states that skin diseases are the second most frequent occupational diseases (following musculoskeletal disorders), representing 10–40% of the recognized occupational diseases (de Craecker, 1993). In the mining and quarrying sector, the incidence rate of 31.5 per 100 000 workers is the highest, with a relatively small number of cases. The sector with the second highest incidence rate (10.4 per 100 000 workers) and a very high number of cases is manufacturing (see Table 2; de Craecker et al., 2008). Table 3 lists occupations with potential dermal exposure and provides some examples of the tasks and substances involved.

4.1.1 Pesticides

Pesticides are a diverse group of chemicals that contribute substantially to public health by limiting the spread of vector-borne diseases and by aiding agricultural development (see the definition of pesticides in Appendix 1). Exposure to pesticides can occur directly from occupational, agricultural and household use, as well as from eating crops treated with pesticides. The main routes of exposure are dermal, oral and by inhalation. As most pesticides have low to moderate vapour pressures, the majority of occupational and residential exposures originate from the dermal route.

Agricultural workers are considered to be an occupational group that receives high exposure to pesticides (Fenske & Day, 2005).

Table 2. Number of cases of skin diseases and incidence rate by economic sector in Europe in 2005[a,b]

Occupational sector	No. of cases of skin diseases	Incidence rate (per 100 000 workers)
Mining and quarrying	55	31.5
Manufacturing	2006	10.4
Other community, social, personal service activities	503	9.5
Construction	834	9.1
Fishing	6	7.1
Hotels and restaurants	305	5.9
Health and social work	558	5.1
Agriculture, hunting and forestry	168	4.1

[a] From de Craecker et al. (2008).

[b] Sectors with incidence rates above 4 are shown.

Dermal exposure may occur as a result of a splash, spill or drift during mixing, loading or applying a pesticide, as well as exposure to residues on application equipment, protective clothing or treated surfaces. Moreover, exposure to pesticides can also concern bystanders and rural workers re-entering the field shortly after treatment. The sources of exposure during post-application activities are different from those during application and include contact with foliage, soil and dust (Tielemans et al., 1999; Ramos et al., 2010; also see sections 4.2.1.4 and 6.2.12). Oral exposure may also occur as a consequence of dermal exposure—that is, through hand-to-mouth activities (see also sections 3.1 and 4.2.3).

Other groups of workers exposed to pesticides include workers in greenhouses, workers in market gardens, home gardeners, chemical workers, animal food mill workers and some food handlers. Workers handling pesticides commercially in residential and institutional settings are often referred to as pest control operators, and their potential for exposure differs significantly from that of agricultural pesticide handlers. Table 4 lists examples of tasks and situations involving possible dermal exposure of pesticide handlers.

Table 3. Occupations, tasks and substances with potential dermal exposure[a]

Occupation	Relevant tasks	Relevant substances
Agricultural industry	Mixing/diluting, loading and spraying	Pesticides and other products (e.g. chemicals with skin notation: allyl alcohol as herbicide, methyl bromide as soil sterilant)
Chemical industry	Handling, loading, mixing/diluting chemical substances, maintenance and servicing	Numerous chemicals (e.g. chemicals with skin notation: acrylamides/ acrylonitriles, allyl alcohol, aniline, benzene, alcohols, carbon tetrachloride, halogenated alcohols and aromatic compounds)
Paints, lacquers and varnishes industry	Mixing/diluting, loading and spraying	Products in use (paints, preservatives, solvents, thinners, additives, paint removers, epoxy resins, pigments and dyes), volatiles (PAHs, formaldehyde), irritants/corrosives or allergenic substances, acrylics, metals
Rubber and plastic materials/ polymers industry	Handling, loading, mixing/diluting chemical substances	Allergens, rubber vulcanization accelerators, additives and antioxidants, acrylonitrile
Cleaning sector	Wet work	Allergens in disinfectants and cleaning agents
Construction sector	Handling, loading, maintenance and servicing	Chromate, cobalt, epoxy resins and rubber, dust, tars, pitches, bitumens, asphalt
Electrical/ electronic engineering industry	Immersing of objects, electroplating, maintenance and servicing	Nickel, trichloroethylene (degreaser), battery electrolytes (sulfuric acid), glues (e.g. cyanoacrylates)
Food sector	Handling of slaughtered animals, their parts and products, contact with animals' body fluids and biological products (e.g. milk and excrement), wet work	Allergens in food (e.g. gluten, crustaceans, eggs, soya, peanuts), animal or vegetal proteins or toxins/residues
Hairdressers	Wet work and using products	Allergens in chemical products for hair, irritants in washing agents

Table 3 (continued)

Occupation	Relevant tasks	Relevant substances
Health care	Wet work, using products	Allergens in disinfectants, medications and fragrances
Leather (processing) industry	Mixing/diluting, loading, maintenance and servicing	Chromium, glues, rubber, turpentine, epoxy resins
Metal/mineral or machine and equipment production industry	Handling, loading, maintenance and servicing	Allergens and irritants in coolants, metals, fuels and benzene, substances in products (e.g. sodium azide used as anticorrosion agent in airbags, acids and solvents used in cleaning products), dust
Textile/clothing industry	Wet work, using products, immersing of objects, handling, loading, mixing/diluting	(Azo) dyes[b], formaldehyde resins, dyes, chromates, nickel
Wood industry	Using products and impregnated products, immersing of objects, spraying, handling, loading, mixing/diluting, cutting, maintenance and servicing	Wood tar (creosote), terpenes (pines), wood protection pesticides (chromium, cobalt, nickel, mercury), wood dust

PAHs, polycyclic aromatic hydrocarbons

[a] From Plinske (2006); Sithamparanadarajah (2008).

[b] Azo dyes can be metabolized to potentially carcinogenic aromatics.

Specific regulations in some countries require training of professionals to ensure that they apply the appropriate pesticides and amounts using the correct equipment, but this is not necessarily the case in other countries (see section 8.1). Exposure to pesticides and fatal reactions are especially relevant and frequently reported in developing countries where workers use manually carried equipment under high-risk conditions. These include missing or inadequate protective clothing, repairing contaminated equipment with their bare hands and using leaky sprayers without avoiding contact with the pesticide solution (van Wendel de Joode et al., 1996; Aragón et al., 2001). Additional factors are the lack of adequate training on pesticide safety and lack of knowledge on specific products and methods for pest control, as well as easy access to acutely toxic (and in most cases cheaper) pesticides.

Table 4. Identification of tasks performed by pesticide handlers that involve dermal contact with pesticides[a]

Task	Description
Mixing/loading	The most common activity for farmers. Typically, it includes tasks involved in pesticide application, such as weighing or measuring the product, mixing/diluting the concentrated product, loading the product into the equipment (either manually or via machinery), adding additional diluent and mixing it in the application equipment.
Application	Involves driving a vehicle containing the application equipment, such as trucks (with tank and mounted spray rig), tractors (which pull a tank and spray rig), other self-contained units and aircraft (helicopters or fixed-wing planes). Relevant also for workers using, for example, backpack sprayers, hand-held tank sprayers, push-type applicators and belly-grinders.
Post-application (re-entry)	Occurs during maintenance activities that require re-entering treated areas shortly after application (e.g. for crop inspection/harvesting activities). General public may also be exposed, for example, during re-entry into recreational areas such as playing fields, golf courses and parks.
Flagging	Occurs when workers on the field (with flags) are assisting pilots in obtaining complete coverage of the target area during aerial application of pesticides. Recent advances in global positioning system technology have greatly reduced the need for flaggers.
Other activities	Cleanup of large equipment, procedures requiring an immediate second operation, such as soil incorporation of a herbicide immediately after application or irrigation of a pesticide into a lawn soon after treatment.

[a] Adapted from Fenske & Day (2005).

Child labour in developing countries can result in significant exposure of children to pesticides, as has been highlighted in recent International Labour Organization activities (ILO, 2011).

Several methods have been developed for the assessment of exposure to pesticides. Sections 5.1, 6.2.11, 6.2.12 and 6.2.13 provide an in-depth review of these methodologies and their potential limitations. Overall, implementation of all these methods depends largely

on the availability of trained personnel and expensive equipment. In developing countries, however, methods for exposure assessment are expected to be inexpensive and easy to use. Semiquantitative and qualitative methods, such as a visual scoring system (Fenske, 1988) and field observations, are among the few examples of such simple methods. Aragón et al. (2006) modified Fenske's (1988) system by including patterns of dermal contamination and used it to estimate the dermal exposure of Nicaraguan farmers to pesticides. Blanco et al. (2005) identified the main determinants of dermal exposure to pesticides for Nicaraguan subsistence farmers through field observations and later proposed the Dermal Exposure Ranking Method (DERM) as an easy-to-use method to identify important determinants leading to dermal exposure and as a tool that could also be used to define priorities for prevention and training programmes (Blanco et al., 2008; see section 6.2.2).

4.1.2 Organic solvents

Organic solvents are another category of substances or products for which dermal exposure may be significant. The term solvent is used generally for substances capable of dissolving one or more other substances, and organic solvents refer to those that are carbon based. Solvents are widely used in industrialized countries, where millions of workers are potentially exposed to solvent-containing products such as paints, varnishes, lacquers, adhesives, glues and degreasing or cleaning agents. The majority of these products contain ethanol, isopropanol, acetone, toluene and xylene, or mixtures of these. Workers in occupations where these agents are used include printers, painters and paint manufacturers, microelectronics workers, degreasers, dry cleaners, carpet layers, coating workers, gluers, dye workers, carpenters, anaesthesia and laboratory personnel, petrol station workers and textile workers. Table 5 lists some common sources of organic solvent exposures.

As most solvents tend to be volatile, exposure assessments in the past have primarily focused on inhalation. However, because of their lipophilic nature, organic solvents can pass the skin barrier and may become systemically available in considerable amounts.

Table 5. Common organic solvents and their adverse health effects on the skin[a]

Compound	Industrial use	Type of skin damage
1,1,1-Trichloroethane	Degreaser and propellant, solvent for inks, adhesives, coatings	Skin irritation, blistering, burns, contact urticaria
Acetone	Cleaning solvent	Skin irritation, dryness, erythema
Acrolein	Manufacturing resins, pharmaceuticals, biocide, chemical warfare	Severe skin irritation
Benzene	Fuel, detergents, paint removers, manufacture of other solvents	Erythema, blistering (acute), drying, defatting, dermatitis (chronic)
Carbon disulfide	Viscose rayon, explosives, paints, preservatives, textiles, rubber cement, varnishes, electroplating	Inflammation, cracking of skin, second- and third-degree chemical burns on extended contact
Ethanol	Solvent, chemical intermediate for drugs, plastics, perfumes, cosmetics	Skin irritation, dermatitis, contact urticaria on prolonged contact
Formaldehyde	Chemical manufacturing, skin/hair care products, cosmetics, pathology laboratories	Irritant, chemical burns, allergic contact dermatitis, contact urticaria
Gasoline/petrol	Fuel, industrial solvent	Depletion of stratum corneum lipids, dryness and fissuring of the skin, nail disorders, hyperkeratosis, onychosis and dermatitis
Isopropanol	Industrial solvent and intermediate, cosmetics, pharmaceuticals, catalyst	Skin irritation, dermatitis, urticaria
n-Hexane	Glues and vegetable extraction, components of naphtha, lacquers, metal cleaning compounds	Mild irritation of mucous membranes, dermatitis on prolonged contact
Paraffin	Component of fuels, paints, dyes and inks; application in medicine, toiletries and cosmetics	Follicular and acneform lesions after prolonged contact
Styrene	Fibreglass component, polymers, plastics	Skin irritation, contact allergy, irritant dermatitis on extended contact (defatting)

Table 5 (continued)

Compound	Industrial use	Type of skin damage
Tetrachloroethylene	Dry cleaning, degreaser, textile industry, oil/fat extracting agent	Irritant dermatitis (defatting) on prolonged contact
Toluene	Paint, fuel oil, cleaning agents, lacquers, paints and paint thinners	Skin drying even from vapour, irritant dermatitis on extended contact
Trichloroethylene	Cleaning agent, paint component, decaffeination, rubber solvents, varnish	Irritant dermatitis from defatting, blistering on prolonged contact
Turpentine	Solvent, chemical intermediate	Strong skin irritation/ sensitization, defatting, dryness, fissures
Xylene	Solvent for paints, lacquers, varnishes, inks, dyes, adhesives	Irritant dermatitis from defatting, contact urticaria

[a] From Rowse & Emmett (2004); Rutchik & Ramachandran (2012).

Factors affecting skin permeability and irritation include anatomic location, individual skin status (e.g. sex, age, genetics, skin type and pre-existing skin damage), environment (e.g. temperature, humidity, ventilation) and the physical and chemical characteristics of the solvent (e.g. volatility, molecular weight and structure, pH and acid dissociation constant, lipophilic properties). Amphiphilic solvents (e.g. glycol ethers and dimethylformamide), being both lipophilic and water soluble, are a particular concern, because they can easily penetrate the skin. Table 6 compares the contribution of dermal and respiratory uptake to overall exposure for different solvents from human volunteer studies. The uptake of the glycol ethers methoxyethanol and ethoxyethanol via the dermal route exceeds uptake via inhalation when inhalation exposure is to concentrations at the occupational exposure limits (OELs).

Numerous solvents are labelled with “skin notations” in lists of OEL values (Table 7; see also section 8.2.2).

Skin reactions such as contact dermatitis (irritant and allergic) and effects on the central nervous system are the two general types of toxic responses associated with exposure to solvents. Adverse effects

Table 6. Comparison of dermal and respiratory uptake for some liquid solvents

Solvent	Exposure conditions		Dermal uptake (% of respiratory uptake)
	Dermal: duration, area exposed	Inhalation: duration, exposure concentration	
1,1,1-Trichloroethane	3 min 360 cm^2 8×/8 h	8 h OEL	5[a]
Trichloroethylene			119[a]
Tetrachloroethylene			46[a]
Toluene			5[a]
Xylol			5[a]
Methoxyethanol	1 h 2000 cm^2	8 h OEL	11 100[b]
Ethoxyethanol			2 200[b]

OEL, occupational exposure limit

[a] Kezic et al. (2001).

[b] Kezic et al. (1997).

on the skin are most frequently associated with the defatting function of the solvents and their capability to dissolve or destroy the surface lipids of the stratum corneum. The consequence is loss of the skin barrier function, resulting in water loss and dryness of the skin. Examples of solvents causing skin dehydration include propanol, isopropanol, alcohol, acetone and chloroform. Other effects include irritation, contact urticaria and irritant or allergic contact dermatitis (Table 5). Immunological contact urticaria has been associated with exposures to several alcohols, such as ethyl, butyl, isopropyl and benzyl alcohol, formaldehyde, methyl ethyl ketone, polyethylene glycol, 1,1,1-trichloroethane and xylene. Some higher-boiling petroleum distillates, such as cutting and lubricating oils, have lesser lipid-extracting capabilities, but are rather keratinogenic, causing folliculitis, epitheliomas and keratoses. Table 5 gives examples of cutaneous injury caused by several organic solvents and the occupations in which they are used. Effects of solvents on the skin and their potential for systemic toxicity from dermal absorption are reviewed by Rowse & Emmett (2004). Details about the diseases resulting from dermal contact with solvents are discussed in more detail in chapter 7.

Table 7. Solvents with threshold limit value (TLV) and "skin notation" according to the German TRGS 900[a]

Substance name	Substance name	Substance name
Acetonitrile	1,4-Dioxane	*N*-Methylaniline
2-Aminoethanol	1,3-Dioxolan	Methyl chloroacetate
Bis(2-methoxyethyl) ether	Ethan-1,2-diol (ethylene glycol)	Methyl formate
Butanone	2-Ethoxyethanol	4-Methylpentan-2-one
2-Butoxyethanol	2-Ethoxyethyl acetate	*N*-Methylpyrrolidone (vapour)
2-(2-Butoxyethoxy)ethanol	1-Ethoxypropan-2-ol	Morpholine
2-(2-Butoxyethoxy)ethanol acetate	Ethylbenzene	Nitrobenzene
Carbon disulfide	Ethyl chloroacetate	Nitroethane
Carbon tetrachloride	Ethyl-3-ethoxypropionate	1-Nitropropane
Chloromethane	Ethyl formate	Oxydipropanol (dipropylene glycol)
Cumene	Heptan-2-one	Pentan-2,4-dione (acetylacetone)
Cyclohexanone	Hexan-2-one	2-Phenoxyethanol
Di-*n*-butylamine	4-Hydroxy-4-methylpentan-2-one (diacetone alcohol)	2-(Propyloxy)ethanol
1,2-Dichlorobenzene	2-Isopropoxyethanol	2-(Propyloxy)ethanol acetate
Dichloromethylbenzene (ring substituted)	Methanol	1,1,2,2-Tetrachloroethane
2,4-Dichlorotoluene	2-Methoxyethanol	Tetrahydrofuran
Diethylamine	2-(2-Methoxyethoxy)ethanol	Tetrahydrothiophene
2-Diethylaminoethanol	2-Methoxyethyl acetate	Toluene
N,N-Diethylacetamide	2-Methoxypropanol	Trichloromethane (chloroform)
N,N-Dimethylaniline	2-Methoxypropyl acetate	Triethylamine
N,N-Dimethylformamide		Xylene (all isomers)

[a] Technische Regeln für Gefahrstoffe (German Technical Rule for Hazardous Substances) 900 (BAuA, 2006).

4.1.3 Wet work

Although an internationally agreed-upon definition of wet work is still lacking, the German guidance document "Technical Rule for Hazardous Substances 401" (TRGS 401) specifies wet work as "activities where workers spend a major part of the working time in wet environments or wear moisture-resistant impervious gloves or clean their hands frequently and intensively" (BAuA, 2011a). According to Flyvholm & Lindberg (2006), wet work further includes exposure to water-soluble irritants.

Prolonged and/or repeated contact with water can damage the skin, and this effect can be significantly enhanced by co-exposure to

Table 8. Exposures leading to occupational irritant contact dermatitis in Denmark[a]

Work type/irritating substance	Percentage
Wet work	43.0
Food	11.9
Impervious gloves	10.6
Oils	10.3
Mechanical irritation	6.2
Chemicals	4.4
Other	4.0
Disinfectants	0.7

[a] Adapted from Skoet et al. (2004).

cleaning substances, disinfectants, solvents, alkalis and acids. In addition, frequent handwashing or wearing impervious gloves for lengthy periods can also impair the barrier function of the skin. Contact with water and wearing impervious gloves are part of the everyday working life of many occupational groups, such as cleaning personnel, hairdressers, health-care professionals, cooks or kitchen help, food manufacturers and metalworkers. Current evidence suggests that exposure to water ranks first among several irritant exposures found at the workplace (Table 8).

TRGS 401 (BAuA, 2011a) recommends that workers should not have their hands wet for more than 2 hours or more than 20 times each day and that impervious gloves should not be worn for more than 4 hours per day. If the definition for wet work is met, a set of requirements regarding information to the employees, screening, physical examination, time limits, etc. is enforced.

Workers classified as wet work employees are in a broad spectrum of occupations and include health-care and nursing professionals, hairdressers, gastronomy workers and cleaning personnel. Health-care workers are a prominent example of a high-risk group subjected to frequent wet work, glove use and high hygiene demands. Nursing activities are associated with prolonged use of occlusive gloves and exposure to irritants such as water, disinfectants and detergents,

and health-care workers have a significant risk of developing hand dermatitis (Jungbauer et al., 2004a,b). The most frequent cause of allergic contact dermatitis (see section 7.2.2) is exposure to rubber additives in gloves and medical devices (see section 8.5.6). Biocides contained in moisturizers or in medical formulations are another important source of contact sensitization (see definition of biocides in Appendix 1). Other allergens to which health-care personnel may be sensitized are nickel (in instruments), fragrances (in moisturizers), acrylates (in dental products and products for bone implantation) and colophony (present in bandages).

Hairdressers are another group of professionals that are subject to excessive exposure to water in addition to numerous cosmetic products, including shampoos, conditioners, dyes, bleaches and permanent wave solutions, as well as detergents and glove components. Although physical factors such as heat, sweating and dry air from work procedures can also contribute to skin irritation, the most important factor remains the frequent and repetitive exposure to water. Duration and frequency of exposure of skin to wet work–related activities have been recognized as key determinants of risk to the skin.

The overall characteristics of wet work are diverse and can lead to different types of skin disease. Occupational dermatoses are generally manifested as inflammatory skin reactions in the form of reddening, itching, peeling, blisters and eczema. Both irritant and allergic contact dermatitis of the hands can occur; in most cases, however, contact dermatitis is caused by chronic exposure to irritants through a non-allergic pathway (see chapter 7). Hand eczema due to wet work may cause chronic suffering, require a change of jobs and/or sick leave and lead to a dramatically reduced quality of life.

Prevention of skin diseases in wet work occupations requires preventive measures different from those applied to more severe irritants (such as corrosives), many of which are covered by occupational health regulations (discussed in section 8.1). Questionnaires and observations are common means of assessing the degree of exposure to wet work, and the method of continuous observation is frequently regarded as the gold standard (Jungbauer et al., 2004a,b). One of the problems in the prevention of skin effects from milder irritants and wet work is that workers frequently accept cumulative irritation effects from repeated

exposures as "part of the job". Prevention programmes can focus on reducing the frequency of wetting the hands—for instance, by promoting the use of impervious gloves to protect against hand dermatitis (see also section 8.5.4). Prevention programmes should be updated regularly based on available scientific evidence, and their implementation requires considerable effort and ongoing attention.

4.1.4 Metals

Exposure to metals is important not only for those directly employed in the mining or metals industry, but also for those in several other occupations.

Dermal exposure to mercury may occur for those employed in the electrochemical and electromechanical industries or for those working in the laboratory (see chapter 7 for the effects from dermal exposure to mercury).

Exposure to chromium salts (chromates) may occur for those employed in the building industry or for craftsmen, as chromium is an ingredient in the manufacture of many products, such as cement, mortar, leather, paints and anticorrosives, with the potential to cause chrome sensitivity. Contact with hexavalent chromium can cause both dermatitis and burns. Hexavalent chromium is known to be the most common cause of allergic dermatitis in men. Research has shown that between 5% and 10% of construction workers may be sensitized to cement containing hexavalent chromium and that plasterers, concreters and bricklayers are particularly at risk (Winder & Carmody, 2002).

Exposure to cobalt may occur in the production of cobalt powders, in the hard metal/diamond polishing industry or from cobalt salts in paints, special metals or rubbers.

4.2 Non-occupational sources

The general population is exposed via the dermal route to numerous products containing a huge variety of chemicals. Moreover, consumers

are exposed in many cases to the same substance in different products (e.g. fragrances are present in cosmetics as well as in scented textiles, detergents or toys). Thus, a clear differentiation between product categories or pathways (see section 3.1.2) is not possible. As the scope of dermal exposure is very wide, a general overview on products and situations with relevant dermal exposure is provided first. Substance groups that are considered to be important based on their potential for causing diseases are then described. Dermal exposure of children is discussed separately in section 4.2.3.

4.2.1 Relevant product groups and exposure situations

Table 9 provides an overview of products associated with dermal exposure of consumers. Exposure differs with respect to whether it is intended or unintentional, the physical state of the product, exposure duration and surface contact. Further, exposure can be by direct dermal contact with substances or products (e.g. when applying cosmetics to the skin) or by indirect contact (e.g. by contact with contaminated material after the application of a pesticide). If available, duration of exposure, frequency of use, duration of dermal contact and amounts used are provided in the table (Weegels & van Veen, 2001; Loretz et al., 2005, 2008; Loretz, 2006), which may be used for risk assessment of individual ingredients if the content is known. The relevance of the individual product groups in Table 9 is discussed in the following sections.

4.2.1.1 *Personal care products and cosmetics*

The definitions of “cosmetics” and “personal care products” can vary considerably in different countries (see Appendix 2). A personal care product can be defined and regulated as a cosmetic, a prescription drug or an over-the-counter (non-prescription) drug, depending on the ingredients and the claims of the product. In this document, the terms cosmetics and personal care products are used as synonyms and represent in a broader sense products that consumers apply onto their body, resulting in dermal exposure to the ingredients.

Soaps, creams, lotions, antiperspirants, sunscreens, perfumes/fragrances and hair preparations/dyes are some examples of these

Table 9. Sources of dermal exposure of consumers

Products	Physical state	Exposure duration	Exposed skin area	Type of skin contact (pathway)	Mean number of applications per day	Mean amount used per application (g)	Mean amount used per day (g)	Reference
Personal care products								
Soap	Solid	Seconds to minutes	Whole body	Direct	—	—	—	—
Body wash	Liquid	Seconds to minutes	Whole body	Direct	1.37	11.3	14.5	Loretz (2006)
Creams, lotions	Liquid	Whole day	Face	Direct	1.77	1.22	2.05	Loretz et al. (2005)
			Hands	Direct	2.12	—	—	
			Arms	Direct	1.52	—	—	
			Feet	Direct	0.95	—	—	
			Legs	Direct	1.11	—	—	
			Neck and throat	Direct	0.43	—	—	
			Back	Direct	0.26	—	—	
			Other body areas	Direct	0.4	—	—	
			Overall	Direct	—	4.42	8.69	

Table 9 (continued)

Products	Physical state	Exposure duration	Exposed skin area	Type of skin contact (pathway)	Mean number of applications per day	Mean amount used per application (g)	Mean amount used per day (g)	Reference
Perfumes	Spray	Whole day	Parts of body to whole body	Direct	1.67	0.33	0.53	Loretz (2006)
Aftershave	Liquid	Seconds to whole day	Face	Direct	—	—	—	—
Antiperspirant	Solid/liquid	Whole day	Direct	Direct	1.3	0.61	0.79	Loretz (2006)
Cosmetics								
Skin bleaching creams	Liquid	Seconds to minutes	Parts of body to whole body	Direct	—	—	—	—
Sunscreens	Liquid	Minutes to whole day	Parts of body to whole body	Direct	—	—	—	—
Makeup	Liquid/ (powder)	Up to whole day	Face	Direct	1.24	0.54	0.67	Loretz (2006)
Lipstick, lip salve	Solid, liquid	Up to whole day	Lips	Direct	2.35	—	—	Loretz et al. (2008)
Mascara	Solid	Up to whole day	Eyes	Direct	—	—	—	—
Eyeshadow	Powder	Up to whole day	Eyes	Direct	1.2	0.03	0.04	Loretz et al. (2008)
Kajal (kohls)	Solid	Up to whole day	Eyes	Direct	—	—	—	—

Table 9 (continued)

Products	Physical state	Exposure duration	Exposed skin area	Type of skin contact (pathway)	Mean number of applications per day	Mean amount used per application (g)	Mean amount used per day (g)	Reference
Facial cleanser	Liquid: lathering/ non-lathering	Minutes to whole day	Face	Direct	1.6	2.57	4.06	Loretz et al. (2008)
Nail polishes, lotions	Liquid	Whole day	Nails	Direct	—	—	—	—
Shampoo	Liquid	Minutes	Hair: rinse out	Direct	1.11	11.76	12.8	Loretz (2006)
Conditioner	Liquid	Minutes	Hair: rinse out	Direct	1.1	13.13	13.77	Loretz et al. (2008)
			Hair: leave in	Direct	—	—	—	—
Hairspray	Liquid	Up to whole day	Hair/head	Direct	1.49 (aerosol) 1.51 (pump)	2.58 (aerosol) 3.64 (pump)	3.57 (aerosol) 5.18 (pump)	Loretz (2006)
Hair gel	Liquid	Up to whole day	Hair/head	Direct	—	—	—	—
Hair dyes	Liquid	Up to whole day	Hair/head	Direct	—	—	—	—
Household products								
Dishwashing agents	Liquid	Minutes	Hands	Direct	0.63	5	—	Weegels & van Veen (2001)

Table 9 (continued)

Products	Physical state	Exposure duration	Exposed skin area	Type of skin contact (pathway)	Mean number of applications per day	Mean amount used per application (g)	Mean amount used per day (g)	Reference
Laundry detergents	Liquid	Minutes	Parts of body to whole body	Direct: spillages Indirect: textiles	—	—	—	—
All-purpose cleaner	Liquid	Minutes	Hands	Direct: mixing Indirect: spillages Residues on package, treated surfaces	0.35	27	—	Weegels & van Veen (2001)
Toilet cleaner	Liquid	Minutes	Hands	Direct: splashes Indirect: as above	0.28	—	—	Weegels & van Veen (2001)
Polishing creams, do-it-yourself products, air fresheners	Liquid, solid	Depends (e.g. on type of work) (minutes up to whole day)	Hands to whole body	Direct: hands when using Indirect: as above	—	—	—	—
Pesticides/insect repellents	Liquid/solid	As above	As above	As above	—	—	—	—

Table 9 (continued)

Products	Physical state	Exposure duration	Exposed skin area	Type of skin contact (pathway)	Mean number of applications per day	Mean amount used per application (g)	Mean amount used per day (g)	Reference
Textiles, shoes and other consumer products								
Textiles (for both clothes and furniture)	Solid	Up to whole day	Parts of body to whole body	Direct	—	—	—	—
Shoes	Solid	Up to whole day	Feet	Direct	—	—	—	—
Jewellery, piercings	Solid	Up to whole day	Specific parts	Direct	—	—	—	—
Everyday items	Varies	Minutes to hours or days	Ears, hands	Direct	—	—	—	—
Environment								
Soil/plants	Solid	Minutes to hours	Parts of body to whole body	Indirect	—	—	—	—
Dust	Solid	Whole day	As above	Indirect	—	—	—	—
Water (e.g. pools)	Liquid	Minutes	As above	Indirect	—	—	—	—
Air	Gas	Whole day	As above	Indirect	—	—	—	—

products (de Groot, 1998; Table 9). Generally, products can be subdivided into leave-on products (e.g. creams, lotions) and rinse-off products (e.g. soap, shampoo), the latter involving much shorter exposure duration. The highest dermal exposure for leave-on products, with an average of $8\,g \cdot d^{-1}$, is for creams and body lotions (Loretz et al., 2008; Table 9). In addition to the dermal pathway, exposure via the oral route can occur for products used in and around the mouth, as well as from hand-to-mouth contact. According to the database on cosmetics ingredients in the EU (EC, 2013a), personal care products are usually complex systems containing many ingredients, depending on the intended function (e.g. emollient, deodorant, preservative).

Negative effects reported from the use of personal care products include irritation (section 7.2.1), sensitization (section 7.2.2) and mechanical injury (e.g. mascara wand scratching the eye), but rarely any other toxicological effects (Ross, 2006). Allergic contact reactions to personal care products are increasingly being observed (Nielsen et al., 2001; Goossens, 2011). As a result of changes in product ingredients, new and unusual allergens are continuously emerging (Pascoe et al., 2010).

The use of skin lightening or bleaching products for cosmetic purposes is frequently practised by women from Africa, the Middle East, Asia and Latin America, but also among dark-skinned populations in Europe and North America (WHO, 2011a). It is reported, for example, that 25–96% of women from sub-Saharan Africa use these products (Ly et al., 2007). Bleaching products usually contain corticosteroids (79%), hydroquinone (58%), products based on vegetable extracts (31.7%), caustic products (8.5%) and also products of unknown composition (Ly et al., 2007). Consequences from use may include hyperpigmentation, striae atrophicae and skin atrophy (Ly et al., 2007). Owing to the mass distribution of these products, this is a global public health issue. For example, in Mexico, these products are widely available in pharmacies, beauty aid stores and health stores (Peregrino et al., 2011).

Another special product involving dermal exposure of consumers is tattoos. The number of tattooed individuals has increased significantly, especially among youth. In the United States of America

(USA), approximately 24% of the population is tattooed, whereas in Europe, the proportion is about 10% (Vasold et al., 2008). Application of tattoos may cause viral or bacterial infections, allergic reactions and various other diseases of the skin (Papameletiou et al., 2003; Kazandjieva & Tsankov, 2007; de Cuyper, 2008).

Relevant ingredients in cosmetics that may cause sensitization are fragrances (see section 4.2.2.1), preservatives (see section 4.2.2.2), dyes (see section 4.2.2.3) and metals in some special cases (see section 4.2.2.4). Kohl, for example, which contains lead, is used in Indo-Pakistan and other Muslim cultures as an eye preparation (IPCS, 1995).

4.2.1.2 *Household products*

Consumers may have contact with a variety of household chemicals in products such as dishwashing liquids, laundry detergents, toilet cleaners, pesticides, glues, textiles and air fresheners.

Weegels & van Veen (2001) investigated consumer contact with household products. Whereas, for instance, direct contact with dishwashing liquid occurs when the hands are inserted into the dishwashing solution, indirect contact is also possible from spills on the package or when drying dishes. Contact with all-purpose cleaner occurs when mixing or checking the soapsuds, rinsing the measuring cap, contacting spills on the package, rinsing the cloth in the soapsuds, wiping with the cloth and clearing away the soapsuds and cloth.

Information on amounts used that may be helpful for risk assessment related to dermal contact with these products is provided in Table 9. Often on account of their intended use for cleaning and/or disinfection, household products may contain substances with corrosive or sensitizing properties, particularly bath and toilet or drain cleaners (Hahn et al., 2010). Relevant substance groups with respect to consumer health are acids and bases as well as detergents that may lead to skin irritation if not properly used (Velvart, 1993).

There is also concern for the indoor use of pesticides (Hahn et al., 2010). Pesticides used indoors degrade to a lesser extent than

those used outdoors and often remain within the house, circulating with dust and air. Therefore, homeowners and their families may be subject to prolonged exposures after the actual process of application. Children in particular may receive considerable exposure to pesticide residues because of their unique behaviours (i.e. mouthing objects and crawling on floors) that increase contact with treated surfaces, such as turf, carpets and floors (see also section 4.2.3).

Further, household products frequently contain fragrances (see section 4.2.2.1) and preservatives (see section 4.2.2.2).

4.2.1.3 *Textiles, shoes and other consumer products*

Dermal contact with clothes and shoes as well as bedclothes can last for several hours at a time. Pressure, friction, warmth and perspiration are conditions conducive to contact dermatitis and/or absorption into the skin (Zhong et al., 2006; Warshaw et al., 2007; Reich & Warshaw, 2010).

Textile fibres themselves are not usually allergenic, but they may be responsible for irritant contact dermatitis. Persons with an atopic constitution and/or sensitive skin often complain of intolerance to clothes, especially woollen garments and synthetic fibres (Ryberg, 2009).

Of toxicological interest are, in particular, those chemicals that are involved in the dyeing and printing processes, optical brighteners and chemical finishes (Krätke & Platzek, 2004; Brookstein, 2009; Ryberg, 2009; Reich & Warshaw, 2010; BfR, 2012a; see also Table 10 in section 4.2.2 below).

Footwear dermatitis is mostly caused by leather processing chemicals, metal buckles, black dyes of shoes and socks, adhesives, plastic, rubber shoes and polishing agents (Freeman, 1997; Chowdhuri & Ghosh, 2007; Warshaw et al., 2007).

Numerous other consumer products (e.g. jewellery and piercings, mobile phones, mattresses, furniture and carpets) may contain chemicals that can cause adverse effects (see Table 10 in section 4.2.2 below).

4.2.1.4 Environment

Dermal exposure may also occur via the environment. Sources include water, soil, plants, house dust and air.

Dermal exposure is obvious for swimming/bathing activities and is especially relevant if the water is contaminated. Persons may, for example, be exposed to organic sun-blocking agents while swimming in lakes (Kameda et al., 2011) or to disinfectants and disinfection by-products when bathing in pools (Erdinger et al., 1998; Bernard, 2007; Richardson et al., 2010; Cardador & Gallego, 2011; Florentin et al., 2011; Dalmau et al., 2012). Some swimmers suffer from eye and skin irritation in water treated with chlorine (Erdinger et al., 1998; Bernard, 2007).

Dermal exposure to soil or plants treated with pesticides is relevant for gardeners. Gardeners frequently lack experience in the proper use of pesticides or tend to ignore instructions provided. They typically wear no protective clothing, have no training to handle the application equipment correctly and have difficulties in accurately interpreting application rates. Pesticide exposure may also be relevant in the case of indirect contact; a study with golfers playing on turf grass treated with pesticides showed that dermal exposure was the dominant exposure pathway for the golfers, accounting for approximately 60% of the absorbed dose of chlorpyrifos and 100% of the absorbed dose of carbaryl (Putnam et al., 2008).

An important source of dermal exposure is house dust. Dust is formed through mechanical processes or through dispersion of solid material in the air and is a complex mixture of soil, biological materials and settled indoor aerosols. Several studies have identified house dust as an important source of pesticides (see also section 4.2.1.2), polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs) and other flame retardants, polycyclic aromatic hydrocarbons (PAHs), plasticizers (phthalates) and metals (Butte & Heinzow, 2002; Lorber, 2008; Johnson-Restrepo & Kannan, 2009; see also section 4.2.2). Furthermore, indoor surfaces become coated with a thin film of organic matter. Semivolatile organic compounds may be transferred to the skin and subsequently taken up. This pathway can exceed intake by inhalation for several semivolatile

organic compounds commonly found indoors, such as butylated hydroxytoluene, chlorpyrifos, diethyl phthalate and nicotine (in its free base form). Another group of semivolatile organic compounds (e.g. benzo(*a*)pyrene, chlordane, chrysene, diazinon, di-*n*-butylphthalate and nonylphenol) can also contribute to the total dermal uptake, but to a lesser extent. For a third group (e.g. bisphenol A), skin contact may contribute to elevated levels in skin surface lipids (Weschler & Nazaroff, 2012).

While the relevance of dermal exposure to liquids, solids or powders is obvious, direct dermal exposure to gases and vapours may be considerable as well, especially for compounds that are both hydrophilic and lipophilic (Kezic et al., 1997; Nomiyama et al., 2001; Bader et al., 2008).

4.2.2 Relevant substances/substance groups

Table 10 provides an overview of different substance categories, relevant chemicals in these categories, their occurrence in consumer products and their possible toxicological relevance, as indicated by their potential to cause diseases. Mention of a disease does not, however, mean that any exposure to these substances will cause the disease. Besides the hazardous properties of the substance itself, concentrations of the substance in the product, the duration of exposure to the substance and the susceptibility of persons exposed are additional determinants for the occurrence of a disease. The major concern is allergic contact dermatitis (see section 7.2.2). Allergic contact dermatitis is easily attributable to previous skin contact, and numerous patch tests have confirmed the sensitivity of previously exposed individuals. Irritating properties can also easily be detected because of the immediate reaction following exposure. Diseases may also occur from systemic uptake following dermal exposure. In contrast to allergic contact dermatitis, where relatively low concentrations in a product may be sufficient to induce or elicit allergy, diseases following systemic uptake are usually caused by much higher concentrations. To assess the risk, dose levels taken up have to be compared with the no-observed-adverse-effect level (NOAEL) of the substance of concern.

Table 10. Overview of substances in consumer products and their toxicological relevance

Substance category	Relevant substances	Products containing substances, other sources	Toxicological relevance for respective use	References
Adhesives	Epoxy resin, formaldeyde, *p*-tertiary-butylphenol-formaldehyde resin	Rubber glues, neoprene adhesives for shoes	Allergic contact dermatitis	Warshaw et al. (2007)
Botanical ingredients	Extracts from *Achillea millefolium*, *Arnica montana*, *Calendula officinalis*, *Chamomilla recutita*, oils from *Melaleuca alternifolia*, *Mentha piperita* oil, geranium, *Litsea cubeba*, *Myroxylon pereirae*	Soap, shampoo, skin care products, herbal remedies	Allergic contact dermatitis, irritation, photoirritation, photosensitization	Mantle et al. (2001); Lalko & Api (2006); Antignac et al. (2011); Travassos et al. (2011)
	Propolis	Face creams, ointments, balsams, toothpaste, mouthwash	Allergic contact dermatitis	Czarnobilska et al. (2012)
Detergents	Phosphates, zeolites	Laundry detergents, textiles	Irritation, allergic contact dermatitis	Belsito et al. (2002)
Dyes, pigments	*p*-Phenylenediamine, *o*-nitro-*p*-phenylenediamine and *p*-toluenediamine	Hair dyes, tattoo inks, shoes	Allergic contact dermatitis, systemic effects	Corrente et al. (2007); Kiec-Swierczynska et al. (2008); Kluger et al. (2008); Calogiuri et al. (2010); Nohynek et al. (2010); Kind et al. (2012); Turan et al. (2013)

Table 10 (continued)

Substance category	Relevant substances	Products containing substances, other sources	Toxicological relevance for respective use	References
	Disperse dyes (azo dyes, anthraquinone dyes)	Textiles, tattoo inks	Allergic contact dermatitis (disperse dyes), carcinogenicity (azo dyes)	Hatch & Maibach (1995); Hatch (2003); Vasold et al. (2008); Brookstein (2009); Ryberg (2009); BfR (2012a); Malinauskiene et al. (2013)
	Carbon black	Tattoo inks	Presumably no toxicological relevance	Vasold et al. (2008)
Easy care finishes	Dimethylol dihydroxy ethylene urea and modified dimethylol dihydroxy ethylene urea, formaldehyde	Textiles	Allergic contact dermatitis	Scheman et al. (1998); Lazarov et al. (2002); de Groot et al. (2010b); BfR (2012a)
Excipients, emulsifiers and humectants	Dicaprylmaleate, wool alcohols, fatty alcohols (e.g. cetyl alcohol), propylene glycol, isononyl isononanoate, trioleyl phosphate, butylene glycol, pentylene glycol	Tanning lotions, moisturizers, foundations, sunscreens	Systemic effects	Davies & Johnston (2011); Goossens (2011)
Flame retardants	Organophosphate flame retardants (e.g. tris(1,3-dichloroisopropyl) phosphate)	House dust, textiles, electronics, mattresses, furniture, carpets, baby products	Systemic effects[a]	Johnson-Restrepo & Kannan (2009)

Table 10 (continued)

Substance category	Relevant substances	Products containing substances, other sources	Toxicological relevance for respective use	References
	Hexabromocyclododecanes	House dust, textiles, electronics, mattresses, furniture, carpets	Systemic effects[a]	Stapleton et al. (2011)
	PBDEs[b]	House dust, textiles, electronics, mattresses, furniture, carpets	Systemic effects	Lorber (2008); Johnson-Restrepo & Kannan (2009); Daso et al. (2010); Kalantzi & Siskos (2011)
Fragrances	*Natural fragrances* Fragrance mix I (geraniol, hydroxycitronellal, isoeugenol, cinnamyl alcohol, cinnamal, *Evernia prunastri* or oakmoss) Fragrance mix II (citronellol, hexylcinnamal, coumarin, Lyral™, citral, farnesol) Linalool, limonene, butyl phenyl methyl propional (Lilial®), α-isomethyl ionone, γ-methyl ionone, eugenol, benzyl benzoate, benzyl alcohol, benzyl cinnamate, *Evernia furfuracea* or treemoss, 4-methoxybenzyl alcohol, amylcinnamyl alcohol, methyl heptane carbonate	Personal care products, cosmetics, household products, air fresheners	Allergic contact dermatitis	Bridges (2002); Schnuch et al. (2004); Brunn Poulsen & Schmidt (2007); Buckley (2007); Rastogi et al. (2007); Belsito et al. (2008); Davies & Johnston (2011); Nardelli et al. (2011); Yazar et al. (2011); SCCS (2012)

Table 10 (continued)

Substance category	Relevant substances	Products containing substances, other sources	Toxicological relevance for respective use	References
	Synthetic musks Galaxolide, Tonalide, Phantolide, Celestolide, (Crysolide), Traseolide	Soaps, shampoos, perfumes, aftershaves, laundry detergents	Bioaccumulative, systemic effects[a]	Ford (1998); Wormuth et al. (2005); Lu et al. (2011)
Metals	Nickel	Jewellery, tattoo inks, eye makeup, coins, bra fasteners, zippers, snaps, buttons, hairpins, eyeglass frames, pens, utensils, paper clips, keys, tools, mobile phones, headsets, finger paints, contaminant in personal care products in some countries	Allergic contact dermatitis	Rastogi (1992); Lidén & Norberg (2005); Marcer et al. (2006); Thyssen & Maibach (2008); Corazza et al. (2009); Forte et al. (2009); Thyssen et al. (2009); Ayenimo et al. (2010); Thyssen & Menné (2010); Jensen et al. (2011); BfR (2012b); Holbrook et al. (2012)
	Chromium salts	Leather products, tattoo inks, finger paints, contaminant in cosmetics in some countries	Allergic contact dermatitis	Rastogi (1992); Hansen et al. (2002); BfR (2007; Warshaw et al. (2007); Corazza et al. (2009); Hwang et al. (2009); Thyssen et al. (2012)
	Cobalt	Jewellery, snaps, buttons, hair dyes, dental alloys, joint replacements, tools, ceramics, enamel, cement, paints and resins, tattoo inks	Allergic contact dermatitis	Forte et al. (2009); Thyssen & Menné (2010); Thyssen (2011)

Table 10 (continued)

Substance category	Relevant substances	Products containing substances, other sources	Toxicological relevance for respective use	References
	Palladium	Jewellery, dental restorations	Allergic contact dermatitis	Faurschou et al. (2011)
	Lead sulfide	Kohl, contaminant in personal care products in some countries	Systemic effects[a]	Al-Ashban et al. (2004); Hardy et al. (2006); de Caluwé (2009); Ayenimo et al. (2010)
	Mercury(I) salts	Antiseptic, fungicidal and bactericidal products, skin lightener creams[c]	Allergic contact dermatitis, hyperpigmentation, erythroderma	IPCS (1991, 2003); Al-Saleh & Al-Doush (1997); Chan (2011); Ladizinski et al. (2011); Peregrino et al. (2011); WHO (2011a)
Pesticides	Pyrethroids (e.g. tetramethrin, allethrin, prallethrin)	Household pesticides, house dust, plants treated with pesticides, surfaces, pets treated with pesticides, impregnated clothing	Systemic effects[a]	Hahn et al. (2010); Morgan (2012)
	Organophosphates (e.g. chlorpyrifos, dichlorvos, phoxim)		Systemic effects[a]	Putnam et al. (2008); Hahn et al. (2010)
	Carbamates (e.g. carbaryl)		Systemic effects[a]	

Table 10 (continued)

Substance category	Relevant substances	Products containing substances, other sources	Toxicological relevance for respective use	References
Phthalates	Diethylphthalate, dimethylphthalate, diisobutylphthalate,di-*n*-butylphthalate, di(2-ethylhexyl)phthalate	Plastics, house dust, fragrances, nail polish, hairspray, hair mousse, skin cleansers	Systemic effects, weak endocrine properties for some phthalates[a]	Api (2001); Koo & Lee (2004); Schettler (2006); Wormuth et al. (2006); SCCP (2007); Lyche et al. (2009); CPSC (2010); Hubinger (2010); Witorsch & Thomas (2010); Guo & Kannan (2011); Koniecki et al. (2011); Zhang et al. (2013)
Plastic and plastic materials	Epoxy resin, formaldehyde	Shoes	Allergic contact dermatitis	Chowdhuri & Ghosh (2007)
	Isocyanates	Products made of polyurethane, e.g. cushioning in furniture items	Allergic contact dermatitis	Bello et al. (2007); Brookstein (2009)
Preservatives/ disinfectants	Isothiazolinones (methylisothiazolinone and methylchloroisothiazolinone)	Cosmetics	Allergic contact dermatitis	Hahn et al. (2010); Lundov et al. (2011); Travassos et al. (2011); Švecová et al. (2013)
	Methyldibromo glutaronitrile[d]	Cosmetics	Allergic contact dermatitis	SCCP (2005); Hahn et al. (2010); Travassos et al. (2011)

Table 10 (continued)

Substance category	Relevant substances	Products containing substances, other sources	Toxicological relevance for respective use	References
	Formaldehyde and formaldehyde releasers (2-bromo-2-nitropropane-1,3-diol (bronopol))	Cosmetics, household products	Allergic contact dermatitis	de Groot et al. (2010a); Hahn et al. (2010); Travassos et al. (2011)
	Iodopropynyl butylcarbamate	Cosmetics, cleansing wipes	Allergic contact dermatitis	Davies & Johnston (2011)
	Thimerosal	Cosmetics	Allergic contact dermatitis	Kiec-Swierczynska et al. (2006)
	Phenoxyethanols	Cosmetics, deodorants	Allergic contact dermatitis	Rastogi et al. (2007); Hahn et al. (2010)
	Parabens	Cosmetics, deodorants	Systemic effects (weak estrogenicity)	Chowdhuri & Ghosh (2007); Cowan-Ellsberry & Robinson (2009); Boberg et al. (2010); SCCS (2011); Travassos et al. (2011)
	Dimethylfumarate	Shoes (mould-proof agent)	Allergic contact dermatitis	Bruze & Zimerson (2011); Silvestre et al. (2011); D'Erme et al. (2012)
	1-Bromo-3-chloro-5,5-dimethyl hydantoin	Swimming pools	Allergic contact dermatitis	Dalmau et al. (2012)

Table 10 (continued)

Substance category	Relevant substances	Products containing substances, other sources	Toxicological relevance for respective use	References
Repellents	Icaridin, ethyl 3-(*N*-butylacetamido)propionate and diethyltoluamide	Personal use insect repellents, house dust	Systemic effects[a]	Hahn et al. (2010)
Rubber and rubber chemicals	Mercaptobenzothiazole, thiuram mix, black rubber mix, dithiodimorpholine	Shoes	Allergic contact dermatitis	Chowdhuri & Ghosh (2007); Warshaw et al. (2007)
Siloxanes	Cyclic methylsiloxanes (hexamethylcyclotrisiloxane [D3], octamethylcyclotetrasiloxane [D4], decamethylcyclopentasiloxane [D5], dodecamethylcyclohexasiloxane [D6]) Linear methylsiloxanes	Soaps, hair care products, skin lotions, toothpastes, cosmetics, nursing nipples, cookware, household sanitation products, such as cleansers, furniture polishes	Systemic effects[a]	Horii & Kannan (2008); Wang et al. (2009); Lu et al. (2011)
Skin lighteners	Corticosteroids	Face cream	Allergic contact dermatitis, hyperpigmentation	Ly et al. (2007); Ladizinski et al. (2011)
	Hydroquinone	Face cream	Irritant contact dermatitis, systemic effects[a]	Ly et al. (2007); Ladizinski et al. (2011)

Table 10 (continued)

Substance category	Relevant substances	Products containing substances, other sources	Toxicological relevance for respective use	References
Surfactants	Betaines, alkyl sulfates	Personal care products, household chemicals	Irritation	Jacob & Amini (2008); Schnuch et al. (2011a)
UV filters (organic)	*p*-Aminobenzoic acid, oxybenzone	Sunscreens, makeup	Allergic contact dermatitis, photosensitization	Avenel-Audran et al. (2010); Morabito et al. (2011); Travassos et al. (2011)
	Benzophenone-4	Sunscreens, makeup	Allergic contact dermatitis, photosensitization, urticaria	Davies & Johnston (2011); Goossens (2011)
	Octocrylene	Sunscreens, makeup	Contact dermatitis	Goossens (2011)

EU, European Union; PBDEs, polybrominated diphenyl ethers; USA, United States of America

[a] Systemic effects depend on dose. Risk assessment necessary for respective use.

[b] Banned in several states of the USA and the EU.

[c] Banned in many countries.

[d] Banned in Europe in personal care products.

An attempt has been made here to make consumers aware of the variety of chemicals to which they are dermally exposed, in particular those that have been reported in the literature to have toxicological effects in some people. There are relatively few quantitative exposure assessments available, and these are out of the scope of this introductory survey and are not given here. The literature cited is by no means comprehensive, but has been chosen to give the interested reader a starting point for further reading. Products containing new chemicals are continually being manufactured and put on the market, and full information on their contents is difficult, if not impossible, to obtain.

Some substance groups with high consumer relevance (i.e. fragrances, preservatives/disinfectants, dyes/pigments, metals) are described in more detail below. For pesticides, the reader should refer to section 4.1.1.

4.2.2.1 *Fragrances*

Fragrances are the most frequently occurring allergens in consumer products and have long been recognized as a problem (e.g. Bridges, 2002; Nardelli et al., 2011; SCCS, 2012; see chapter 7).

Whereas the term fragrance refers to individual substances, a fragrance formula may consist of 10–300 different fragrances. A perfume is a special product used to give a pleasant scent that contains a mixture of fragrant essential oils or aroma compounds, as well as fixatives and solvents.

The fragrance industry has published a list of 3194 fragrances based on about 90% of the world's production. Eighty per cent of the total fragrance chemical volume is used in personal care and cosmetic products, and 20% in household products (IFRA, 2013). Fragrances can also be found in products designed for use by children (Brunn Poulsen & Schmidt, 2007). Moreover, they are also used in detergents, fabric softeners and a variety of other household products, as well as textiles; in addition, they are often added only to mask a product's unpleasant smell from raw materials.

The use of fragrances in cosmetics is regulated in many countries (Bridges, 2002). In Europe, any personal care products that contain fragrances will have the word "perfume" in the ingredients list. Twenty-six fragrance allergens have been regulated in Europe since 2003 (EC, 2003b). The presence of any of these fragrances in personal care products must be indicated in the list of ingredients when its concentration exceeds 0.001% in leave-on products or 0.01% in rinse-off products. In a recent study of 300 personal care products on the European market, it was found that 50–89% of these contained at least 1 of the 26 fragrance allergens that must be declared in the EU (Buckley, 2007). This study shows clearly how widespread the exposure to fragrances is in modern society.

Limonene, linalool, hexylcinnamal, γ-methyl ionone and Lilial® are very frequently used fragrances in consumer products (Rastogi, 2002; Buckley, 2007; Magnano et al., 2009; Yazar et al., 2011).

In addition to natural fragrances, artificial fragrances such as polycyclic musks (e.g. Galaxolide, Tonalide, Phantolide, Traseolide, Celestolide [Crysolide]) are used in many consumer products, such as soaps, shampoos, perfumes, aftershaves and laundry detergents (Ford, 1998; Wormuth et al., 2005; Lu et al., 2011).

4.2.2.2 *Preservatives/disinfectants*

After fragrances, preservatives are the most important allergens, especially in cosmetic products (Nardelli et al., 2011).

Preservatives are used to ensure that the products are safe to use for a length of time. They protect products from contamination by microorganisms present in the air, in the water and on our own skin. Although there are about 50 preservatives available, relatively few are chosen (Lundov et al., 2009). Compounds frequently used include 2-phenoxyethanol, hydroxybenzoates (parabens), isothiazolinones and 2-bromo-2-nitropropane-1,3-diol (or bronopol). The concentration range can be estimated fairly well (Hahn et al., 2010; Yazar et al., 2011) based on the maximum concentration

of active ingredients stipulated in the European Cosmetics Directive (EC, 2003b). Frequently, personal care products contain more than one active substance—for example, groups of compounds, such as several isothiazolinones or several parabens, or combinations of differently acting biocides, such as isothiazolinones and formaldehyde-releasing agents (Hahn et al., 2010).

4.2.2.3 *Dyes/pigments*

Dyes are another important substance group with allergenic potential.

Hair dyes may induce allergic contact dermatitis on the face, scalp and neck of consumers (SCCP, 2006). The most common allergens are the *p*- and *o*-benzenediamine dyes, in particular *p*-phenylenediamine and its derivatives, which remain an important cause of occupational allergy among cosmeticians and hairdressers. *p*-Phenylenediamine is used mainly for permanent hair dyeing and, under the EU Cosmetics Directive (EC, 2003b), is allowed in hair dye products with a concentration limit of 6%. In Japan, hair dyes are not considered cosmetics, but, along with skin bleaching, hair growing and anti–hair loss agents, are regulated as "quasi-drugs" (Nohynek et al., 2010; see Appendix 2). Other hair dyes in this group include *o*-nitro-*p*-phenylenediamine and *p*-toluenediamine.

From as early as 1869, textile dyes and subsequently finishes have been reported to cause various manifestations of allergic contact dermatitis, from mild to severe and debilitating (Hatch & Maibach, 1995; Malinauskiene et al., 2013). As dyes are extensively used to colour fabrics of polyester, nylon, cellulose acetate and acrylic fibres as well as cellulose, usually cotton (Johansson & Zimerson, 1995; Hatch, 2003; Le Coz, 2011), exposure to dyes is high. In the EU, their use is regulated by law; in the USA, only a voluntary agreement with industry exists.

Disperse dyes do not chemically bond to the fibres, and their small, lipophilic molecules can therefore easily migrate onto the skin of the person who is wearing the garment. Approximately 60% of all disperse dyes are azo dyes, and about 25% are anthraquinone dyes,

with the remainder being quinophthalone, methine, naphthalimide, naphthoquinone and nitro dyes.

Some azo dyes may separate under certain conditions to produce carcinogenic and allergenic aromatic amines (for more information, see Slowicki et al., 2009). The EU Azocolourants Directive (EC, 2002) sets out that azo dyes, which may release 1 or more of these 22 aromatic amines in detectable concentrations (i.e. above 30 parts per million [ppm]) in the finished articles or in the dyed components, may not be used in textile and leather articles that may come into direct and prolonged contact with the human skin or oral cavity. Since Annex XVII of REACH came into force in 2009 (EC, 2009a), the Azocolourants Directive (EC, 2002) has been replaced by the REACH Regulation.

Pigments, in contrast to dyes, are not soluble in water. Azo pigments, as well as many other pigments, are used in tattoo inks (Vasold et al., 2008). Black colours consist of carbon black as well as by-products of soot production (Vasold et al., 2008). There is, so far, no detailed regulation of tattoo colourants in the EU. The EU Scientific Committee on Cosmetic Products and Non-food Products Intended for Consumers (Papameletiou et al., 2003) noted that the chemical structure, identity and toxicological profile of many colourants used in tattooing are incomplete or unknown, thereby precluding proper risk assessment. Tattoo colourants and piercing materials are a legal paradox, at least in the EU. Although the colourants used for tattooing are placed in the human body by injection, this procedure is outside the scope of the Cosmetics Directive (EC, 2003b) and thus is not further regulated.

4.2.2.4 *Metals*

A wide range of products, such as cosmetics and tattoo inks, detergents, jewellery and piercing materials, leather tanning, articular prostheses and dental implants, may induce contact dermatitis due to their metal contents (Forte et al., 2008; see Table 10).

In addition to the metals presented in Table 10, other metals, such as aluminium, beryllium, cobalt, copper, gold, iridium, platinum,

rhodium and titanium, may cause skin hypersensitivity (Forte et al., 2008). In general, few data exist on the content of metals in consumer products. Ayenimo et al. (2010) detected iron, lead and nickel in personal care products commonly used in Nigeria, such as soaps, creams and detergents. The authors speculated that prolonged use of these products may pose a threat to human health.

(a) Nickel

Metal contact dermatitis is a common dermatosis, and nickel is the most common cause of contact allergy. It is estimated that up to 17% of women and 3% of men are allergic to nickel (Thyssen & Menné, 2010). Dermal contact with metals from ear piercing and the use of nickel-plated jewellery were the major contributors (metals that release nickel include white gold, gold plating, German silver, nickel plating and stainless steel; Thyssen & Menné, 2010). Nickel is also found in common, everyday items, including coins, bra fasteners, zippers, snaps, buttons, hairpins, eyeglass frames, pens, utensils, paper clips, keys and tools (see Table 10). Additionally, as body piercing has become increasingly popular, cases of metal allergy have soared. In 1994, the EU Nickel Directive (EC, 1994) was passed to protect European citizens from nickel allergy. This intervention led to a significant decrease in the proportion of consumer items that released an excessive amount of nickel ($>0.5\,\mu g$ nickel per square centimetre per week, for example, in Sweden; Lidén & Norberg, 2005; Thyssen et al., 2011). However, other sources of nickel allergy have emerged, such as mobile phones and headsets as well as body piercings. In 2009, the Nickel Directive became part of Annex XVII of the REACH Regulation and was revised to include nickel-releasing mobile phones; however, in countries where there are no restrictions, this is a persistent cause of nickel allergy and dermatitis. Before regulation of nickel release from mobile phones, 8 of 41 (19.5%) mobile phones marketed in Denmark between 2003 and 2007 released nickel in concentrations that could result in nickel allergy and dermatitis (Jensen et al., 2011).

(b) Lead

Although inhalation and ingestion are the most important exposure routes for lead, dermal exposure can also occur (Meyer et al., 2008).

Inorganic lead (e.g. on dust) can be absorbed through the skin (Stauber et al., 1994; Filon et al., 2006). The people most commonly exposed are those who are poor and who live in developing countries. The sources of lead exposure vary among and within countries, depending on past and current uses.

Major sources of lead in dust, for example, are leaded petrol (Duzgoren-Aydin, 2007) and lead-based paints, although for most purposes, according to regulations in many countries, these products should no longer contain lead. However, lead-based paints are still present in older houses and for instance remain as the most common source of lead exposure in the USA (Gulson et al., 1995; Jacobs et al., 2002). In homes in Delhi, India, the lead content of the dust is much higher than in the USA, and the levels pose a hazard to children (Kumar & Scott Clark, 2009). In addition, lead-based paints (especially for exterior surfaces) were widely sold in Africa until fairly recently, and lead chromate remains unregulated in most African countries. The cities in Africa are notoriously dusty, and mud and dirt invariably cover the hands, faces and clothes of toddlers and young children when they play outside or even in their homes, thus representing a serious health hazard (Nriagu, 1992; Ogunsola et al., 1995; Nriagu et al., 1996; see also section 4.2.3).

Another important source of exposure to lead is the use of kohl (also known as al-kahl, kajal or surma) as an eye cosmetic. In a large number of traditional kohl products available on the free market, lead sulfide is the main component. Use of kohl as an eye cosmetic was originally very common, especially among women, children and babies in North Africa (Morocco, Algeria, Egypt), in the Near East and Middle East, as well as in India and Pakistan. The cultural custom is very old and has been in use in Egypt since the Ancient Empire. In a survey of traditional eye cosmetics in six of the seven emirates of the United Arab Emirates, 20 of 53 (38%) were found to contain a lead compound (galena, lead sulfide) as the main component (Hardy et al., 2006). Similarly, analysis of a total of 107 kohl samples from Saudi Arabia showed lead levels up to 53% (Al-Ashban et al., 2004). The blood analyses of regular kohl users revealed a high lead concentration (Al-Ashban et al., 2004), which is a risk, particularly for women and children (de Caluwé, 2009).

(c) Chromium

Chromium is another important allergen. Chromium dermatitis is often due to exposure in the occupational environment, with cement being one of the most common chromium sources (see section 4.1.4). However, most patients showing chromium allergy are sensitized and develop contact dermatitis following consumer exposure to chromium in finished leather products. Nearly 90% of global leather production is tanned using chromium(III) sulfate. Chromium(VI) either appears as an impurity in the tanning substance or is formed through oxidation from chromium(III) in the ensuing processing stages. In a survey in Denmark, 15 of 43 (35%) leather goods contained chromium(VI) (Hansen et al., 2002). In a study in Germany, chromium(VI) was detected in more than half of the leather goods (850 samples) examined; in one sixth of the leather goods tested, the concentrations were higher than 10 mg·(kg leather)$^{-1}$ (BfR, 2007).

(d) Mercury

Inorganic mercury (e.g. ammoniated mercury) is often an ingredient in skin lightening soaps and creams (WHO, 2011a). Mercury salts inhibit the formation of melanin, resulting in a lighter skin tone (IPCS, 2003; Engler, 2005; Ladizinski et al., 2011). The products are supposed to be applied to the skin to dry overnight. In a study in which 16 skin lightening creams from a local Mexican market were analysed, the mercury content in 6 of the samples varied between 878 and 36 000 ppm. According to the authors of this publication, these values highly exceed the limit from the United States Food and Drug Administration (USFDA) for mercury in creams of less than 1 ppm (Al-Saleh & Al-Doush, 1997; Peregrino et al., 2011; CDC, 2012). Organic mercury (e.g. thiomersal) is used as a preservative in cosmetics, such as eye makeup cleansing products and mascara (Glahder et al., 1999; UNEP, 2008; WHO, 2011a). In addition, organic mercury may also be used in antiseptic, fungicidal and bactericidal products (IPCS, 1991). Further information about the toxicological profile of and exposure to mercury can be found in ATSDR (1999), IPCS (2003), Counter & Buchanan (2004), Clarkson & Magos (2006), WHO (2007a) and Chan (2011).

4.2.3 Dermal exposure of children

4.2.3.1 Reasons for special attention to children

The term "children" is used to describe humans at various stages of maturity for almost two decades of life. With regard to dermal exposure, it is particularly relevant to define the stage of development, as different exposures are involved with different age groups. There are several points to consider (SCCS, 2011), as described below.

Different absorption and distribution factors due to the immaturity of the physiological functions of young children may result in a higher internal exposure from the same external dose of certain chemicals in young children compared with adults. The skin of premature neonates is not fully developed, is thin and fragile and can be much more permeable than that of full-term neonates (Hoang, 1992). This potential for increased uptake may be an important consideration if these neonates are dermally exposed to contaminants in bath water or to chemicals in hygienic or diaper (nappy) rash products. Further, the defence against proliferation of microbes is reduced (Fluhr et al., 2010). The results of limited in vitro testing on skin from neonates and adults suggest that full-term newborns have a well-developed stratum corneum and that children's skin has a permeability similar to that of adults' skin (Hoang, 1992). However, there is accumulating evidence that the skin's barrier protection function remains immature throughout at least the first 2 years of life (Fluhr et al., 2010; Paller et al., 2011).

Dermal permeability may be enhanced when skin is damaged or highly hydrated (e.g. in an infant whose skin under a diaper is more likely to be excessively hydrated and possibly compromised by irritation and rash) (Hoang, 1992; Daston et al., 2004; SCCS, 2011).

The surface area to body weight ratio can be up to 2.3-fold higher in newborns (from birth to 1 month) than in adults, decreasing to about 1.8-fold for 12-month-old infants (USEPA, 2011a). Thus, dermally applied compounds may result in a higher exposure per kilogram of body weight (Makri et al., 2004).

Depending on the chemical, the half-lives of bioavailable substances may be 3–9 times longer in premature and full-term newborns than in adults (Renwick et al., 2000; Makri et al., 2004). Human infants up to about 6 months of age are typically, but not always, more sensitive than adults to chemical toxicity (Scheuplein et al., 2002).

4.2.3.2 *Specific exposure situations*

Baby skin care products are often applied to a large area of the infant's body, in comparison with adult skin care products, which are usually applied only to selected sites.

Behavioural factors may lead to higher exposure in children than in adults. Infants, toddlers and children may play and crawl on the ground, leading to a high percentage of the body being covered with soil or settled dust and giving them the opportunity for greater exposure. Children are also more likely to wear less clothing (e.g. barefoot walking, shorts) than adults. Furthermore, dermal exposure can contribute to ingestion exposure due to transfer from the skin to the mouth via the fingers (Daston et al., 2004). This may be an important pathway for uptake of pesticides by children (see section 4.1.1).

When playing, children can come into contact with chemicals that can be released, for example, from their toys in smaller or larger amounts during skin contact and/or when taken into the mouth. Considering the fact that children play with toys for several hours per day or even sleep with them in bed, the duration of dermal exposure can be very prolonged. Hazards include carcinogenic substances, such as PAHs (BfR, 2009), heavy metals, such as lead, cadmium and nickel (Kawamura et al., 2006; BfR, 2010, 2012b), plasticizers (Johnson et al., 2011; Abe et al., 2012) and fragrances (BfR, 2010). The use of 55 allergenic fragrances and ingredients is banned by the EU Toy Directive (EC, 2009c), and 11 further fragrances must be declared due to their allergenic potential.

Flammability standards in some countries require the use of flame retardants in children's nightwear and in the polyurethane products that come into contact with children (e.g. car seats, changing table

pads, sleep positioners, portable mattresses). Following the phaseout of PBDEs in 2004 in the USA and Europe, alternative flame retardants were introduced (Stapleton et al., 2011). In a study investigating the content of flame retardants in different baby products containing polyurethane foam, the most commonly found flame retardant was tris(1,3-dichloroisopropyl) phosphate. As infants have a longer dermal (and hand-to-mouth) contact with baby products compared with older children or adults (e.g. with furniture), it was estimated that exposure to tris(1,3-dichloroisopropyl) phosphate may be higher than the acceptable daily intake derived by the Consumer Product Safety Commission in the USA.

Finger paints and face paints are paste- and/or jelly-like coloured substances specially designed for children to use with their hands and fingers and on their faces and bodies. They contain complex formulations, including colouring agents, fillers, binders, humectants, preservatives, surfactants and embittering agents. Several potentially toxic substances, especially metals, have been identified in some paints (Rastogi, 1992; Corazza et al., 2009).

5. ANALYTICAL APPROACHES TO ESTIMATE DERMAL EXPOSURE

The purpose of this chapter is to present an overview of current analytical approaches to estimate dermal exposure. After the general principles are explained, considerations for selecting suitable approaches are summarized at the end of the chapter. This chapter does not highlight which methods are preferred by various regulations.

Basically, the exposure scenario determines how the dermal exposure has to be or can be estimated. The exposure scenario includes the physical state of the substance or product, the exposure duration, the exposure frequency and the skin area exposed (see section 3.2).

A substance or product can act either locally or systemically and either acutely or chronically. The corresponding hazard or effect values are described using different measures (e.g. percentage or milligrams per kilogram of body weight). Therefore, the exposure value needed (e.g. local peak exposure or daily exposure per local body site or whole body) depends on the specific toxicological or medical question relevant to the situation to be assessed.

Substance concentrations are mainly used for comparisons with reference values for local effects such as irritation, but also for sensitization. The total amount of the substance absorbed per day is used for risk assessment of systemic effects.

The physicochemical properties of the substance or product influence the choice of a suitable analytical method. Volatility, adsorption (adherence to the skin surface) and absorption (penetration into deeper skin layers) behaviours or stability, and the physical state of the substance or product influence the study design as well as the specific measure needed for dermal exposure (e.g. overall amount, peak exposure, maximum concentration). As a result, and also because of the lack of harmonized or precise guidance, a huge variety of sampling approaches can be found in the literature.

The need for harmonization and the difficulties in reaching this goal are reflected by the latest efforts in the development of the

corresponding norm of the International Organization for Standardization (ISO). This norm summarizes available approaches, provides typical applications and limitations and gives general advice for quality and strategy issues. Therefore, this chapter focuses on the principal features of and differences among the analytical approaches most frequently applied to estimate dermal exposure.

The process of dermal exposure can be assessed at different stages with respect to the time and site of the sample collection—that is, during or immediately after the exposure process (e.g. analysis of the deposited amount on the skin, such as the patch technique), at the beginning (e.g. analysis of the contaminated soil or transfer processes) and after the subsequent absorption process (e.g. analysis of body fluids).

Thus, three completely different analytical approaches can be distinguished for assessing dermal exposure. This chapter focuses on the direct measurement techniques used to estimate dermal exposure during or immediately after the exposure process (see section 5.1). In addition, however, the surrogate methods analysing the processes of migration and transfer as they influence dermal exposure are explained in section 5.2. Finally, biomonitoring of the absorbed dose is briefly described in section 5.3. The standard analytical methods used to determine analyte concentrations are not covered in this chapter.

5.1 Direct measurements of dermal exposure

In general, the process of any analytical determination can be divided into three main steps: sampling, sample preparation and the analysis itself. Sampling is the first and the most important step, and representative surface sampling—especially of the skin—is technically much more sophisticated than sampling of a volume (air or water). Parameters such as the sensitivity of the skin to mechanical or chemical damage and the shape of the human body have to be considered and hamper quantitative, reproducible and correct sampling.

Methods or procedures used for the subsequent steps, sample preparation and analysis, also depend on several parameters, such as the type of the measured substance or surrogate as well as the

magnitude of its expected concentration. Several aspects of good scientific practice must be considered and well documented: the purpose of the assessment, the sampling strategy and the sampling method, including analytical laboratory requirements regarding capabilities and desired limits of detection. However, the methods used for sample preparation and analysis are similar to the methods used in other fields of study and are usually available in the relevant analytical literature (often standard operating procedures). Therefore, sample preparation and analytical techniques are not further described in this document.

Nevertheless, the first step, the sampling of dermal exposure, is a challenging task due to the small amounts of sample material, the impact of skin sampling on the skin (surface) condition and the technical sophistication that is required for quantitative sampling.

Some methods that are based on different physical principles have been developed to determine dermal exposure directly on the skin surface. According to the latest guideline for measurement (analytical methodology) of dermal exposure, these methods are classified into three groups (ISO/TR 14294:2011):

- *interception (formerly surrogate skin) techniques*: provide a measure of the integrated exposure mass over a specific exposure duration;
- *removal techniques*: assess the integrated exposure loading over the exposure duration;
- *in situ techniques*: measure integrated exposure loading over the exposure duration; the pattern of exposure can be immediately recognized.

The principal differences between the different methods for sampling the skin are illustrated in Figure 2. The patch reflects the interception techniques (patches, clothing), which collect all mass deposited in a given time on a given area. It is important to consider that the adsorption and absorption capacities of interception material are often higher than the adsorption capacity of the skin. Thus, the process of desorption from the skin may be poorly reflected by these techniques. In addition, this approach is the only one that prevents the absorption of the substance by the skin.

The wipe represents the solvent-based removal techniques. These sampling methods are applied after a certain exposure duration and measure the remaining mass on a given area; the equilibrium between deposition and desorption or absorption is not artificially changed. The same applies to the tape strip method. This method is a special case, as it is usable for analysis of exposure as well as absorption, depending on the number of tape strips (number of layers taken from the skin) used for the analysis.

The in situ methods also measure, in principle, the remaining amount on the skin after a given exposure duration. Additionally, in situ techniques can be used to measure the time dependency of exposure, a fact that cannot be illustrated in Figure 2. However, the similarity of the fluorescent or other light-active substance to the target substance has to be proved. In general, the fluorescent or dye substances could also be used in combination with the interception or removal techniques. When applied alone, fluorescence techniques measure deposited (1 in Fig. 2) and absorbed (2 in Fig. 2) mass; as the absorbed (2) part depends largely on the specific fluorescence technique used, in situ methods are not depicted in Figure 2.

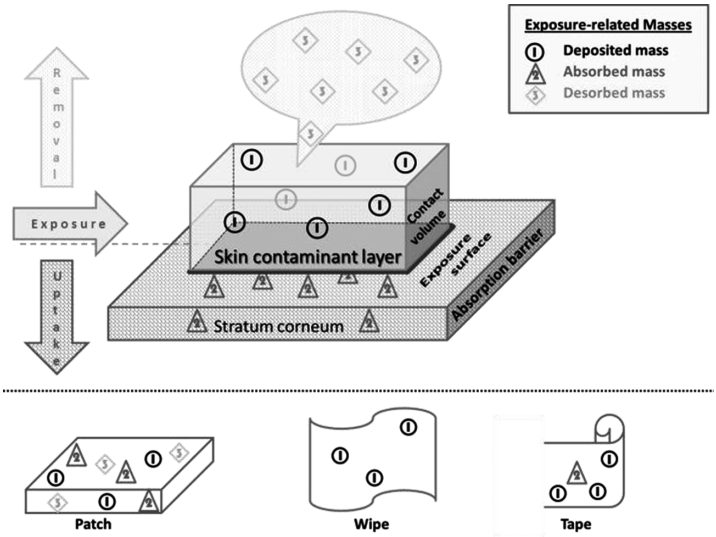

Fig. 2. Exposure sampling.

A major point to consider when assessing the suitability of the different methods is the recovery of the analysed compounds. In general, the recovery is influenced by:

- the effectiveness of the sampling;
- the retention of the compound on the sampling material;
- the effectiveness of extraction of the analyte from the sampling material (patches, gloves, rinsing water);
- the effectiveness of the analytical methodology.

The losses in sampling and/or sample preparation may be higher in field studies than in laboratory studies, as both steps depend on the physicochemical properties of the substance (e.g. volatility) and the environmental conditions (e.g. temperature, wind). In addition, time between exposure and sampling or measurement may have an impact on the recovery. If the sample preparation and analytical techniques used for different sampling procedures are identical, it can be assumed that the difference in overall recovery is caused by the difference in the efficiency of the sampling procedure. In general, it must be noted that there are many studies available for which the sampling efficiency has not been determined or reported. The deposition sites as well as the amounts that are deposited on the skin depend on parameters such as worker behaviour and wind properties. The United States Environmental Protection Agency's (USEPA) Series 875 Occupational and Residential Exposure Test Guidelines (USEPA, 1996) recommend field fortification samples to address potential losses in the field.

In the following sections, these direct sampling methods are briefly described, and their strengths and weaknesses are compared.

5.1.1 Interception techniques

The principle of these sampling methods is to replace the target skin by a surrogate layer, which can be easily removed for analysis (see Fig. 2). The surrogate layer is likewise the collection medium, which is then extracted with an appropriate solvent and transferred into a suitable form for analysis, depending on the analytical technique used.

Interception (formerly surrogate skin) techniques are the recommended techniques in the standard protocols published by WHO (1982), USEPA (1996) and OECD (1997), where patches and/or whole-body suits are used as collection media.

Independent of the material used for collecting the sample, the recovery of the analyte has to be documented and should be as high as possible (e.g. 95%) (OECD, 1997; Soutar et al., 2000). Ideally, the substance of concern is analysed. However, in some cases, surrogate substances (or tracers) may be used, such as zinc chloride (Popendorf & Selim, 1995) or a fluorescent tracer (Berger-Preiß et al., 2005). This approach is useful if the analytical detection of the target compound is not possible or is practically difficult or if the method has an insufficient detection limit.

In some cases, the physicochemical properties (e.g. dissolution, interacting or binding behaviour) of the target substance and the surrogate substance might be different. Therefore, the distribution patterns of the substance and the tracer should be similar, and their ratio has to be known and verified both in the applied formulation and on the target (skin or clothing). These tracers can easily be analysed by classical analytical techniques, or, in the case of fluorescent tracers, a complex "field" of new analytical approaches has been developed (see section 5.1.3).

With respect to interception techniques, two different approaches are applied: using and extracting complete suits (whole-body dosimetry; see section 5.1.1.1) and extracting single patches followed by extrapolation to the total body surface (patch sampling; see section 5.1.1.2). An overview of interception techniques is given by Soutar et al. (2000).

5.1.1.1 (Disposable) overalls and gauntlets or gloves

(a) (Disposable) overalls

Whole-body dosimetry using overalls answers the following questions:

- What is the total amount to which the human body was exposed?
- What is the pattern of deposition (e.g. to identify relevant or high exposure areas on the human body)?

Sample preparation depends on the initial purpose of the measurement. Either the complete overall or only specific exposed parts of the overall (e.g. the higher exposed areas) are used for extraction. Lightweight overalls or similar wear is typically used to estimate exposure of the body. Exposure of the head is measured by either a hood attached to the overalls or a separate hat, and exposure of the hands and feet can be measured using gloves (see section 5.1.1.1(b)) and socks, respectively (Soutar et al., 2000).

Disposable overalls and gauntlets represent a collecting medium that usually consists of only one material layer. Depending on the target substance and the sampling conditions, the material as well as the exposure duration have to be adjusted to avoid losses via breakthrough. After sampling, the surrogate layers are carefully removed by another person, avoiding cross-contamination between the different areas of the body surface.

According to the WHO (1982) protocol, the overalls have to be sectioned immediately following exposure into 10 parts: both legs, above and below knee; both arms, above and below elbow; and torso, front and back. A more detailed sample preparation was published by Hughes et al. (2006, 2008) (Fig. 3).

Commercially available suits consist of a variety of materials. The following materials were found in the literature: 100% cotton (Popendorf & Selim, 1995), a cotton and polyester mix (Fenske, 1993; OECD, 1997), Strentex or "Corovin" (Abbott et al., 1987), Tyvek® (van Rooij, 1994; Links et al., 2007) and Sontara® (Egea González et al., 1999a,b).

The material itself can influence the analytical determination. Potential undesired interactions between the solvent and the material or the solvent and the substance can be prevented by prewashing in the extraction solvent. For each material and substance, the recovery

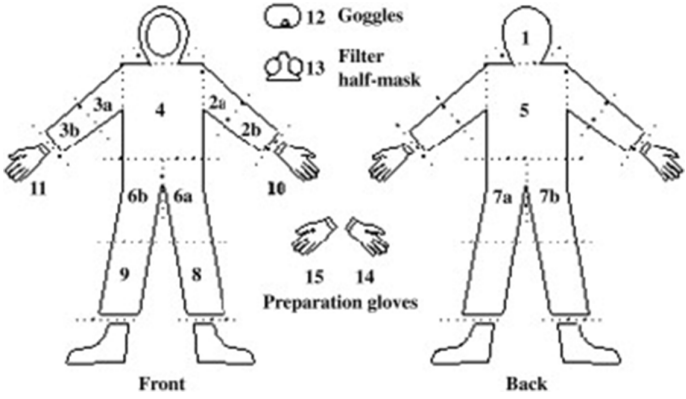

Fig. 3. Sectioning overalls (Hughes et al., 2008).

Reprinted from The Science of the Total Environment, Volume 391, E.A. Hughes, A.P. Flores, L.M. Ramos, A. Zalts, C.R. Glass & J.M. Montserrat, Potential dermal exposure to deltamethrin and risk assessment for manual sprayers: influence of crop type, Pages 34–40, Copyright 2008, with permission from Elsevier.

should be validated (Egea González et al., 1999a). Additionally, the retention of the substance could depend on the material that is exposed; however, no experimental data have been found in the literature regarding this point.

For the whole-body sampling method, also termed whole-body dosimetry, several variations are reported. Egea González et al. (1999a) used Sontara as the outer absorbent garment and Tyvek as the inner impermeable garment to retain the majority of the liquid contamination by the outer garment and to collect any liquid penetrating the Sontara by the inner garment.

For work clothing (Machera et al., 2003), inner and outer dosimeters can be distinguished. A coverall (applied as an outer shell) that acts as a surrogate for the clothing is an outer dosimeter. An inner dosimeter, which is considered as a surrogate for the skin itself, is usually represented by the underwear. In the normal clothing approach (Chester et al., 1990), the normal clothing and underwear are analysed as outer and inner dosimeters, respectively.

The normal clothing approach is especially useful during a dermal exposure investigation of children or toddlers. The analysis of three studies on children's exposure to pesticides showed the potential

information that can be obtained from such studies (e.g. factors such as activity level, surface loading, body suit section, age of the children) as well as the difficulties (e.g. high variability and standard deviations) associated with analysing the data (Egeghy et al., 2007). A limitation of these studies was that the retention as well as the analytical recovery from these different materials were not reported.

The whole-body sampling method is also frequently combined with fluorescent tracer as a surrogate for the substance of concern (e.g. Lesmes-Fabian et al., 2012).

(b) Gloves

Gloves are used as part of the whole-body dosimetry as well as a stand-alone method to assess the exposure of hands. Materials such as cotton, nylon and leather have been used (summarized by McArthur, 1992). However, studies comparing the sampling or analytical properties of these materials are not available.

The data gained by these techniques often reflect maximum exposure loading and can be considered to represent potential dermal exposure. For instance, Zweig et al. (1985) and Davis (1980) found that glove samplers worn for short periods of time (exposure duration ranged from 1–2.25 hours to 4 hours, respectively) gave consistently high estimates of pesticide exposure. In contrast, glove samplers were found to underestimate hand exposure in a case where moisture on the gloves from early-morning dew inhibited the ability of the gloves to collect pesticide (Zweig et al., 1985). Recently, bovine top-grain leather gloves were used to measure dermal exposure of hands to timber preservatives, and analytical data such as recovery, breakthrough and storage stability were validated (Schäferheinrich et al., 2012).

5.1.1.2 Exposure patches

Exposure patches usually consist of at least two layers: the sampling layer and an inert foil. The sampling layer consists of one or more soaking or collecting materials, and an aluminium foil is often used as the inert foil. To prevent contamination before use, a cover foil can protect the sampling layer. The patches are applied immediately before and removed immediately after the exposure.

With respect to the sampling layer, earlier guidelines recommend only α-cellulose (WHO, 1982; Reinert, Nielsen & Davis, 1986), whereas later ones suggest alternative materials, such as 100% cotton or polyester and cotton (OECD, 1997). This technique is also recommended in the Occupational and Residential Exposure Test Guidelines developed by the Office of Chemical Safety and Pollution Prevention (USEPA, 1996). An alternative approach is the HSE (1999) method, which recommends using several different patch materials (fabric, polymer, paper, charcoal cloth or composite materials) instead of one material for all substances.

The technical specification ISO/TR 14294:2011 lists several collecting materials and mentions specific procedures for some pesticides, beryllium and carbon nanotubes, but no advice is given as to which material should be used for which substance class. The suggested patch materials are intended to collect all substances that are deposited. However, a material capable of simulating both skin properties and the redistribution pattern of substances on the skin (e.g. simple falling off of dusts) was not found in the literature.

A new patch sampler was recently designed to sample the exposure of road pavers to PAHs. Samplers positioned on each worker's wrist or forearm and worn during a full work shift were used for both potential (outside of clothing) and actual (underneath the long-sleeve cotton shirt) exposure measurements. The five-layer sampler was designed to capture the full range of potential hot-mix asphalt emissions as well as other workplace exposures, such as diesel oil. The outer polypropylene layer served as a protective barrier intended to be analogous to human skin. The middle layers included polyurethane foam to provide high-capacity and reasonable collection efficiencies and a C-18 solid-phase extraction disc to capture most of the remaining organic compounds, including PAHs. The innermost layer consisted of activated carbon cloth to capture any volatiles that were not retained by the middle layers. An ethylene tetrafluoroethylene layer served to isolate the solid-phase extraction disc from the activated carbon cloth layer (Kriech et al., 2011; Olsen et al., 2011; Cavallari et al., 2012).

Common materials used for collecting a variety of different substances have been reviewed by Popendorf & Ness (1994) and

Table 11. Patch materials[a]

Material	Target	Reference
Filter paper and multilayered gauze	Substances with low vapour pressure via airborne mists or dusts	Popendorf & Ness (1994)
Polypropylene	Semivolatile substances	Popendorf & Ness (1994)
Polypropylene	PAHs	Jongeneelen et al. (1988); van Rooij et al. (1993a,b); van Rooij (1994)
Charcoal	Volatile compounds	Cohen & Popendorf (1989)
Layers of gauze	Cyclohexane-soluble matter	Kromhout et al. (1994)
Layers of gauze	3,3′-Dichlorobenzidine	London et al. (1989)
Layers of surgical gauze	Dry particles: dust	OECD (1997)
Surgical cotton gauze	Pesticides	Delhomme et al. (2011)
Gauze doped with glycerine	4,4′-Methylene bis(2-chloroaniline)	Clapp et al. (1985)
Gauze immersed in 10% ethylene glycol in acetone	Parathion and dimethoate	Carman et al. (1982); Serat et al. (1982)
α-Cellulose with lanolin in isohexane[b]	To simulate the slightly greasy surface of the skin	Fletcher et al. (1959)
Aluminium foil	Oily formulations, synthetic pyrethroid spray	Prinsen & van Sittert (1980); WHO (1982)
Glass fibre filters impregnated with ethylene glycol	2,4-D amine salt	Grover et al. (1986)
Polyester felt impregnated with isocyanate derivatizing solution	1,6-Hexamethylene diisocyanate	Thomasen et al. (2011)
Five-layer sampler	PAHs	Kriech et al. (2011)
Teflon membranes	Pyrethroid	Armenta & Blanco (2012)
Filter paper	Imidacloprid	Aprea et al. (2009)
High absorbent papers	Water (as surrogate)	García-Santos et al. (2011)

2,4-D, 2,4-dichlorophenoxyacetic acid; PAHs, polycyclic aromatic hydrocarbons

[a] Adapted from Ness (1994). The original has been modified by the addition of more recent references.

[b] Resulted in higher variation due to two factors: lanolin interferes with chemical determination, and lanolin is absorbed by the skin (Fletcher et al., 1959).

Ness (1994); examples are summarized in Table 11. For enhancing the number of substances that can be analysed with a single patch and the sampling efficiency, a broad range of sampling materials, additives and their combinations was tested. Occasionally, additives are used to stabilize the substance or to increase the collecting properties of the material. However, this diversity makes standardization difficult.

The number of patches recommended differs between the various guidelines and within the available literature, ranging from 6 (HSE, 1999), 8 (WHO, 1982), 10 or 12 (USEPA, 1996) to possibly 13 (OECD, 1997). The HSE (1999) approach suggests the use of either a full set of patches (11) or a reduced set of patches (6). Overall, the higher the number of patches, the better the quality of the result; however, the practicability diminishes.

The positions of the patches are only roughly specified (e.g. front of left leg, above ankle). The positions should be representative of the different exposed regions of the body. The OECD (1997) protocol suggests adding further patches to additional sites if significant exposure is expected. Another approach is suggested by Soutar and co-workers (2000): "The selection of sites for patch placement should ultimately depend on the likely pattern of exposure during a particular activity". Additionally, the patches may be placed over the outer layer of the clothing to measure potential dermal exposure, and another set can be placed against the skin under the clothing to measure actual dermal exposure (Popendorf & Selim, 1995).

The overall exposure is then calculated by extrapolating the values determined for the representative body regions using appropriate scaling factors for these regions (Popendorf & Selim, 1995; Popendorf et al., 1995; Soutar et al., 2000). This approach assumes that contamination is uniformly distributed over the area represented by the patch. However, the patches represent only a small portion of the body surface area and therefore may not be fully representative of the exposure of the respective body region. Extrapolation from the residues on the relatively small surface area of the trapping device to entire body region areas is a potential source of error in the use of patches for sample collection. For example, it could lead to an

Table 12. Variability of exposure analytical methodology over anatomic regions during airblast mixing and application of a pesticide[a]

Anatomic region	*N*	Mean total area (cm^2)	% of area exposed			
			Mean	Median	Range	SD
Forearms	21	1298	21.8	17.2	2.9–49.8	15.7
Upper arms	14	1087	12.2	10.3	1.3–34.5	9.5
Torso	17	3755	4.3	2.6	0.2–23.7	5.8

N, number of samples; SD, standard deviation

[a] From Fenske (1990).

underestimation of exposure, should droplets miss the patch when spraying, or an overestimation, should a splash land on the patch. Fenske (1990) demonstrated that for certain tasks, the proportion of the surface areas of specific body regions receiving exposure is relatively small (4–22%) and highly variable (Table 12).

The calculation of body surface area is based on different figures in different protocols. For example, the surface areas provided in WHO (1982), OECD (1997) and USEPA (2011a) vary (Table 13). USEPA (2011a) is the completely revised edition of the Exposure Factors Handbook, which includes information on total body surface areas.

The sampling efficiency depends on the type of compound to be sampled (liquid, gas or solid/powder) and on the sampling material. For example, for charcoal, the recovery of volatile compounds is inversely related to their vapour pressure, the number of layers in the patch, air velocity, humidity and volume of liquid applied. The sampling efficiency for an exposure duration of 3–6 hours ranged from about 38% for hexane to 87% for decane using 25 µl of solvent on four-layer patches at 20 °C, 50% relative humidity and 0.15 $m \cdot s^{-1}$ air velocity (Cohen & Popendorf, 1989). However, it is questionable whether this represents a huge overestimation of the real dermal loading because of the special binding capacities of charcoal, which may be much higher than that of skin. In contrast, Serat et al. (1982) reported

Table 13. Areas assigned according to different guidelines

Guideline basis	WHO (1982), based on Berkow (1931)	Skin area (cm^2)	OECD (1997)	Skin area (cm^2)	USEPA (2011a): 95th percentile male	Skin area (cm^2)
Head (add 10% if not measured)	Head, neck	1 100	Head	1 300	Head	1 540
	If hat worn	825	Face	650	—	—
Torso	Upper chest (V of neck)	150	Front of neck	150	—	—
	Top of shoulders near neck	300	—	—	—	—
	Back just below neck	100	Back of neck	110	—	—
	—	—	Chest/stomach	3 550	Trunk including neck	11 000
	—	—	Back	3 550	—	—
Arms	—	—	(Upper) arms	2 910	(Upper) arms	2 200
	Forearms	1 200	Forearms	1 210	Forearms	1 970
Hands	Hands	800	Hands	820	Hands	1 310
Legs	Upper legs from knees up	3 500	Thigh	3 820	Thigh	5 230
	Legs from knees down	2 300	Lower legs	2 380	Lower legs	3 240
Feet	—	—	Feet	1 310	Feet	1 610
Sum of parts considered	—	10 275	—	19 900	—	15 560
Whole body	—	18 000	—	Not given	—	25 200

a substantial loss of pesticides from fabric patches within 4–6 hours after exposure.

If only an indication of magnitude is needed, an even simpler approach may be appropriate. García-Santos and co-workers (2011) tested the so-called "weight method" as a screening method to estimate dermal exposure to pesticides (aqueous solutions). High absorbent papers (5 × 5 cm, blotting paper) were used as patches, and the weight gain due to liquid absorption was used as a measure of dermal exposure. The airborne drift and deposition were estimated by the weight method. Compared with the fluorescent tracer uranine on the high absorbent papers, this method showed a recovery of 86%. The method is a rapid, low-cost screening tool to assess exposure caused by sprayers and is very useful in developing countries, where the lack of staff and analytical equipment as well as the costs of chemical analyses make it difficult, if not impossible, to monitor exposure to contaminants (García-Santos et al., 2011).

Depending on the guideline followed, parameters such as patch size, sampling material (layers and combinations), backing, holder and other means used to attach the patches, sampling locations (body part and above or beneath the clothing), sampling period and preparation for analysis have to be documented (WHO, 1982; USEPA, 1996; OECD, 1997). The need for better documentation is reflected in the latest international guideline (ISO/TR 14294:2011). Here, for example, a detailed description of the sampling procedure is also required.

5.1.2 Removal techniques

In principle, the removal techniques collect the fraction of a compound that remains on the skin after a particular exposure. This means that the mass that has evaporated, fallen off or been absorbed during the exposure process is not sampled.

In order to remove a substance from the skin, adsorption forces have to be broken through external (e.g. mechanical, aerodynamic or hydrodynamic) forces or wet chemistry interaction. The desorption efficiency has to be determined, as well as the recovery in the sampling medium.

5.1.2.1 Wiping technique

The wiping technique is based on the removal of adhesive substances from the skin by the impact of mechanical, fluid dynamic and/or chemical forces under moist conditions.

Usually, small defined surfaces of the skin are wiped with moist or soaked sampling media, such as cotton cloths, filter paper, sponges, surgical swabs or cotton wool swabs. Flexible and non-flexible templates of different shapes are used in order to limit the surface areas to be wiped. Deionized water, pure alcohols or mixtures of them are most frequently used as wiping solvents due to their low skin irritating impact.

Wipe sampling efficiencies from several procedures and for several compounds are summarized in Table 14.

Campbell et al. (2000) used pigskin to study the dependence of the recovery on the solvent used for wiping and on the water solubility of the analysed substance. Four different solvents were compared: 1-propanol, polyethylene glycol (average molecular weight 400); 10% Ivory® (soap) and D-TAM® (a commercial decontamination product containing propylene glycol and surfactant). The recoveries were between 36% and 69%, and no significant pattern was recognized (Table 15). In all studies, sampling was performed 90–240 minutes after application. During this time, a considerable fraction of the substances may already have been absorbed and thus would not have been accessible by wiping of the skin surface.

Overall, it seems to be advisable to use a solvent that is appropriate for the chemical nature of the measured compound. For example, Boeniger et al. (2008) used corn oil to enhance the removal efficiencies of lipophilic PAH (i.e. pyrene) compounds.

Depending on the physicochemical properties of the substance, different adsorption was expected with different wiping materials. In one study (Boeniger, 2006), three brands of commercially available wipes were compared: two made of cellulose fibre and one made of a non-woven polyvinyl alcohol fibre (Table 14). Boeniger (2006) measured

Table 14. Wipe sampling efficiency studies[a]

Substance	Mass deposited (µg)	Exposure	Solvent	Wipe material	No. of wipes Body region wiped Duration Delay	Wiping efficiency (%) ± SD	Reference
Chlorpyrifos	2.5, 5	Hands pressed to aluminium foil with test substance	2-Propanol	SOF-Wick® cellulose sponge	2 Hands — Droplets 25 and 50 µl were allowed to dry	104 ± 11 (n = 12)	Geno et al. (1996)
Pyrethrin I	35, 70	Hands pressed to aluminium foil with test substance	2-Propanol	SOF-Wick® cellulose sponge	2 Hands — Droplets 25 and 50 µl were allowed to dry	92 ± 28 (n = 12)	Geno et al. (1996)
Pyrene in used gasoline engine oil (430 mg·kg^{-1})	17.17	Palms, distribution by 10 s rubbing	2 ml corn oil; 15 s rubbing	Whatman cellulose filter paper	3 Palms, rubbing 30 s per wipe 10 + 15 s	69 ± 20 (n = 3)	Boeniger et al. (2008)

Table 14 (continued)

Substance	Mass deposited (µg)	Exposure	Solvent	Wipe material	No. of wipes Body region wiped Duration Delay	Wiping efficiency (%) ± SD	Reference
Pyrene in used gasoline engine oil (430 mg·kg^{-1})	15.76	Palms, distribution by 10 s rubbing	2 ml corn oil; 15 s rubbing	Alpha polyester fabric wipes	3 Palms, rubbing 30 s per wipe 10 + 15 s	54 ± 30 (n = 3)	Boeniger et al. (2008)
Lead oxide powder	200, 2979	Rubbing of the palms of both hands for 30 s	Not known, probably alcohol	Three commercially available wipes, prewetted: Palintest, Wash 'n Dri, GhostWipes	4 Two palms 30 s per wipe 30 s	69.9–78.6 ± 2.7–12.5 (n = 2[b])	Boeniger (2006)
Nickel Chromium Cobalt	1.5, 5	Applied to 3 cm^2 of palms or arms	1% nitric acid	Cellulose wipes	3 (and three strokes per wipe) Palms and arms — Solutions left to dry; <15 min	Palms: 93–103 ± – (n = 4 × 2) Arms: 90–93 ± – (n = 4 × 2)[c]	Lidén et al. (2006)

n, number of samples; SD, standard deviation

[a] Unless otherwise stated, sampling was started immediately after application.

[b] Similar values for all three wipes and both deposition levels.

[c] Similar values for all three metals and both deposition levels.

Table 15. Wipe sampling with different wetting liquids: porcine model[a,b]

Substance	Water solubility[c]	Average recovery percentage ± SD			
		1-Propanol	PEG	10% Ivory®	D-TAM®
Methyl parathion	37.7 mg·l^{-1} (20 °C)	57 ± 17 (*n* = 9)	41 ± 18 (*n* = 9)	50 ± 19 (*n* = 9)	41 ± 15 (*n* = 9)
Glyphosate	1.2 × 10^4 mg·l^{-1} (25 °C)	44 ± 12 (*n* = 9)	41 ± 11 (*n* = 9)	49 ± 14 (*n* = 9)	36 ± 9 (*n* = 9)
Alachlor	240 mg·l^{-1} (25 °C)	57 ± 13 (*n* = 9)	55 ± 8 (*n* = 9)	52 ± 12 (*n* = 9)	51 ± 6 (*n* = 9)
Trifluralin	0.184 mg·l^{-1} (25 °C)	69 ± 10 (*n* = 9)	51 ± 15 (*n* = 9)	56 ± 13 (*n* = 9)	45 ± 13 (*n* = 9)

D-TAM® commercial decontamination product containing propylene glycol and surfactant; Ivory® soap; *n*, number of samples; PEG, polyethylene glycol (average molecular weight 400); SD, standard deviation

[a] From Campbell et al. (2000).

[b] Without pretreatment of the skin with solvent. Delay > 90 min. 6.25 cm^2 cotton gauze moistened with 0.5 ml solvent, 15 passes with the same wiping pattern.

[c] From SRC Physprop database (http://esc.syrres.com/fatepointer/search.asp).

a similar result for lead oxide in dust wiped from the palms (n = 4) for all three wipes, indicating a minor influence of the wiping material. Furthermore, the amount loaded did not influence the recovery. Regardless of the loading of 200 or 2979 µg lead oxide, total recoveries ranging from 69.9% to 78.6% were attained. Most of the lead oxide was recovered during the first wipe (first wipe: 52.2–62.5%; second wipe: 7.8–13.3%; third wipe: 3.2–7%; and fourth wipe: 1.7–3.7%).

Similarly, in a study on pyrene in used gasoline engine oil, no major differences for Whatman cellulose or Alpha polyester fabric wipes were found, with recoveries of 69% ± 20% and 54% ± 30%, respectively (Boeniger, 2006; Boeniger et al., 2008). High recovery was achieved for chromium, cobalt and nickel sampled on palms and lower arms by wiping with cellulose injection wipes wetted with 1% nitric acid. This method was found to be more effective on hands than tape stripping (Lidén et al., 2006).

Considering the wide variety of sampling materials available, the different solvent mixtures and the number of substances of concern, standardization is a challenging task. One specific limitation of standardized wipe sampling is the person-dependent variability

Table 16. Interindividual and intraindividual variability for wiping: wipe sample recoveries of chlorpyrifos from spiked aluminium foil[a]

Trial	Technician	Mean % recovery[b]	Coefficient of variation
1	1	96.0	2.0
2	1	94.5	3.1
3	1	96.2	3.5
4	2	96.3	3.6
5	3[c]	67.2	14.6
6	3	85.7	4.8

[a] From Fenske et al. (1991).

[b] Mean of three samples in each case.

[c] Recoveries of technician 3 were significantly lower than those of technician 1 (analysis of variance: Student-Neuman-Keuls test, $P < 0.05$).

of applied pressure for wiping. Interindividual variability as well as intraindividual variability during wipe sampling were investigated by Fenske et al. (1991), who found that the recovery attained depended on the technician (Table 16).

The wipe sampling strategy (wiping pattern) is also considered to be important in terms of the sampling efficiency. Some patterns (S/Z movement or just from left to right) are summarized by Ness (2000). However, a comparison of the sampling efficiencies related to these approaches and/or the associated uncertainties could not be found in the literature.

Direct reading indicators in the form of wipes are available for isocyanates. After contact, the colour of the wipe changes, qualitatively confirming the exposure to isocyanate. This easy, inexpensive and fast technique is listed by OSHA (1997). The SWYPE™ colorimetric indicators (CLI, Des Plaines, Illinois) are useful for assessing surface contamination (Liu et al., 2000) and can also be used in a semiquantitative manner by introducing scores for the differences in staining (Liu et al., 2007).

5.1.2.2 *Handwash technique*

The handwash technique is based on the removal of adhesive substances from the skin by the impact of mechanical, fluid dynamic and/or chemical forces under wet conditions. The procedure ranges

from simple handwash movements to a detailed six-step technique (EN 1499:2013). Principally, washing and rinsing are distinguished (with or without mechanical impact), and the following fluids are used: deionized, distilled or tap water or organic solvent with a weak skin irritating impact, such as pure alcohols or dilutions of them.

Several processes are involved when dermal exposure loading is measured by handwashing: the elution efficiency (how much can be desorbed with the eluent from the contamination source), the transfer efficiency (how much is transferred from the contamination source to the hand), the removal efficiency (how much can be desorbed from the hand) and the extraction efficiency (the recovery in the handwash solution) (see Fig. 4; Fenske & Lu, 1994; and Fig. 5; Fenske et al., 1998).

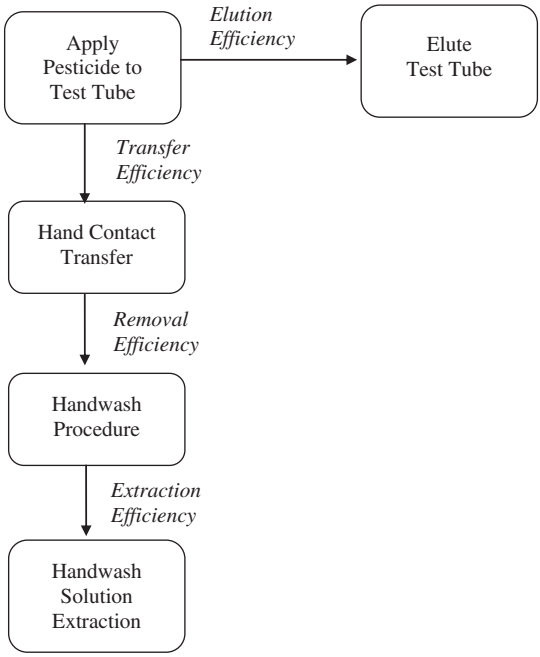

Fig. 4. Standard procedure for handwash removal efficiency studies (Fenske & Lu, 1994).

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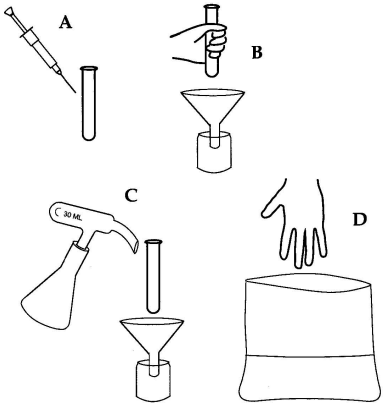

Fig. 5. Schematic diagram of the study design investigating handwash removal efficiency. **A)** With a micropipettor, the pesticide captan in acetone solution is applied to the outside of a test tube and allowed to dry in a laboratory hood. **B)** Captan is transferred to the hand of the study participant; a funnel and sample jar capture any pesticide that falls off the tube. **C)** Pesticide remaining on the tube is removed by elution, i.e. two rinses of the test tube using 30 ml toluene from a volumetric dispenser for each rinse, plus two rinses of the funnel, each using 10 ml toluene. **D)** Hand is washed twice in 250 ml of 10% isopropanol/distilled water with vigorous shaking for 30 seconds in a polyethylene bag. Captan is then extracted from the handwash solution with toluene and a saturated sodium chloride/distilled water solution. Handwash removal efficiency is then calculated (Fenske et al., 1998).

This protocol has been used for assessing the efficiency of handwashing, and the authors showed the overall difficulties in introducing a standard handwash method for the determination of dermal exposure. Besides that protocol, it is also possible to determine the transfer efficiency from an external matrix to the skin by measuring the amount remaining on the matrix after hand contact.

The sampling efficiency of the handwash technique has been found to depend on the washing solution, duration of exposure, prewashing of the hands, skin loading levels and number of washings (Fenske & Lu, 1994; Fenske et al., 1998).

Table 17 shows some of the parameters expected to influence the handwash sampling efficiency: precleaning, mass, delay after exposure, wetting liquid and number of wipes per site. Prewashing with ethanol can improve removal efficiency (e.g. for chlorpyrifos: with ethanol, 54%, versus without ethanol, 27%), and, as expected, the efficiency can decrease with the time passed after exposure (e.g. for chlorpyrifos, with ethanol: 54% at t = 0 hour versus 34% at t = 1 hour) (Fenske & Lu, 1994).

From the values summarized in Table 17, no final conclusion can be drawn regarding the potential influence of the applied mass on the handwash removal efficiency. Based on these figures, the wetting liquid has only a minor influence. A comparison of the figures obtained with soaps and alcohol indicates that soaps can be more effective than alcohol. However, a removal efficiency of higher than 90% is seldom achieved.

5.1.2.3 *Immersion technique*

The immersion technique is a special removal technique that is like handwashing but without the application of mechanical forces or like rinsing but without the use of hydrodynamic forces.

This rapid and simple sampling procedure was developed by Staton et al. (2006) for the determination of nickel on the skin. In this study, nickel deposited on the skin of workers handling nickel-releasing coins was determined. In the immersion procedure, the thumbs and index fingers are directly immersed in ultrapure water contained in graduated sample tubes, and the nickel concentration in the solution is analysed using inductively coupled plasma–optical emission spectrometry.

Changing the immersion duration from 2 to 5 minutes showed no difference in the extraction efficiency; thus, an optimal value was reached after 2 minutes. The results indicate that this method is usable at least for substances for which low detection limits are available, such as nickel and other metals.

The immersion technique was compared with wipe sampling using wipes soaked with acid. It was found that the average measured

Table 17. Handwash sampling efficiency studies[a]

Substance, reference	Solubility (in water, if no solvent is stated)	Solvent	No. of washes (no. of hands)	Delay of washing (h)	Amount on hand (µg)	Efficiency (mean ± CV) (%)	Prewashing
Captan Fenske et al. (1998)	5.1 mg·l^{-1} (25 °C)	10% isopropanol/ water, 1 hand, 250 ml, PE bag	1 (12)	0	4 370	78	Yes: soap/water
		Mass balance approach from transfer of a contaminated tube	2 (12)	0	4 370	91 ± 22	Yes: soap/water
			1 (6)	0	5 250	67 ± 22	Yes: soap/water
			2 (3)	0	5 250	78 ± 14	Yes: soap/water
			1 (12)	1	5 620	60	Yes: soap/water
			2 (6)	1	5 620	68 ± 5	Yes: soap/water
Captan Brouwer et al. (2000a)	—	2-Propanol rinsing, 1 hand, 250 ml, PE bag; direct repeated spiking of 0.5 ml on the hands	4 4	—	1 500 15 000	94 ± 11 63 ± 13	—
Carbendazim Brouwer et al. (2000a)	29 mg·l^{-1} (24 °C)	2-Propanol rinsing, 1 hand, 250 ml, PE bag; direct repeated spiking of 0.5 ml on the hands	3 3	—	500 5 000	94 ± 8 59 ± 13	—

Table 17 (continued)

Substance, reference	Solubility (in water, if no solvent is stated)	Solvent	No. of washes (no. of hands)	Delay of washing (h)	Amount on hand (µg)	Efficiency (mean ± CV) (%)	Prewashing
Chlorothalonil Brouwer et al. (2000a)	0.6 mg·l^{-1} (25 °C)	—	4	—	4 400	74 ± 11	—
Chlorpyrifos Fenske & Lu (1994)	1.12 mg·l^{-1} (24 °C)	Ethanol rinsing, 1 hand, 250 ml, PE bag	2 (10)	0	1 120	54	Yes: ethanol
			2 (12)	0	1 140	27 ± 5	No
			2 (12)	1	1 576	34	Yes: ethanol
			2 (12)	1	1 370	31 ± 6	No
		10% 2-propanol rinsing, 1 hand, 250 ml, PE bag	2 (12)	0	1 610	43 ± 24	No
			2 (12)	1	1 520	23 ± 9	No
			1 (10)	0	132.25	21 ± 7	No
			1 (12)	0	21.9	23 ± 7	No
			1 (12)	0	2.3	38.5 ± 5	
Mancozeb Brouwer et al. (1992)	6.2 mg·l^{-1} (25 °C)	2 hands shaken 30 s in PE bags with 500 ml 0.1 mol·l^{-1} EDTA solution	2 (10)	0.25	0.5 ml 1% TRIDEX® (45 g/l) = 225	81 ± 10	—
Mancozeb Brouwer et al. (2000a)	—	2-Propanol rinsing, 2 hands, 500 ml, PE bag	3 (4)	—	2 275	66 ± 5	—

Table 17 (continued)

Substance, reference	Solubility (in water, if no solvent is stated)	Solvent	No. of washes (no. of hands)	Delay of washing (h)	Amount on hand (µg)	Efficiency (mean ± CV) (%)	Prewashing
Mancozeb Marquart et al. (2002)	—	Mimic normal hygienic washing with soap and cold tap water; 2 hands	4 × 12 persons	0.5	5, 15 and 30 mg	86 ± 5	No
Methiocarb Brouwer et al. (2000a)	27 mg·l^{-1} (20 °C); 1.3 g·l^{-1} (20 °C) in *n*-hexane; 33 g·l^{-1} (20 °C) in toluene; >200 g·l^{-1} (20 °C) in dichloromethane; 53 g·l^{-1} (20 °C) in 2-propanol	With soap and cold tap water, 2 hands; direct repeated spiking of 0.5 ml on the hands	3 (4)	—	500 1 800 7 000	77 ± 3 84 ± 3 84 ± 6	—
Methomyl Brouwer et al. (2000a)	5.8 × 10^4 mg·l^{-1} (25 °C); soluble in methanol, acetone, ethanol and 2-propanol	With soap and cold tap water, 2 hands; direct repeated spiking of 0.5 ml on the hands	3 (4)	—	300 1 490	71 ± 3 70 ± 4	—
Prochloraz Brouwer et al. (2000a)	34 mg·l^{-1} (25 °C); ~16 g·l^{-1} in kerosene; ~2500 g·l^{-1} in chloroform, xylene, diethyl ether and toluene; ~3500 g·l^{-1} in acetone	2-Propanol rinsing, 1 hand, 250 ml, PE bag; direct repeated spiking of 0.5 ml on the hands	3 (4)	—	500 5 000	95 ± 14 96 ± 6	—

Table 17 (continued)

Substance, reference	Solubility (in water, if no solvent is stated)	Solvent	No. of washes (no. of hands)	Delay of washing (h)	Amount on hand (µg)	Efficiency (mean ± CV) (%)	Prewashing
Propoxur Brouwer et al. (2000a,b)	1860 mg·l^{-1} (20 °C); soluble in acetone and methanol	With soap and cold tap water, 2 hands; direct repeated spiking of 0.5 ml on the hands	3 (4)	—	175 575 1 400	66 ± 8 71 ± 13 72 ± 10	—
Propoxur Marquart et al. (2002)	—	With soap and cold tap water; mimic normal hygienic washing	4 × 12 persons	0.5	2.5, 5 and 7.5 mg	46 ± 3	No
Vinclozolin Brouwer et al. (2000a,b)	2.6 mg·l^{-1} (20 °C); hardly soluble; soluble in acetone and chloroform	With soap and cold tap water, 2 hands; direct repeated spiking of 0.5 ml on the hands	3 (3)	—	59.2, 227, 384	81 ± 5	—

CV, coefficient of variation; EDTA, ethylenediaminetetraacetic acid; PE, polyethylene

[a] Adapted from Brouwer et al. (2000c).

[b] From SRC Physprop database (http://esc.syrres.com/fatepointer/search.asp).

amounts were almost the same, although standard deviations with both techniques were high (Staton et al., 2006). The authors concluded that this innovative method shows several advantages over alternatives such as wiping and tape stripping in terms of extraction efficiency, speed and ease of operation in the field. However, the applicability of this technique for the analysis of nickel compounds and other substances needs to be evaluated more thoroughly.

5.1.2.4 Tape stripping technique

The tape stripping technique is based on the gradual removal of the stratum corneum, the most exterior skin layer, including the substance deposited in this layer. In this way, the fraction of the compound that cannot be washed off because it is adhering tightly to the upper skin layer may be removed and analysed (as illustrated in Fig. 6). The glue on the tape strips—organic substances with high molecular mass—is applied under pressure and forms a tight mechanical bond with the stratum corneum. This layer of skin is subsequently removed by taking off the strip (Fig. 7). The tape stripping method is used for substances that remain on the skin long enough for sampling, such as viscous substances (adhesives) and particles.

As tape stripping reaches deeper skin areas, the amount of substance removed may also be regarded as the amount absorbed.

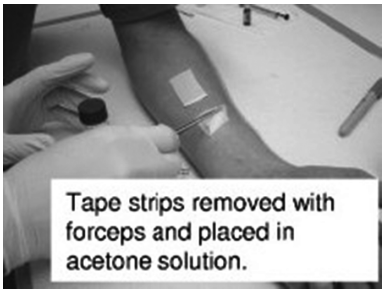

Fig. 6. Removal of tape strips (Kim et al., 2008).

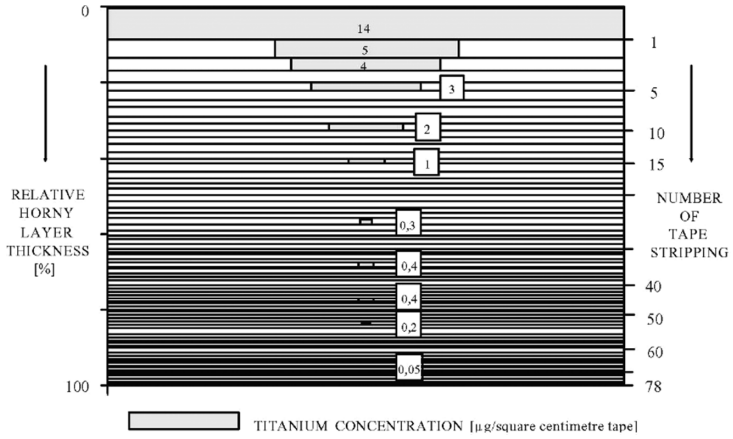

Fig. 7. Horny layer removed by tape strips: penetration of nanoparticle-sized coated titanium dioxide into the horny layer 1 hour after long-term sunscreen application (Lademann et al., 1999).

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Therefore, this technique is also included in the EHC on dermal absorption (IPCS, 2006). For exposure investigations, only the upper layers of the skin are tape stripped. However, a clear definition of what is considered "upper layers" could not be found in the literature (see Fig. 7).

The amount of skin removed is usually determined by weighing. Alternative methods measure the natural light absorption of the proteins bound on the tape (but light scattering of the stratum corneum overshadows the absorption; Marttin et al., 1996) or the intensity of a coloured protein adduct (a modified Lowry assay, the Bio-Rad DC protein microassay; Dreher et al., 1998). This latter method led to false-positive blank results for Cover-Roll™ tape, which contains woven polyester backing and polyacrylate adhesive (Chao & Nylander-French, 2004). Therefore, Chao & Nylander-French (2004) introduced another approach for normalization: they measured the keratin protein via a modified Bradford assay (AMRESCO, Solon, Ohio). In this study, the authors observed a lognormally distributed binding of naphthalene to keratin. The 12 volunteers were of different ages, races, sexes and skin types. Even this group is much too small to allow conclusions to be drawn; the results indicated no difference between

sexes and only minor differences at some time points for the various ages, races and skin types (Chao & Nylander-French, 2004).

As the depth and time course of skin absorption depend largely on the nature of the substance, the number of tape strips for particular analytical methodologies should be adjusted in preliminary studies, as shown by Nylander-French (2000).

Hostýnek et al. (2001) investigated the adsorption depth profile of soluble nickel salts applied as solutions. Up to approximately the 20th strip, the number of tape strips correlated strongly with the cumulative mass of stratum corneum removed (r^2 = 0.95–0.99). For nickel chloride solution, the gradients of the depth profiles increased with exposure time. The calculated total recoveries (Table 18) were virtually quantitative for most experimental parameters (time, dose, site and counterion). The incomplete mass balance for nickel nitrate only at the highest concentration indicates that beyond the adsorption

Table 18. Recoveries via wiping and tape stripping for nickel salts[a,b]

Nickel salt	Load (µg·cm^{-2} / site)	Time (h)	Nickel on skin surface (% dose)	Total recovery (% dose)
			Wiping only	Tape stripping
Chloride	19.8 / arm	0.5	89 ± 10.4 (n = 5)	—
	19.8 / arm	3	84 ± 7.1 (n = 2)	—
	19.8 / arm	12	75 ± 6.7 (n = 2)	—
	19.8 / arm	24	58 ± 6.1 (n = 3)	99.7 ± 3.0 (n = 3)
	1.8 / arm	24	94 ± 7 (n = 2)	—
	314 / arm	0.5	54 ± 7.1 (n = 5)	—
	314 / back	24	51 ± 6.3 (n = 3)	103.9 ± 4.8 (n = 2)
Nitrate	38.5 / back	24	42 ± 6.9 (n = 2)	97.3 ± 2.8 (n = 2)
	357 / back	24	30.5 ± 5.5 (n = 2)	87.5 ± 11.8 (n = 2)
	357 / arm	24	27.9 ± 2.6 (n = 2)	72.0 ± 3.0 (n = 2)
Sulfate	37.1 / arm	0.5	89 ± 9.9 (n = 3)	98.6 ± 3.6 (n = 3)
	37.1 / back	24	52.7 ± 8.1 (n = 2)	88.6 ± 7.0 (n = 2)
Acetate	56.1 / arm	0.5	90.1 ± 7.3 (n = 2)	97 ± 4.3 (n = 2)

[a] From Hostýnek et al. (2001).

[b] Analysis for residual nickel on the skin surface, collected by decontamination through swabbing with water-moistened cotton prior to stripping, and nickel recovery from analysis of 20 subsequent tape strips, collected without prior surface decontamination.

process, absorption to deeper regions of the skin has already occurred. In addition, this result shows the difficulties in defining the border between adsorption and absorption. Thus, this method is suitable for exposure estimations of very slowly absorbing substances or for absorption measurements of more rapidly absorbing substances.

As all described processes are related to time, the exposure estimate depends on the sampling time, as the mass deposited on the skin is removed by other processes, such as absorption or evaporation. Several important time lines that have to be considered in analytical methodology include the duration of exposure (t_{exp}), the time needed to completely remove the stratum corneum by tape stripping (t_{TS}) and the lag time for chemical penetration through the stratum corneum (t_{lag}). To describe the optimal sampling conditions, Reddy et al. (2002) derived several equations that can also be taken into account for measures of dermal exposure. Thus, looking at the stratum corneum concentration profile, two thermodynamic states can be distinguished:

1) non-steady-state conditions: $0.06 \leq t_{exp}/t_{lag} \leq 0.6$
2) steady-state conditions: $t_{exp} > 1.7\ t_{lag}$.

Additionally, the time needed for sample preparation has an effect on the experimental results. The concentration profile remains unaffected by the lag time for chemical penetration through the stratum corneum when duration of exposure is higher than t_{lag}. If $t_{TS} < 0.2\ t_{lag}$ for $t_{exp} > 0.3\ t_{lag}$, the diffusion during the tape stripping procedure should not affect the tape strip concentrations.

Parameters that are expected to influence tape stripping efficiency are listed in Table 19. The tape itself (i.e. the material properties, and especially the adhesive glue) has a great influence on the capacity of the tape (Surakka et al., 1999). As shown in Table 20, the removal efficiency for the first tape stripping varied from 29% to 102% of the deposited compound, depending on the tape used. This is quite high variability, considering that glass is a smooth surface.

Practicability is also important. Despite 100% efficiency, difficulties during performing the test can be the cause for non-use ("Although Mex®1 had the highest removal efficiency, it was rejected due to difficulties in sampling and handling"; Surakka et al., 1999).

Table 19. Sampling efficiencies of tape stripping methods

Compound	No. of persons, no. of sites, no. of strips per sample site, type of tape[a]	Exposure duration TS residence	Varied parameter	Sampling efficiency (± CV or range)	Remarks	Reference
TPGDA (t.g.), 5 µl	n.g n.g. 3 strips DSquame®/ Fixomull®	30 min Varied	*TS residence* 5 s 30 s 60 s	 62%/65% ~68%/76% 95%/96%	25 mm × 40 mm Guinea-pigs	Surakka et al. (1999)
TPGDA (t.g.), 2.5 µl	10 persons 8 sites 3 strips DSquame®/ Fixomull®	30 min Varied	*TS residence* 1 min 2 min	 46.4%/72.7% > 70%/> 70%	25 mm × 40 mm	Surakka et al. (1999)
TPGDA (t.g.), 1 µl, 2.5 µl	5 persons Varied sites 1 strip Fixomull®	30 min 2 min	*Sites* 2: 1 µl 4: 2.5 µl	 57 ± 70% 70–96%	25 mm × 40 mm	Surakka et al. (1999)
TPGDA (t.g.), 2 µl	10 persons 3 sites Varied strips Fixomull®	30 min n.g.	*Strips* 1 2	 85 ± 14.1% 92.8 ± 13.5%	25 mm × 40 mm	Surakka et al. (1999)

Table 19 (continued)

Compound	No. of persons, no. of sites, no. of strips per sample site, type of tape[a]	Exposure duration TS residence	Varied parameter	Sampling efficiency (± CV or range)	Remarks	Reference
UV resin (40 ± 50% TPGDA), 2 µl	10 persons 3 sites Varied strips Fixomull®	30 min n.g.	*Strips* 1 2	 62 ± 20.2% 77.6 ± 21.3%	25 mm × 40 mm	Surakka et al. (1999)
Multifunctional acrylates, purified TPGDA (84.3% monomer)	10 persons 5 sites Varied strips Fixomull®	30 min 2 min	*Strips* 1 (49) 2 (29)	 94 ± 16% 102 ± 11%	Precut to 2.5 cm × 4 cm	Nylander-French (2000)
UV resin (29.5% TPGDA monomer)	10 persons 5 sites Varied strips Fixomull®	30 min 2 min	*Strips* 1 (50) 2 (35)	 89 ± 15% 113 ± 14%	Precut to 2.5 cm × 4 cm	Nylander-French (2000)
Naphthalene in jet fuel (JP-8)	22 persons 1 site 3 strips Cover-Roll®	Varied 2 min	*Exposure* 5 min 10 min 15 min 20 min	 69.8 ± 10.6% 33.2 ± 9.8% 3.3 ± 3.3% 0.9 ± 0.8%	Precut to 2.5 cm × 4 cm Application chamber	Mattorano et al. (2004); Kim et al. (2008)

Table 19 (continued)

Compound	No. of persons, no. of sites, no. of strips per sample site, type of tape[a]	Exposure duration TS residence	Varied parameter	Sampling efficiency (± CV or range)	Remarks	Reference
Budesonide in ethanol (corticosteroid), 0.5, 2.07 µg	None 2 × 4 glass plates 5 strips Fixomull®	1 and 30 min 1–2 min	*Mass* 0.5 µg 2.07 µg	 78 ± 13.6% 84 ± 8.7%	Precut to 2.5 cm × 4 cm	Liljelind et al. (2007)
Budesonide in ethanol (corticosteroid), 0.5, 2.07 µg	6 persons 1 site 5 strips Fixomull®	Varied 1–2 min	*Exposure* 1 min (6) 30 min (6)	 40 ± 14% 36 ± 8%	0.5 µg: <LOD	Liljelind et al. (2007)
7-oxo-dehydroabietic acid (oxidized derivate of resin acid), 1, 15 µg	None 6 glass plates 3 strips Leukosilk®	n.g. Varied	*TS residence* 2 min: 1 µg 30 min: 1 µg 2 min: 15 µg 30 min: 15 µg	 94% (91–101%) 76% (67–83%) 98% (95–102%) 100% (93–102%)	Precut to 4 cm × 2.5 cm	Eriksson et al. (2008)
7-oxo-dehydroabietic acid (oxidized derivate of resin acid), 16.2 µg	10 persons 1 site 3 strips Leukosilk®	Varied 2–3 min	*Exposure* Immediately 30 min	 32% (18–45%) 24% (13–34%)	Precut to 4 cm × 2.5 cm	Eriksson et al. (2008)

Table 19 (continued)

Compound	No. of persons, no. of sites, no. of strips per sample site, type of tape[a]	Exposure duration TS residence	Varied parameter	Sampling efficiency (± CV or range)	Remarks	Reference
Dehydroabietic acid (resin acid), 1.6, 16 µg	None 6 glass plates 3 strips Leukosilk®	n.g. Varied	*TS residence* 2 min: 1.6 µg 30 min: 1.6 µg 2 min: 16 µg 30 min: 16 µg	 104% (94–118%) 98% (91–104%) 91% (85–100%) 92% (85–98%)	Precut to 4 cm × 2.5 cm	Eriksson et al. (2008)
Dehydroabietic acid (resin acid), 17.55 µg	10 persons 1 site 3 strips Leukosilk®	Varied 2–3 min	*Exposure* Immediately 30 min	 33% (18–51%) 25% (12–39%)	Precut to 4 cm × 2.5 cm	Eriksson et al. (2008)
Abietic acid (resin acid), 1.6, 16 µg	n.g. Glass plates 3 strips Leukosilk®	n.g. Varied	*TS residence* 2 min: 1.6 µg 30 min: 1.6 µg 2 min: 16 µg 30 min: 16 µg	 56% (47–64%) 40% (33-42%) 108% (97–119%) 78% (52–87%)	Precut to 4 cm × 2.5 cm	Eriksson et al. (2008)
Abietic acid (resin acid), 13.8 µg	10 persons 1 site 3 strips Leukosilk®	Varied 2–3 min	*Exposure* Immediately 30 min	 28% (13–40%) 20% (6–28%)	Precut to 4 cm × 2.5 cm	Eriksson et al. (2008)

Table 19 (continued)

Compound	No. of persons, no. of sites, no. of strips per sample site, type of tape[a]	Exposure duration TS residence	Varied parameter	Sampling efficiency (± CV or range)	Remarks	Reference
Pyrene	None 6 glass plates n.g. Fixomull®	Immediately n.g.	*Mass* 8 ng 400 ng	 89 ± 12% 86 ± 3%	Precut to 3 cm × 5 cm	Kammer et al. (2011)
	None 6 glass plates n.g. Fixomull®	30 min n.g.	*Mass* 8 ng 400 ng	 93 ± 12% 59 ± 9%	Precut to 3 cm × 5 cm	Kammer et al. (2011)
Benzo(*a*)pyrene	None 6 glass plates n.g. Fixomull®	Immediately n.g.	*Mass* 8 ng 400 ng	 92 ± 7% 83 ± 5%	Precut to 3 cm × 5 cm	Kammer et al. (2011)
	None 6 glass plates n.g. Fixomull®	30 min n.g.	*Mass* 8 ng 400 ng	 100 ± 10% 70 ± 12%	Precut to 3 cm × 5 cm	Kammer et al. (2011)
Pyrene	5 persons 1 site 5 strips Fixomull®	Varied 1–2 min	*Exposure* seconds 30 min	 70.2 ± 9.3% 63.3 ± 19.7%	Precut to 3 cm × 5 cm	Kammer et al. (2011)

Table 19 (continued)

Compound	No. of persons, no. of sites, no. of strips per sample site, type of tape[a]	Exposure duration TS residence	Varied parameter	Sampling efficiency (± CV or range)	Remarks	Reference
Benzo(*a*)pyrene	5 persons 1 site 5 strips Fixomull®	Varied 1–2 min	*Exposure* seconds 30 min	 59.6 ± 12.1% 54.4 ± 32.7%	Precut to 3 cm × 5 cm	Kammer et al. (2011)
Methylene bisphenyl isocyanate	None 6 Teflon® surfaces 2 strips Fixomull®	Immediately n.g.	*Mass* 15 ng 150 ng 750 ng	2 Strips (1/2) 34 (27/7) ± 69% 63 (50/13) ± 11% 78 (69/9) ± 11%	2.5 cm × 4 cm	Liljelind et al. (2010)

CV, coefficient of variation; LOD, limit of detection; n.g., not given; t.g., technical grade; TPGDA, tripropylene glycol diacrylate; TS, tape strip

[a] Cover-Roll® was investigated under the product name Fixomull® (Beiersdorf AB, Kungsbacka, Sweden) (Fent et al., 2006).

Table 20. Removal efficiencies of different tapes on glass[a,b]

Adhesive tape	Removal efficiency (%)			
	Strip 1	Strip 2	Strip 3	Total
Bioclusive®	71.3	14.3	ND	85.6
Blenderm®	67.8	19.5	0.5	87.8
D-Squame®	88.0	4.8	ND	92.8
Fixomull®	68.0	18.3	ND	86.3
Mefix®	101.8	ND	ND	101.8
Scanpor®	72.5	15.0	1.3	88.8
Sebutape®	66.8	15.8	ND	82.6
Tegaderm	77.5	13.0	0.8	91.3
Tesa 4287	44.8	20.5	8.3	73.6
Tissue adhesive	29.0	7.8	32	68.8

ND, not detected

[a] From Surakka et al. (1999).

[b] Three sequential strips from glass surface; 5 µg tripropylene glycol diacrylate (20 min exposure).

The exposure duration has a minor effect on the removal efficiency in the case of solids (Liljelind et al., 2007). The delay in analysis (i.e. the time between exposure and sampling) has a pronounced effect on the recovery in the case of substances with a significant vapour pressure or with a certain tendency for absorption (Mattorano et al., 2004). According to the study of Surakka et al. (1999), a sampling duration (i.e. the residence time of the tape on the skin) of 2 minutes seems to have become widely accepted.

The number of strips used in a particular study depends on study design and the substance (low vapour pressure, slow absorption), and the recovery can be improved with a higher number of strips.

The influence of the sampling site (see Fig. 8) was investigated with tripropylene glycol diacrylate (TPGDA), a commercially available UV resin (Nylander-French, 2000). Minor tendencies were found, but no general significant differences were identified between the sites tested on the palm and those tested on the arm (Nylander-French, 2000).

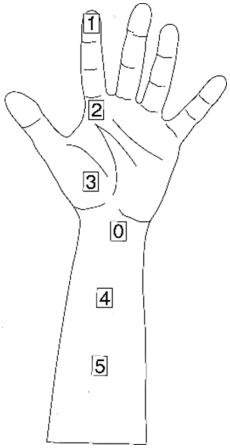

Fig. 8. Tape stripping sites on the volunteer's palms and the lower volar region of the arm. Numbers 1–5 correspond to the sites where 2.5 ml of either tripropylene glycol diacrylate (TPGDA) or UV resin was deposited prior to tape stripping; #1 fingertip, #2 upper palm, #3 lower palm, #4 lower arm, #5 upper arm. The tape strip from site #0 served as an unexposed control site (field blank) (Nylander-French, 2000).

Reprinted from L.A. Nylander-French, A tape-stripping method for measuring dermal exposure to multifunctional acrylates, Annals of Occupational Hygiene, 2000, volume 44, issue 8, pages 645–651, by permission of Oxford University Press.

The ethical acceptance of tape stripping differs worldwide. According to a recently established law in the USA, tape stripping has to be authorized by an ethics review conducted by the Human Studies Review Board (USEPA, 2013a). This requirement could reduce the use of tape stripping in the USA and perhaps some other countries.

5.1.2.5 *Suction method*

The suction method is simply sampling by the application of a vacuum. This method is limited to sampling materials with low adhesion forces, such as solid particles. A vacuum provided by a pump is used to draw air through a nozzle held close to a surface; the suction action generates a combination of lift and drag forces that remove the substance from the skin.

Byrne (2000) first reported the application of this method for skin sampling. Theoretically, this approach could also be applied for

clothing sampling. However, there was no evidence found in the literature that suction sampling has been used to assess contaminant levels on clothing surfaces (Byrne, 2000).

5.1.3 In situ techniques

In situ techniques use the spectroscopic properties of substances and measure absorption in the range between the infrared and UV parts of the electromagnetic spectrum. Either the substance itself or a tracer mixed with the substance can be analysed via spectroscopic methods. Three approaches are currently distinguished:

1) video imaging technique;
2) Fourier transform infrared spectroscopy with attenuated total reflectance (ATR-FTIR);
3) detection via light sensor.

Whereas the first technique is suitable for measurements on large surfaces, the second and third techniques are limited to smaller areas.

Tracers are substances that emit fluorescent light or absorb infrared light. Fluorescent tracers were first employed in occupational health about 20 years ago as a qualitative tool for a dermal exposure study of orchardists (Franklin et al., 1981). As tracers are surrogates for the substance of interest, their ratio to the substance of interest must be known and should be constant during the exposure process: in the formulation, during the transfer and on the skin or clothing. Additionally, the tracer must not change the physicochemical properties of the formulation.

Archibald et al. (1995) showed that combining a tracer with an oil-based concentrate led to a constant uniform distribution of the tracer in the spray solution and in the deposition ratios. In practice, however, it might be difficult to find a tracer with the same deposition and retention characteristics as the substance of interest (Cohen Hubal et al., 2005). Therefore, potential differences in the relative transfer of the tracer and the substance should be assessed in preliminary studies. A qualitative assessment of the potential and limitations of this method was presented by Cherrie et al. (2000). In

essence, this method is very helpful for identifying sources of contamination, investigating mechanisms of emissions, showing the pattern of contamination and linking the contamination to human behaviour. Therefore, it is very useful to show that dermal exposure occurs (e.g. in training courses), to identify the relevant pathways for dermal exposure and to illustrate the relevance of the careful handling of chemicals (e.g. pesticides).

5.1.3.1 *Video imaging technique*

The substances or tracers used for this technique absorb light in the range of visible or UV radiation (see Table 21). The video imaging systems usually consist of sensitive video cameras and computer software for the image analysis. The relevant surfaces are photographed before and after exposure. The feasibility of employing fluorescent tracer and video imaging analysis to quantify dermal exposure to pesticides has been demonstrated and evaluated by Fenske & Teschke (1995). If tracers are used, some preliminary tests are necessary in order to determine the relationship between the substance and the tracer. The images should be corrected for camera noise, non-uniform illumination and variation of illumination with time. Additionally, the mean grey values of the fluorescent spots and of the underlying skin have to be determined (contrast between the grey value of the tracer and the skin may be too low for the camera), and the fate of the tracer on the skin (i.e. possible interaction with keratin of skin cells) should be considered (Bierman et al., 1995, 1998).

The first video imaging technique for assessing dermal exposure was introduced in the late 1980s (instrumental design and tracer validation by Fenske et al., 1986a,b). The fluorescent interactive video exposure system was developed subsequently, in the 1990s, and this system is suitable for measuring whole-body exposure (Roff, 1994). In 1997, Fenske & Birnbaum presented the second-generation video imaging technique for assessing dermal exposure with higher resolution in both picture element array and grey scale, leading to improved exposure quantification.

The video cameras originally used to record the images produced analogue signals, which had to be converted to digital form

Table 21. Tracer properties

Tracer	Properties	Excitation/ extinction	LOQ/LOD	Solubility	Reference
Riboflavin (vitamin B_2)	Non-toxic K_{ow} = –1.46 (Nahum & Horvath, 1980) Absorption: 250–500 nm Strong absorption: 440–480 nm Peak fluorescence emission: 505–560 nm Sufficient emission: 600 nm Photodegradation under fluorescent light and incident sunlight: 10%·h^{-1}	Near 440 nm (blue region) / 600 nm (in the red/orange region)	0.1/0.02 mg·cm^{-2}	Water (150 mg·l^{-1}) and acetone	Ivancic et al. (2004)
Uvitex OB	Emission at 440 nm: Uvitex OB >>> riboflavin Emission at 600 nm: not detectable Heat resistant, chemically stable fluorescent whitener Absorption maximum: 375 nm Fluorescence maximum: 437 nm	Excitation at 380 nm	Not given	Soluble in organic solvents	Ivancic et al. (2004) Product information: Ciba (1999); Mayzo (2009)
Fluorescein	Emission at 600 nm: ~ twice that of riboflavin Not soluble in water Less safe than riboflavin Absorption maximum: 496 nm	496 nm / 520–530 nm	Not given	Soluble in alcohol, DMSO, ether and alkaline solution	Ivancic et al. (2004); Welsch (2006)

DMSO, dimethylsulfoxide; K_{ow}, octanol–water partition coefficient; LOD, limit of detection; LOQ, limit of quantification

(i.e. digitized into pixels). The intensity of the pixels is correlated to the deposited mass. However, it must be noted that the relationship between the pixels' intensity and mass deposited on the skin is not linear (unlike in dilute liquids). The fluorescent or other dye substances on a (skin) surface are (almost) dry dye layers and therefore do not follow the Lambert-Beer law (which applies to dilute liquids). Thus, these layers are high-density light-scattering materials (disperse media). The mass calibration on surfaces can be described by the Kubelka-Monk law, which is lognormal for low concentrations. To model the calibration curve, different software packages are available.

Depending on the experimental setting, linear-logarithmic calibrations have been used (Fenske et al., 1986a; Archibald et al., 1994, 1995; Bierman et al., 1998; Houghton et al., 1999), as well as linear polynomial and log-log polynomial fits of the order 3–5 (Roff, 1994, 1997).

Additional technical aspects have to be resolved by the technical equipment, the software or the study design:

- The linearity of response of the system has to be checked for the filters used for the camera (Fenske et al., 1986a) or for the light sources (Archibald et al., 1994).
- The lens of the camera exhibits a common spherical aberration, which produces an effect known as vignetting; that is, light is passed less efficiently at the edges of the lens than in the centre (Fenske et al., 1986a).
- The intensity of light is indirectly proportional to the square of the distance and also depends on the angle of light direction (Lambert's cosine law). Two solutions have been published: "anthropometric correction" software (Fenske et al., 1986a) and the dodecahedral lighting system (Roff, 1994).
- Anthropometric adjustment is necessary, as the surface of most of the body is non-planar (Fenske et al., 1986a).
- The smaller the angle between the surface and the camera, the smaller the area (Roff, 1994); the full size is seen at 90 degrees.

- The natural background signal of the skin varies with different body regions and between individuals (Roff, 1994).
- The fluorescence might fade with time (Roff, 1997).
- The tracer deposited upon absorbent materials such as woven protective clothing migrates into the bulk of the fabric, masking the fluorescence (Roff, 1997).
- The removability of the fluorescence determines the frequency of experiments, so water-soluble fluorescence can be easily washed off with soap and warm water after the experiments (Archibald et al., 1994; Ivancic et al., 2004).
- The excitation wavelength and photostability determine the type and power of the light source, respectively (see Table 21).
- The intensity and the shape of the absorption and emission spectra can affect accuracy.
- Pale skin has a similar reflectance in the red, green or blue region of the spectrum, whereas dark skin has much less reflectance in the green region, but nearly the same in the blue and red regions (Archibald et al., 1994; Ivancic et al., 2004).
- The light intensity of the light source has to reach its stable phase (Archibald et al., 1994).
- The adsorption and absorption behaviours of the tracer have to be considered.

A semiquantitative "visual scoring system" was introduced by Fenske (1988). The scoring system is a matrix, and the score (1–5) increases both with the exposed area (0–100%) and with the intensity of exposure (low, medium or high). The reliability of the visual scoring system to assess dermal exposure to pesticides was investigated under field conditions in Nicaragua (Fig. 9) by Aragón et al. (2004). They introduced two modifications of Fenske's (1988) system: weighting the area of the exposed body parts according to total body surface area and establishing criteria for reading of the fluorescence intensity. The body surface of 33 farmers, divided into 31 segments, was videotaped in the field after spraying with a pesticide solution containing a fluorescent tracer. Five students rated and evaluated the fluorescent images. The consistency of the results was high, and the overall intraclass correlation coefficient was satisfactory (0.75) but relatively low between the raters (0.54) with respect to the intensity.

Fig. 9. (a) Wind blowing spray cloud. (b) After application: Mist image on the left side of farmer's face (Aragón et al., 2006).

Reprinted from A. Aragón, L.E. Blanco, A. Funez, C. Ruepert, C. Lidén, G. Nise & C. Wesseling, Assessment of dermal pesticide exposure with fluorescent tracer: a modification of a visual scoring system for developing countries, Annals of Occupational Hygiene, 2006, volume 50, issue 1, pages 75–83, by permission of Oxford University Press.

5.1.3.2 *Fourier transform infrared spectroscopy with attenuated total reflectance (ATR-FTIR technique)*

Attenuated total reflectance (ATR) is a sampling technique used in conjunction with infrared spectroscopy that enables solid or liquid

samples to be examined directly. The total reflection is induced in an optical waveguide. The internal reflection element can be a prism, fibre or ATR crystal. Total reflection can cause an evanescent wave behind the reflecting boundary. If a substance partly absorbs the energy of the evanescent wave (infrared range), the total reflection attenuates. The amount of energy absorbed can be correlated with the amount of the substance being considered.

Fourier transform infrared (FTIR) spectroscopy is a special variation of infrared spectroscopy. The signals measured are converted by means of Fourier transformation, resulting in calculated infrared spectra. Further information regarding the principles of FTIR and ATR is available in several textbooks.

The ATR-FTIR technique is applicable for measuring non-volatile infrared-active compounds on the skin. The spectra can be obtained within a few seconds with minimal sample preparation. ATR-FTIR is applicable for simultaneously identifying and quantifying multiple compounds on the skin in vivo using multivariate analysis methods. The sampling area is limited by the size of the ATR crystal to surface areas up to 2 cm^2 (Doran et al., 2000). This technique has also been applied to measure captan exposure on gloves (Phalen & Que Hee, 2005, 2007). Some of the difficulties associated with this technique were reviewed by Carden et al. (2005):

- The (pesticide) spectral band may overlap with spectral features of the skin.
- Skin is occluded during the experiment, which prevents transpiration and leads to higher water content in the skin; this, in turn, gradually changes the spectrum (Potts et al., 1985).
- Interpersonal variability due to different pigmentation, hydration, age, etc. leads to different background levels.

5.1.3.3 *Light sensor technique*

The light sensor technique uses photodetectors to measure the fluorescence emitted by the skin or surface (excluding stray light) that is produced in response to irradiation by a light source. The luminoscope (portable luminescence detector) was introduced by

Vo-Dinh & Gammage (1981) for field monitoring of occupational skin contamination. This technique uses an optic fibre to transport the ultraviolet A (UV-A) light from the source to the surface and back to the detector (see Fig. 10).

This luminoscope technique was established to measure coal contamination on the skin. Coal contains several hazardous PAHs; thus, calibration experiments were performed on mouse skin. A linear range could be demonstrated for concentrations below 100 $ng \cdot cm^{-2}$ (Fig. 11), and the standard deviations reached for the luminoscope itself and the results on the mouse skin were below 5% and 30%, respectively.

5.1.4 Comparison of different sampling techniques

The processes that influence the extent of dermal exposure (deposition, adsorption, desorption, etc.) are differently covered by the methods available for dermal exposure estimation. The magnitudes of these differences depend on the exposure situation—the properties of the substance or product, the activity and the environmental conditions—and the influences of these parameters on the dermal exposure have not been well studied. For practical reasons, the different methods are frequently combined within one exposure study—for example:

- watch-like polypropylene patches on wrists and handwash/wipe method with sunflower oil to study exposure of road pavers to PAHs (Väänänen et al., 2005);
- filter paper patches on body and handwashing with 95% ethanol (Aprea et al., 2009);
- patches on whole body and hand wipe by swabs wetted with 2-propanol (Thomas et al., 2010);
- five-layer patches on wrists and forearms and handwash with sunflower oil (Cavallari et al., 2012).

One critical parameter of sampling methods is the recovery. It directly determines the limit of detection, and its accuracy affects the uncertainty. Therefore, to facilitate comparison of exposure estimates, data on the reliability of the sampling methods are needed (absolute or relative to each other). Furthermore, such comparative studies on the

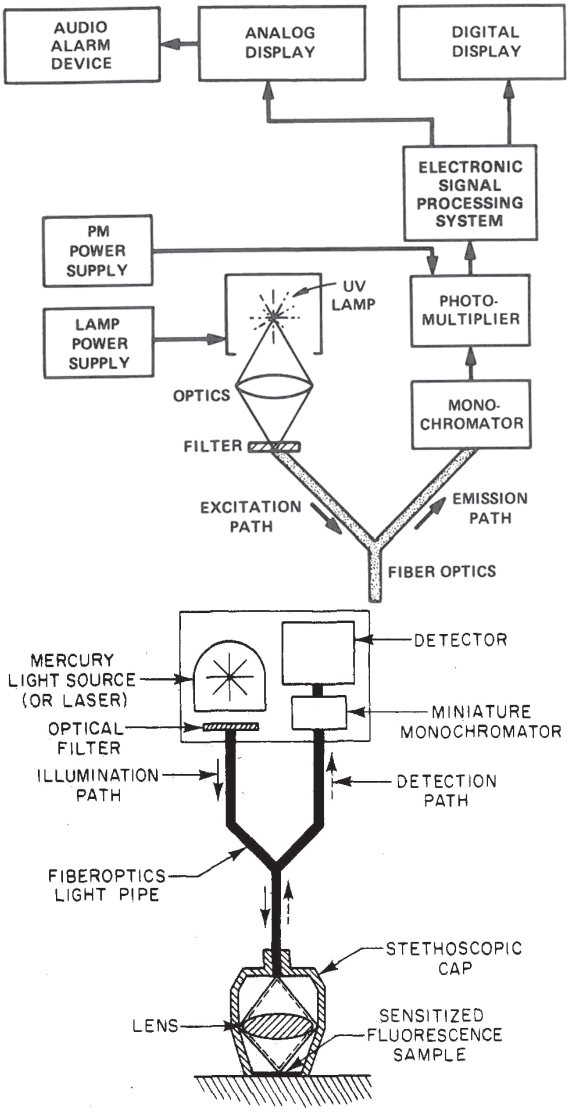

Fig. 10. Luminoscope block diagram (*top*) and schematic diagram (*bottom*): The fibre transmits UV excitation light to the skin and conducts the induced fluorescence to the single photon-counting detector (Vo-Dinh & White, 1986; Vo-Dinh, 1987).

(*top*) Reprinted from Evaluation of an improved fiberoptics luminescence skin monitor with background correction, T. Vo-Dinh, American Industrial Hygiene Association Journal, volume 48, pages 594–598, 1987, reprinted by permission of the publisher (Taylor & Francis Ltd, http://www.tandf.co.uk/journals). (*bottom*) Reprinted with permission from T. Vo-Dinh & D.A. White, Sensitized fluorescence spectrometry using solid organic substrate, Analytical Chemistry, volume 58, number 6, pages 1128–1133, Copyright 1986, American Chemical Society.

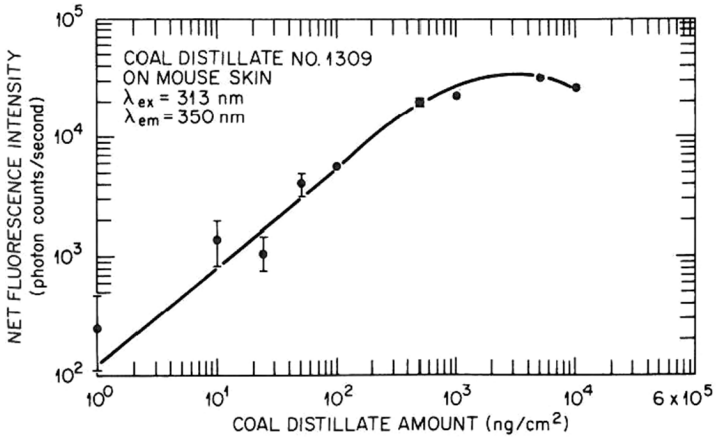

Fig. 11. Load–response curve for a coal distillate on mouse skin (Vo-Dinh, 1987).

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different sampling methods for different exposure scenarios are necessary to identify suitable methods for exposure scenarios that differ with respect to:

- physical appearance of the substance or product;
- absorption/retention/desorption behaviour;
- skin or clothing sampling;
- task-based or shift-based sampling;
- frequency of exposure;
- pathway of exposure;
- environmental conditions;
- quantitative or qualitative assessment;
- limit of detection/recovery;
- frequency and number of measurements;
- local or systemic exposure.

Unfortunately, few comparative studies investigating particle sampling that compare more than two techniques could be found in the scientific literature, which indicates that such studies are seldom performed.

Table 22. Removal efficiencies of particles from skin[a]

Particle size (µm)	Wiping efficiency (%)	Waxing efficiency (%)	Washing efficiency (%)	Vacuuming efficiency (%)
2.5	72.5 ± 8.8	75.8 ± 3.0	31.5 ± 6.3	21.4 ± 3.5
4.5	71.1 ± 8.1	77.0 ± 14.7	36.3 ± 4.2	24.3 ± 1.4
8	76.4 ± 5.3	68.0 ± 9.9	35.7 ± 4.1	22.2 ± 3.3

[a] From Fogh et al. (1999).

With the objective of assessing exposure to radioactive particles, Fogh et al. (1999) investigated the removal efficiencies of four different sampling techniques, depending on the aerosol particle size. The remarkably low removal efficiencies of the washing and vacuuming techniques found in this study (Table 22) led to the conclusion that these techniques are not suitable for particle sampling on the skin.

Lundgren et al. (2006) compared vacuum sampling with patches (adhesive tape on a cover glass), tape stripping and vacuuming. Following a cumulative mass loading of wheat flour of 300 µg·cm^{-2}, they achieved a removal efficiency of 96.4% with the first tape strip and 99.8% with the second tape strip. Comparing tape stripping (two strips) with vacuuming, a small underestimation (an average of 9% lower values) was found with the vacuuming sampler (Fig. 12). Estimates from tape stripping (two strips) and patch sampling differed slightly, with an overestimation (up to 21%) for the patch method. The overestimation with the patch method is explained by possible sticking of the particles to the glue, whereas particles deposited on skin might fall off as the subject moved during exposure. However, according to these results, all techniques are applicable for the sampling of dust particles on skin.

In another study (Gorman Ng et al., 2012a), three commonly used sampling methods (i.e. wipes, rinses and gloves) were compared in side-by-side experiments (left and right hands). Here, wipes and gloves were tested for sampling glycerol solutions, and wipes and rinses were tested for sampling powder (calcium acetate, Epsom salts and zinc oxide). Two methods were not performed, as rinsing with glycerol is impractical due to its high viscosity, and the background levels of

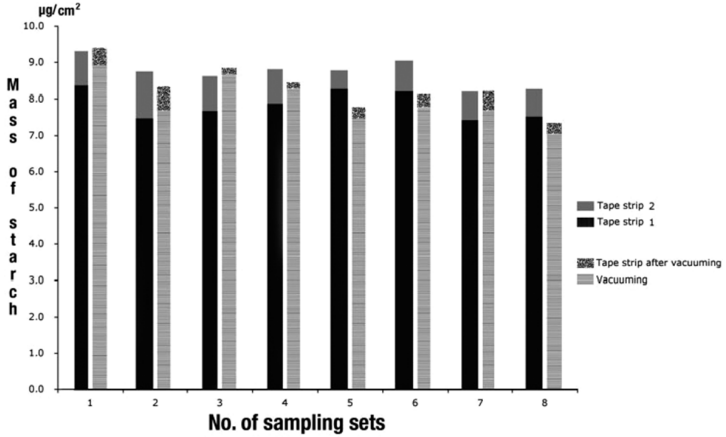


Fig. 12. Comparison of tape stripping and vacuuming (Lundgren et al., 2006).

Reprinted from L. Lundgren, L. Skare & C. Lidén, Measuring dust on skin with a small vacuuming sampler—A comparison with other sampling techniques, Annals of Occupational Hygiene, 2006, volume 50, issue 1, pages 95–103, by permission of Oxford University Press.

magnesium in cotton hamper glove sampling of magnesium powders (background levels often influence the selection of these materials). The measured sampling efficiencies of wipes and gloves for glycerol were similar, but the detection limit using gloves was 30 times higher than the detection limit using wipes (Table 23). For powder sampling, rinsing led to higher efficiencies and lower detection limits than wipes (Table 23). Overall, sampling efficiency was within a similar order of magnitude. However, this study demonstrates that the detection limit for the different methods also has a major influence on selection of the most suitable method.

Summing up, the results of the three studies mentioned above are quite different. According to Fogh et al. (1999), washing and waxing (~75%) are the most appropriate methods for particle sampling, and wiping or vacuuming should be avoided. According to Gorman Ng et al. (2012a), high sampling efficiencies for powders can also be reached by rinsing and wiping, depending on the type of powder. Lundgren et al. (2006) found high efficiencies with tape stripping (above 95%). All of the results indicate that the physicochemical properties of particles influence the sampling efficiency. Furthermore,

Table 23. Comparison of wipes, rinses and gloves[a]

	Detection limit (mg)	Sampling efficiency (%)
Gloves		
Glycerol	0.6	53[b] & 63[c]
Wipes		
Epsom salts (magnesium sulfate)	0.1	53
Zinc oxide	0.16	85
Calcium acetate	0.03	70
Glycerol	0.02	68[b] & 44[c]
Rinses		
Epsom salts (magnesium sulfate)	0.01	85
Zinc oxide	0.01	97
Calcium acetate	0.01	113

[a] From Gorman Ng et al. (2012a).

[b] Samples > 50 mg.

[c] Samples < 50 mg.

the basic differences between these results underline the need for standardization of study designs.

In addition to investigations on absolute recovery, relative recovery of different methods has also been determined. In targeted controlled laboratory experiments, a study was performed on the effects of viscosity and dustiness on dermal exposure via three pathways: immersion, surface transfer and deposition. In this study, volunteers' hands were exposed to non-toxic substances: powders of varying dustiness and liquids of varying viscosity. The dermal exposure was measured with one of three sampling methods: skin rinse, skin wipe or cotton glove dosimeter sampling. To compare these sampling methods, the left and right hands were measured using different sampling methods in side-by-side experiments (Gorman Ng et al., 2012a).

For solutions of varying concentrations of glycerol, gloves and wipes were compared for the two pathways, immersion and deposition. Gloves always resulted in higher values than wipes. Interestingly,

Table 24. Ratios between different sampling methods[a]

Methods	Substance	Substance/product property	Ratio of glove/rinse to wipe	Comment/cause
Cotton glove and wipe	Glycerol solution	Viscosity (mPa·s): 20% glycerol: 2 50% glycerol: 7 87% glycerol: 109	Immersion: 10 5.2 1.4	Absorption and saturation effects in skin and glove; recovery from wipes increasing with increasing glycerol concentrations; no effect of glycerol concentration on recovery for gloves
		Viscosity (mPa·s): 20% glycerol: 2 50% glycerol: 7 87% glycerol: 109	Deposition: 25 26 42	Recovery for deposition increasing with decreasing glycerol concentration for gloves and wipes
Rinse and wipe	Calcium acetate	Fine powder, very soluble in water	Surface contact: 0.22 Immersion: 0.28	Unclear (mechanical force by wiping)
	Zinc oxide	Coarse powder, poorly soluble in water	Surface contact: 0.77 Immersion: 0.71	Unclear (poorly soluble)
	Epsom salts	Granular particles	Surface contact: 1.6 Immersion: 1.1	Difficult to pick up large particles on the skin with wipes, but in real-life scenarios, such large particles are unlikely to remain on the skin

[a] From Gorman Ng et al. (2012a).

for the immersion experiments, the differences became smaller with increasing glycerol concentrations (20%, 50% and 87%; see Table 24).

For powders, the efficiency of the two sampling methods varied by powder properties (dustiness, solubility or other). While rinsing was better for the granular powder, wipes were more efficient for the fine and soluble powders.

5.2 Migration rates and transfer coefficients

In addition to direct measurement, dermal exposure can also be estimated indirectly by measuring the migration rates and transfer coefficients of substances. These approaches are frequently used to estimate dermal exposure to treated surfaces, soils or articles with potentially releasable substances. These scenarios are usually characterized by an exposure concentration or exposure loading on the skin that is often below the detection limit of the analytical method used. To overcome this limitation, three precursor processes are measured instead:

1) the migration (leaching) out of an article;
2) the dislodgeability from a (treated) surface;
3) the transfer from a surface to the skin.

The common idea is to determine the rate or the relevant mass percentage of these processes. Migration rates and transfer coefficients are then used to calculate a dermal exposure estimate. Generally, these approaches need to be used with caution, as this simplification assumes that dermal exposure is linearly dependent on time and/or environmental concentration.

5.2.1 Migration

Low molecular mass substances can migrate through a material to its surface or into the adjoining medium. The migration rate is a measure of how much substance is extractable per product surface area and per time ($\mu g \cdot cm^{-2} \cdot h^{-1}$) or per product amount and per time ($\mu g \cdot g^{-1} \cdot h^{-1}$). The migration rate depends on the physicochemical properties of the substance, the material, the extraction medium and the interactions between these components.

The migration rate multiplied by the considered surface area and exposure duration results in the corresponding exposure mass. Different techniques are proposed to determine migration rates (EC, 2001a): head-over-heels agitation, horizontal shaking (mild conditions) and horizontal shaking (stringent conditions). These three techniques differ in their mechanical treatment of the probe and the chemical force of the extraction medium and were originally developed for mouthing

studies, which investigate potential migration during the mouthing activity of young children. To assess the proper migration rate for estimating dermal exposure, the experimental setting has to reflect dermal exposure conditions: artificial sweat (30 °C) as the extraction medium and less mechanical forces during the treatment. Depending on the exposure question, other experimental conditions might be desired. For instance, for assessment of migration rates for clothing, the German Federal Institute for Risk Assessment (BfR) recommends (BfR, 2012a):

- 0.5 g unwashed textile in 25 ml acidic and basic artificial sweat solution (e.g. ISO 11641:2012);
- 60 minutes of shaking with 90 revolutions per minute (rpm) at 40 °C;
- quantification of the release in relation to 1 g or 1 cm^2 of textile;
- use of the higher value for the exposure estimation for the first 16 hours.

For metals in toys, a norm is proposed: EN 71-3:2013. In this context, dermal absorption is considered to be negligible (van Engelen et al., 2008), and therefore dermal exposure is covered by the corresponding estimation of the reasonable worst case of oral exposure (mouthing)—that is, the migration test is performed with artificial stomach fluid (EN 71-3:2013). In contrast, the corresponding part for organic compounds in toys recommends just water as the extraction medium (EN 71-10:2005).

For scented toys, the BfR adapted the procedure as follows (Masuck et al., 2011):

- discs with surface area of 10 cm^2
- 100 ml ultrapure water as sweat and saliva simulant
- 60 minutes of head-over-heels shaking with 60 rpm
- $MR = (c_{fragrance} \cdot V_{simulant})/(t_{migration} \cdot A_{disc})$
  - MR: migration rate ($ng \cdot cm^{-2} \cdot min^{-1}$)
  - $c_{fragrance}$: concentration of a fragrance in the stimulant ($ng \cdot ml^{-1}$)
  - $V_{simulant}$: volume of simulant solution (ml)
  - $t_{migration}$: duration of the migration process (min)
  - A_{disc}: area of the sample disc (cm^2)

- $E_{derm} = (MR \cdot A_{contact} \cdot t_{exposure})/bw$
  - E_{derm}: amount of dermally exposed fragrance per kilogram of body weight (bw) per day ($mg \cdot (kg\ bw)^{-1} \cdot d^{-1}$)
  - MR: amount of fragrance migrating from the toy sample into sweat via dermal contact ($ng \cdot cm^{-2} \cdot min^{-1}$)
  - $A_{contact}$: area of skin contact with the toy (cm^2)
  - $t_{exposure}$: duration of exposure per day ($min \cdot d^{-1}$)
  - bw: body weight (kg).

Default values for contact area and exposure duration can be found in the *Exposure factors handbook* (USEPA, 2011a) and the *Child-specific exposure factors handbook* (USEPA, 2008).

Other experimental conditions may be more suitable for different articles. However, a norm is needed that summarizes the standard experimental conditions for relevant exposure scenarios.

5.2.2 Transfer

The process for the transfer of a substance from treated surfaces, soils or products to the skin depends on the physicochemical properties of the substance and/or the product, the surface, the receiver and the environmental conditions, as well as the interactions between these components. Some methods have been developed to quantify residue transfer to the skin of individuals performing activities on treated surfaces (USEPA, 2007a, 2011a). Depending on the experimental setting, transfer parameters (e.g. transfer efficiencies, transferable residues, transfer coefficients or transfer rates) or similar parameters are estimated:

- Transfer efficiency is the fraction (or percentage) of surface residues (measured by wipes or rollers) transferred to the skin.
- Dislodgeable residue (DR, $g \cdot cm^{-2}$) is the amount of a substance per surface area that is available for transfer (IPCS, 2001a). For pesticides, it is often called dislodgeable foliar residue (DFR; see section 6.2.12), turf transferable residue (TTR) or transferable residue (TR) for other surfaces.

- Transfer coefficients ($cm^2 \cdot h^{-1}$)[1] represent the ratio of the dermal exposure during a specified time period (the transfer rate, $mg \cdot h^{-1}$) to the environmental concentration ($mg \cdot cm^{-2}$) related to a specific activity (e.g. harvesting a crop, children playing on a lawn that was exposed to pesticides or unintended touching of treated surfaces).
  - Environmental residue levels are measured concurrently with exposure levels for particular job functions or activities.
  - These studies have been conducted primarily for the purpose of estimating exposure to pesticides.
  - USEPA (2012a) developed some generic activity-specific transfer coefficient assumptions to use in exposure assessments based on published and unpublished residue transfer studies.
  - Factors commonly believed to affect dermal transfer are summarized in Table 25.

Combinations of these basic concepts are also used. Therefore, the user of such parameters should check how the term was derived. Independent of the term used to describe the transfer process, the process depends on substance properties, the activity and the environmental conditions.

Several studies have been performed to measure transfer parameters, and the results of these studies were analysed by different approaches (Beamer et al., 2009; Gorman Ng et al., 2011). To derive general conclusions, a probabilistic solution was proposed by Beamer et al. (2009). Based on a literature review, 35 studies comprising 25 different sampling methods, 25 chemicals and 10 surface types were identified. Some distributions were derived for three chemicals (chlorpyrifos, pyrethrin I and piperonyl butoxide) on three surface types (carpet, vinyl and foil). Only the lognormal distribution was

[1] A formerly used term was "transfer factor" ($cm^2 \cdot h^{-1}$), expressing the intensity of the contact with the treated surfaces—i.e. the equivalent area of treated surfaces (foliage) that a worker contacts while performing a given activity in a given crop. However, this parameter has been replaced by the term "transfer coefficient" in order to exclude the causality that transfer factor erroneously implied (EFSA, 2008) (see Appendix 3, section A3.2.3).

Table 25. Factors affecting dermal transfer[a]

Category	Parameter	Source
Surface	Level of contamination	Goede et al. (2003); Egeghy et al. (2007)
	Type of surface: roughness, carpet vs hard surface	Brouwer et al. (1999); Rodes et al. (2001); Gorman Ng et al. (2012a)
Contaminant	Formulation	Marquart et al. (2003)
	Physical state: solid, liquid	Marquart et al. (2003)
	Particle characteristics: particle size distribution, moistness, dustiness	Kissel et al. (1996); Gorman Ng et al. (2012a)
	Liquid characteristics: viscosity and related properties	Marquart et al. (2003); Gorman Ng et al. (2012a)
	Physical properties of active ingredient: vapour pressure, water solubility, lipophilicity	Egeghy et al. (2007)
Skin	Moistness	Camann et al. (1996); Clothier (2000); Rodes et al. (2001); Egeghy et al. (2007); Gorman Ng et al. (2012a)
	Body region, hair density, skin folds and crevices (water adherence)	Gujral et al. (2011)
	Contact area	Brouwer et al. (1999)
Contact	Frequency: number of contacts or objects	Brouwer et al. (1999); Rodes et al. (2001); Egeghy et al. (2007)
	Interval between contacts	Camann et al. (1996)
	Motion: press, smudge, drag	Lu & Fenske (1999)
Protection	Clothing: use, area covered, material	Marquart et al. (2003)
	Handwashing: frequency	Egeghy et al. (2007)

[a] Adapted from Egeghy et al. (2007).

consistently accepted for each chemical and surface type combination, where the fitted distributions were significantly different (Kruskal-Wallis test). Based on these analyses, probability distribution functions of transfer efficiencies were proposed for the three surface types (Beamer et al., 2009).

Another approach to analyse the huge number of data is a database collecting transfer efficiencies, published by Gorman Ng et al. (2011). A database of transfer efficiency data relevant for dermal and inadvertent ingestion exposure was developed, containing 534 transfer efficiencies empirically measured between 1980 and 2010 and reported in the peer-reviewed and grey literature. The majority of the reported transfer efficiencies (84%) relate to transfer between surfaces and hands, and the average transfer efficiency from surface to skin was analysed (23%, standard deviation 31%) (Gorman Ng et al., 2012b).

In the database, two types of efficiencies are distinguished (Gorman Ng et al., 2012b):

1) Mass per unit area: The mass per unit area detected on the receiver divided by the mass per unit area present on the surface area involved in contact.
2) Total mass: The mass detected on the receiver divided by the total mass present on the donor (not only on the surface area involved in the transfer).

In Europe, several exposure assessment studies (mainly of personnel in hospitals and pharmacies) are available in which surface contamination as well as dermal exposure (using the interception technique) were measured for evaluating the possible transfer of drugs from contaminated surfaces to the skin (Villarini et al., 2011; Sottani et al., 2012; and citations therein), but none was found to investigate activity-specific transfer parameters or coefficients.

The USEPA's Residential Standard Operating Procedures (USEPA, 1997b, 2012a) also provide guidance for estimating dermal exposure from pesticide residue transferred to the skin of individuals who contacted previously treated indoor surfaces (e.g. carpets, floors, furniture and other surfaces) during standard activities such as recreation, housework or other occupant activities. If

chemical-, surface- and activity-specific measurements for the transfer parameters are not available, default values or general approaches for estimation are provided, as well as default values for the transfer coefficients for different subpopulations.

Although this approach has been developed for pesticides, dermal exposure to other chemical substances in indoor environments can also be estimated using transfer coefficients, assuming similar activities after application of the chemical substance, but noting the physicochemical property differences and the need for measured indoor surface transferable residue data.

5.3 Biomonitoring

Biomonitoring is an important tool for measuring systemic exposure to chemical agents. In the context of dermal exposure, it reflects both processes of dermal exposure and subsequent absorption into the systemic circulation. Typically, systemic levels of a chemical are the aggregate result of all exposure pathways, and frequently dermal exposures may not be distinguishable from exposures by the inhalation or ingestion route. Numerous review articles and scientific handbooks have been developed with respect to biomonitoring (e.g. IPCS, 2001b), and a brief section on the use of biomarkers for the assessment of dermal absorption is provided in IPCS (2006). Therefore, biomonitoring is only briefly described here.

Monitoring of biological parameters is frequently used for exposure assessment. The analytical parameters can be distinguished in dose biomarkers (the concentrations of the substance itself or its metabolites), effect biomarkers (e.g. protein adducts, deoxyribonucleic acid [DNA] adducts, cytogenetic parameters or immunological parameters) or susceptibility biomarkers (e.g. enzyme pattern and enzyme activity). Biomarkers can be measured in different body fluids (urine, blood, breast milk, exhaled breath or saliva). Ideally, biomarkers of exposure are chemical specific, detectable in trace amounts and quantitatively associated with the exposure pattern (as shown in Franklin, 1984).

Absorption and metabolism are processes that occur subsequent to external exposure. Therefore, the extrapolation of results caused by

dermal exposure and obtained via biological monitoring must be carefully performed. The lack of a detailed understanding of the chemical's metabolism and pharmacokinetics in humans could cause misinterpretation of the analytical results in body fluids. In contrast, if precise data on dermal exposure and metabolism are available, biomonitoring data can increase knowledge about absorption and pharmacokinetics. For example, the dermal absorption values for chlorpyrifos from different comparative studies were found to range from 1% to 10% (Nolan et al., 1984; Ross et al., 1991; Griffin et al., 1999; Krieger et al., 2000; Geer et al., 2004).

In general, biological monitoring is used to evaluate the efficiency of PPE, to determine whether workers have been exposed to harmful substances and, during epidemiological studies, to establish a link between exposure and health effects. The samples are collected from volunteers before, during and after exposure. Monitoring levels in blood or urine allows systemic exposure to be quantified (not distinguishing between the exposure routes) over a specific exposure period. Systemic exposure values are periodically measured in the United States National Health and Nutrition Examination Survey, the Canadian Health Measures Survey and the German Environmental Survey. For substances that are readily absorbed through the skin and become systemically available, comparing biomonitoring results with concentrations in inhaled air can reveal the relevance of the dermal route of exposure. For example, measuring the excretion of pyrene in the urine of workers exposed to PAHs indicated that the dermal pathway was more relevant than the inhalation route (van Rooij et al., 1993a,b).

Biological monitoring is a useful method to confirm exposure and is also sometimes regarded as the "gold standard" for systemic dose estimates (Sexton et al., 2004). However, if dermal exposure is to be estimated based on biomonitoring, extensive additional studies (i.e. on absorption, metabolism and physiologically based pharmacokinetics) are needed.

5.4 Considerations for selecting suitable approaches

Some statements with respect to the applicability of single methods can be found in the literature:

> Interception samplers such as the pads [. . .] are likely to overestimate exposure [. . .]. The fluorescent tracer method provides some advantages in terms of convenience but may still overestimate exposure if the fluorescent compound preferentially binds to the skin, as is often the case. The wipe sample may underestimate exposure because of removal of contaminant prior to sampling from washing or wiping of hands or because of uptake of the contaminant through the skin. [Cherrie & Semple, 2010]

> The pad technique has major drawbacks, since the contamination over the body is not uniform and erroneous data may be obtained, especially for a small number of replicates. [van Hemmen, 1993]

> Overall, tape-strips of exposed skin measured lower levels of monomeric and polymeric HDI [1,6-hexamethylene diisocyanate] than impregnated patch samplers at the same sampling site on the skin. Unlike tape-strips, impregnated patches are not as prone to evaporative or reactive losses or losses due to rapid penetration into the skin. Further investigations are warranted to evaluate these and other methods to measure dermal exposure to workers under occupational conditions to better understand the relationship between dermal exposure and internal dose. [Thomasen et al., 2011]

The in situ techniques provide the opportunity to investigate the sources and pathways of exposure. Tracer techniques are favoured if the substance of interest is quickly absorbed compared with the tracer. In that case, the tracer loading on the skin is valuable additional information to biological monitoring data. The advantages of these optical methods are that they provide near real-time quantitative results, and the need for sample preparation is minimal. However, an extra sampling accessory is required, which is less attractive. Depending on the type of accessory, either it could be relatively expensive (e.g. the ATR crystal) or it would have to be specially designed (e.g. chalcogen-based glass as infrared optical sensor; Wu & Chiu, 2007).

However, these statements/conclusions refer to certain exposure scenarios and cannot be generalized. Therefore, this section focuses on the general aspects that should be considered. Some important features of the different sampling techniques for direct measurements are summarized in Table 26. Each method has its own strengths and limitations, the importance of which depends on the goal of the study (e.g. screening, training, quantitative estimate).

Beyond the features listed in Table 26 and practicability with respect to the activity, important analytical parameters such as

Table 26. Overview of important features of sampling techniques for direct measurements of dermal exposure

	Interception techniques		Removal techniques					In situ techniques		
	(Disposable) overalls and gauntlets or gloves	Exposure patches	Wiping technique	Handwash technique	Immersion technique	Tape stripping techniques	Suction method	Video imaging technique	ATR-FTIR technique	Light sensor technique
Estimate/ result	All deposited amount (mass) in certain time frame		Exposure loading at a definite time point					Exposure loading at a definite time point or time resolved		
Sample area	Whole body or body regions	$\sim 10 \times 10$ cm^2	$\sim 5 \times 5$ cm^2	<2000 cm^2	Immersible body parts	2.5×4 cm^2 3×3 cm^2	$\sim 20 \times 20$ cm^2	Whole body possible	<2 cm^2	<0.5 cm^2
Body regions	Whole body or body regions	Whole body or body regions	Uncovered body regions	Uncovered hands, wrists, forearms	Uncovered fingers (hands, forearms)	Uncovered body regions	Uncovered body regions	Whole body possible	Uncovered body regions	Uncovered body regions
Deposition pattern of body exposure	Yes	Partly	No	No	No	No	No	Yes	No	No
Deposition surface	Clothing	Patch	Skin	Skin	Skin	Skin	Skin	Skin/clothing	Skin	Skin

Table 26 (continued)

	Interception techniques		Removal techniques					In situ techniques		
	(Disposable) overalls and gauntlets or gloves	Exposure patches	Wiping technique	Handwash technique	Immersion technique	Tape stripping techniques	Suction method	Video imaging technique	ATR-FTIR technique	Light sensor technique
Substances	Substances extractable from the surrogate material	Substances extractable from the surrogate material	Substances soluble in skin-compatible solvents	Substances soluble in skin-compatible solvents	Substances soluble in skin-compatible solvents	Adherent substances, such as particles or viscous substances	Solids with low adhesion: powders or particles Particle size–dependent sampling possible	Fluorescent substances (inherent or tracer)	IR-active liquids, pastes or solids (strong and specific IR spectra)	Fluorescent substances (inherent or tracer)
Necessary add-ons	None	None	Precleaning of the skin	Precleaning of the skin	Precleaning of the skin	Precleaning of the skin	Precleaning of the skin	Set of photographs before exposure	Premeasure-ments	Premeasure-ments
Equipment	Standard analytical equipment	Standard analytical equipment	Standard analytical equipment	Standard analytical equipment	Standard analytical equipment	Standard analytical equipment	Specialized technique; seldom available	Specialized technique; seldom available	Specialized technique; seldom available	Specialized technique; seldom available
Analysis	Extraction media	Extraction media	Skin-compatible solvent	Skin-compatible solvent	Skin-compatible solvent	Glue of the tape + extraction media	Particle filter + extraction media	Photographs and computer files	Light signal and computer files	Light signal and computer files

Table 26 (continued)

	Interception techniques		Removal techniques					In situ techniques		
	(Disposable) overalls and gauntlets or gloves	Exposure patches	Wiping technique	Handwash technique	Immersion technique	Tape stripping techniques	Suction method	Video imaging technique	ATR-FTIR technique	Light sensor technique
Experience available	Several studies available	Several studies available	Several studies available	Several studies available	Few studies available	Some studies available	Some studies available	Some studies available	No study found	Limited studies available
Measurement affected by dermal absorption	No	No	Yes	Yes	Yes	Could also be detected	Yes	Fluorescent tracers tend to bind tightly to the skin	No information	No information
Interaction with the skin	No	No	Skin might be damaged by the technique Reaction to substances possible					Reaction to substances possible		
Requirements for detecting "real exposure"	Skin-simulating surrogate material needed		Use of standards					Limited to light-absorbing substances Tracer = surrogates Quantification limited		
Influencing factors	Clothing material Size of cut clothing parts Solvent	Patch material Size and number Body region Solvent	Wipe material Solvent Duration Repeating Area of skin Pressure	Solvent Volume of solvent Washing or rinsing Duration Repeating	Solvent Volume of solvent Duration	Tape material Glue in the tape Pressure Duration	Particle size Adhesion forces	Tracer Fading Quenching Background signals Distance and angle	Not documented	Small signal background ratio High background variability

Table 26 (continued)

	Interception techniques		Removal techniques					In situ techniques		
	(Disposable) overalls and gauntlets or gloves	Exposure patches	Wiping technique	Handwash technique	Immersion technique	Tape stripping techniques	Suction method	Video imaging technique	ATR-FTIR technique	Light sensor technique
Other features to be considered	Deposition pattern and exposure amount simultaneously	Different materials for different substances available	Hazardous potential of the solvents			Allergic reactions to the glue	—	Source target analyses UV light doses Tracer to substance ratio Toxicity of tracer	Substance identification and quantification simultaneously Specific ATR crystal needed	Fast and portable

ATR-FTIR, Fourier transform infrared spectroscopy with attenuated total reflectance; IR, infrared; UV, ultraviolet

Table 27. Influence of study purpose on method selection

Study purpose	Possible methods
Whole body exposure – screening – accurate estimates and pattern	Patches and gloves Overalls
Epidemiological or surveillance studies	Biomonitoring
Inhalation pathway excluded	Biomonitoring
Rough screening of formulation exposure	Weighing patches
Penetration through clothing	Patches above and beneath
Whole-hand exposure	Handwashing
Only fingertips exposed	Immersion
Training, pathway finding, exposure pattern, surveillance	Video imaging technique

Table 28. Influence of substance properties on method selection

Substance/properties	Possible methods
Toxic substances	Interception techniques
Long-lasting substances[a]	Removal and fluorescence techniques
High absorption / low desorption[a]	Interception and fluorescence techniques
High desorption rate (removal, resuspension, evaporation)[a]	Biomonitoring
Soluble substance	Wiping/rinsing/handwashing
Highly adsorbing substances	Tape stripping; interception techniques
Viscous substance pathway dependent	Wiping; interception techniques
Particles and fibres	Suction method
Fine particles	Wiping
Granular particles	Handwashing/rinsing
Contact with contaminated surfaces/materials	Transfer
Products: low dermal exposure expected	Migration

[a] Schneider et al. (2000).

sensitivity and selectivity (background levels or signals), variability or uncertainty should be compared. Ideally, the selection process for a suitable method follows a criteria catalogue. At present, only a few comprehensive studies are available, which allow only a limited conclusion on the most suitable method for particular study goals. Possible methods for different study purposes (see Table 27) and different substance properties (see Table 28) may help in selecting an adequate analytical approach to estimate dermal exposure.

6. MODELS AND TOOLS TO ESTIMATE DERMAL EXPOSURE

Measuring and modelling are complementary approaches to assessing dermal exposure (see section 3.4). In cases where direct exposure measurements cannot be obtained or where it is impracticable to collect sufficient analytical measurement data to give a statistically robust assessment, modelling is a valuable approach to estimating exposure. A "model" is a mathematical abstraction derived from assumptions and approximations in order to represent exposure. The term "tool" refers to computer-based software or other product (e.g. a spreadsheet) that is intended to simplify the estimation procedure and can even implement various models (see section 3.5 and Appendix 1).

In this chapter, the general aspects of modelling in relation to dermal exposure are presented (section 6.1). Following this, various examples of models and tools dealing with dermal exposure are introduced (section 6.2). Models of uptake into the body are not considered, as these have been fully described in EHC 235, entitled *Dermal absorption* (IPCS, 2006). A more general description of exposure modelling is provided in EHC 214 on *Human exposure assessment* (IPCS, 2000) and Harmonization Project Document No. 3 on *Principles of characterizing and applying human exposure models* (IPCS, 2005). A broader description of basic principles and definitions can be found in Appendix 1 (e.g. explanations for the different model types: mechanistic, empirical, deterministic and probabilistic). Additionally, issues surrounding uncertainty in exposure assessment are provided in Harmonization Project Document No. 6 on *Uncertainty and data quality in exposure assessment* (IPCS, 2008). A good overview on the individual models is provided in BROWSE (2011a,b,c) and EFSA (2008).

6.1 Aspects of modelling dermal exposure

6.1.1 Model approaches

Figure 13 is a schematic diagram of the processes involved in developing models and tools. It shows the process of conceptualizing

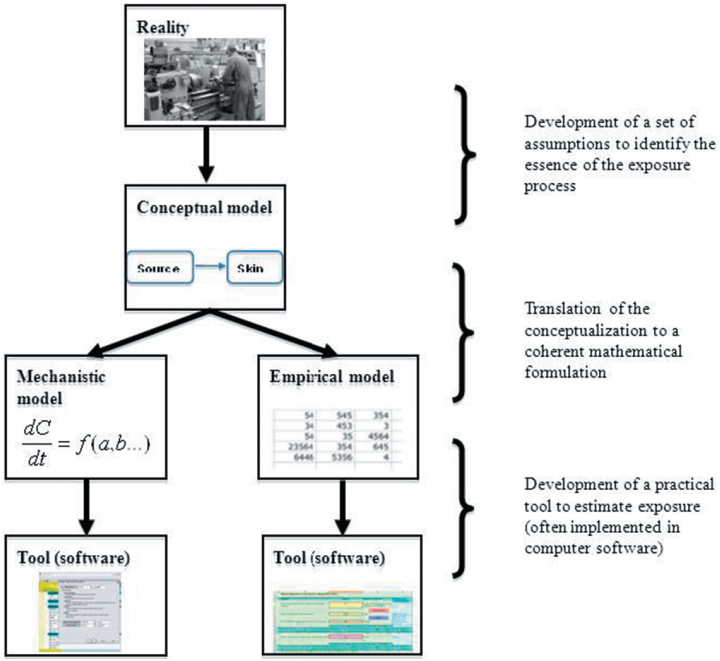


Fig. 13. A schematic diagram of the processes involved in developing exposure models and tools.

the realistic exposure situation and then formulating a mathematical model to describe the relationship between exposure and the various explanatory variables. Finally, the model may be implemented as a practical tool, either in computer software or as a set of instructions to calculate exposure.

Mathematical modelling approaches provide quantitative estimates of exposure using a set of input parameters. Models are classified as either mechanistic or empirical, and in both cases the models can be applied as deterministic or probabilistic (stochastic) tools (IPCS, 2005). Thus, the model may rely on a set of mathematical mass balance equations (mechanistic model) or some set of empirical rules to derive its output (empirical model). A given set of input variables can produce a single output, and this output will always be the same for the same set of inputs (deterministic model). Alternatively, the output

is described by a statistical distribution, and the input variables may be either unique values or some probability distributions (probabilistic model). Models are limited by day-to-day changes in exposure (variability) or by the lack of knowledge about the correct value for a specific exposure parameter (uncertainty). Although the consequence of both variability and uncertainty in a model may be the same, it is important to keep these sources of variation separate; it is always possible to reduce uncertainty by collecting more information, whereas variability cannot be reduced without intervening in the way in which the substance is used (see terminology in Appendix 1).

Some tools rely on analytical measurements, and their output is defined by statistical analysis of the data set or selected subsets. The selection of subsets should increase the analogy between the exposure scenarios of the data set and the scenario that is to be modelled. Other approaches are based on a theoretical analysis of the exposure process, normally encompassed within a system of mathematical equations. The potential to adapt all or only some input parameters of the underlying model differs between the tools.

Bayesian statistics provides a formal theoretical framework for updating a prior judgement (e.g. a probabilistic model estimate of exposure) with new empirical exposure data, and this approach is becoming more common in exposure modelling.

6.1.2 Model scope, applications and features

Exposure modelling should reflect the purpose of the assessment—for example, regulatory risk assessment, risk management or research studies. The purpose of an exposure assessment may be to estimate the actual exposure, to assess the impact of risk-reducing measures or to identify limits of substances in products. Many regulations use a tiered approach to decide whether there is concern about potential risk. Initially, simple conservative modelling approaches are used to obtain a rough estimate of the exposure and to characterize the risk. If the initial conservative assessment indicates a risk, then the assessor may move to a higher-tier assessment involving a more sophisticated model estimate or generate data by analytical measurements.

Exposure assessments are often carried out in respect of populations, and the data used in models should be representative, with the intention to ensure safety for the whole population. In probabilistic modelling, this can be considered by taking high-end percentiles of the output exposure distribution; in deterministic modelling, defaults are selected where expert judgement has revealed sufficient conservatism.

Models can be very general in their application, seeking to provide estimates of exposure for a wide domain of scenarios (e.g. for all workplace exposures), or may focus on more specific circumstances, such as a process (e.g. spraying) or a class of substances (e.g. pesticides). There are a few approaches that try to unify all aspects of dermal exposure across consumer, worker[1] and environmental scenarios experienced by the same group of people. The model boundaries (applicability domains) thus differ.

All types of models have their uses, but some models are more broadly applicable than others. It is important to remember that all models are based upon assumptions and that their outputs are at best an approximation of the actual (true) exposure and may be inaccurate in particular circumstances. Of course, the same could be said of exposure measurements from a small number of workers on a few days at one time of year that are used to represent the exposure of all workers doing that task. The reliability of exposure models can be assessed from validation studies, and this is the topic of the next section.

6.1.3 Model validation

It is imperative that models are evaluated to assess their reliability in predicting exposures prior to being used. According to Leijnse & Hassanizadeh (1994), a model is called valid in all aspects ("strong validation") if the model outputs can be demonstrated to closely relate to the outputs of a given system (see also Appendix 1).

[1] It should be noted that the term "worker" is used differently in different regulations, such as REACH (EC, 2009a) and the EU agricultural pesticide regulation (EC, 2009b). In this document, the term is used as a synonym for "occupational user".

It is often assumed that analytical exposure measurements are essentially the "gold standard" and that model outputs should approximate measurement data. However, measurements are not without error, and a data set containing few measurements may not be a reliable basis on which to test validity (IPCS, 2005).

Strictly speaking, we wish to show that the analytical measurements and the model predictions are associated with each other—that is, that they are measuring the same underlying parameter (e.g. the "true" exposure). These are inter-method reliability studies. They are used to identify two factors: the bias (systematic difference) of one method in relation to the other and the degree of correlation between the two methods. The bias can be assessed by the difference between the mean model estimate and the mean measured exposure for a defined set of exposure measurements. It is often the case that models are "designed" to have some inherent positive bias in relation to measured data. This is the case particularly in situations where models are used for regulatory purposes, such as the European REACH Regulation (ECHA, 2012a) and the Canadian Environmental Protection Act, 1999 (Government of Canada, 1999). Ideally, the degree of bias should be consistent throughout the model domain and should only be sufficient to ensure that the majority (e.g. 95%) of model estimates are above the corresponding measured data. The degree of conservatism in the model should be defined and documented.

The same applies for exposure tools, as often the models implied in the tools are based on data that are implicitly limited to the domain described by the data set (e.g. analytical methodology or design); in other words, the resulting applicability domain of the model reflects the applicability boundaries of the tool. Tools that are based on some theoretical analysis of the process of exposure may be more robust in predicting exposure beyond the original set of observations that were used to parameterize the model. An important part of assessing the reliability of any tool should be an evaluation of the underlying model structure and the validation of the implemented model. In choosing a tool or model, the applicability to the specific system in question always has to be checked (IPCS, 2005).

A typical approach of validation is to compare the modelled output with a set of measured data that has not been used to derive the model

or tool (IPCS, 2000). For models where the parameters are derived from a data set, a typical approach is to divide the data into a "training" set and a "validation" set. It is expected that a valid model should accurately predict the results in the validation set. In addition to the preferred option of using measurements, comparison of results from different assessment methods or modelling approaches can also be used to evaluate validity, or at least agreement (IPCS, 2000). Another important way of validating a model is to review the degree to which it is realistic, is logical and incorporates the key determinants of exposure, as well as to confirm that the equations used describe the model correctly (see section 3.3 and section A3.2 in Appendix 3). This is sometimes referred to as "construct validity". These assessments of model validity are complementary and are not a substitute for each other. Ideally, the validity of models should be judged using both approaches.

6.2 Examples of models and tools

In this section, models and tools for estimating dermal exposure are presented. Where possible, models and tools that are closely related with respect to the underlying concept, data basis (EASE and ECETOC TRA) or regulatory use (pesticide models) are presented together. Also where possible, for each model or tool, the following information is provided:

- general description and scope of application;
- underlying data basis, concept and derivation of dermal exposure estimates;
- validation status.

The links for downloading the tools are provided in section A3.1 of Appendix 3. The underlying algorithms are presented in section A3.2.3 (for the influencing factors and determinants used, see specifically section A3.2.3). Considerations on utilization are provided in section 6.4. Section 6.3 provides an overview of all described models and tools.

In the majority of cases, the tools are available free of charge and have been designed to have a relatively simple user interface and to

be based on widely available software, such as Microsoft Excel or as stand-alone applications on the Microsoft Windows operating system. Where this is not the case, the operating system and/or software requirements are described in the text.

6.2.1 DREAM

6.2.1.1 General description and scope of application

The DeRmal Exposure Assessment Method (DREAM)[1] was developed by van Wendel de Joode and colleagues (2003) and is based on the conceptual model described by Schneider et al. (1999) (see section 3.1). It was intended for use by trained users for assessing dermal occupational exposure (e.g. in occupational hygiene and epidemiological surveys) (van Wendel de Joode et al., 2003). The DREAM model is not readily available as a software tool, although the algorithm is transparently described by van Wendel de Joode et al. (2003) and can be reproduced in spreadsheet form. By ranking tasks and jobs, DREAM is meant to additionally supply information for analytical measurement strategies (van Wendel de Joode et al., 2003). DREAM provides only relative assessments of exposure as a numerical estimate (in DREAM units) and does not indicate exposure in units of mass or any other physical property.

6.2.1.2 Underlying data basis, concept and derivation of dermal exposure estimates

DREAM is described as a semiquantitative (generic) method to assess dermal exposure by systematically evaluating exposure determinants using preassigned default values (van Wendel de Joode et al., 2003; see section A3.2 in Appendix 3). It consists of a multiple-choice questionnaire on exposure determinants (inventory module) that is to be completed by an occupational hygienist after observing the workers and an evaluation algorithm (van Wendel de Joode et al., 2005a). For the inventory module, basic data for estimating dermal exposure are to be collected, as shown in Table 29.

[1] Not to be confused with the Dose-related Risk and Exposure Assessment Model for environmental exposure assessments, which is also abbreviated as DREAM.

Table 29. Information needed for the DREAM inventory module[a]

Module	Data to be obtained on. . .
Company	General information about company and observer
Department	Chemical or biological agents that occur in work environment Cleaning activities in department
Agent	Physical characteristics of substance for which dermal exposure is assessed, such as concentration of active ingredient in substance, physical state, boiling point, viscosity, formulation type (powder, granules), dustiness, stickiness
Job	Hygienic behaviour Number of people with this job title
Task	Percentage of time that task is performed Number of people performing task (event per unit of time)
Exposure to a substance assessed for a certain task	Probability and intensity of dermal exposure routes (per body part)
	Use of clothing (per body part) (covered versus uncovered body parts, clothing material, repeated use of clothing) Contamination of work environment

[a] From van Wendel de Joode et al. (2003).

The exposure is assessed using a complex series of algorithms for nine body parts, giving a matrix of exposure: head, upper arms, forearms, hands, front torso, back torso, lower body part, lower legs and feet. The model estimates potential (exposure mass on clothing and skin) and actual (exposure mass on skin) dermal exposure by summing contributions from emissions from the source, plus deposition and transfer processes, while taking account of the protection afforded by clothing and gloves (see Fig. 14, including algorithm). Each determinant in the model is assigned a numerical value according to a list of categories. These factors follow the approach for exposure to contaminants in air of Cherrie et al. (1996), who proposed to weigh effects of exposure determinants on a logarithmic scale. The directions of the default values of DREAM (increasing versus decreasing exposure) are derived from the literature and expert judgement. For example, the probability of exposure of a specific body part is scored as follows (factors given in parentheses): unlikely, i.e. $<1\%$ of task duration (0); occasionally, i.e. $<10\%$ of task duration (1); repeatedly, i.e. 10–50% of

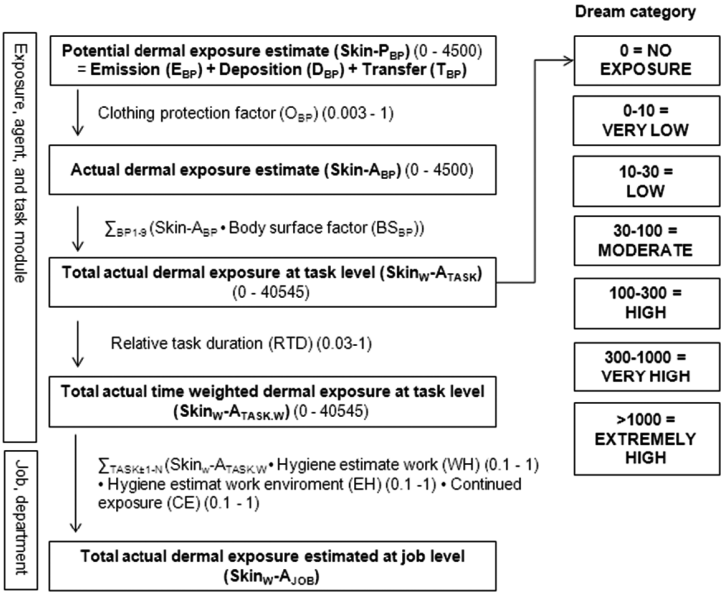


Fig. 14. Summary of the evaluation model of DREAM, with the ranges of the estimates in DREAM units in parentheses (van Wendel de Joode et al., 2003).

Reprinted from B. van Wendel de Joode, D.H. Brouwer, R. Vermeulen, J.J. van Hemmen, D. Heederik & H. Kromhout, DREAM: a method for semi-quantitative dermal exposure assessment, Annals of Occupational Hygiene, 2003, volume 47, issue 1, pages 71–87, by permission of Oxford University Press.

task duration (3); almost constantly, i.e. ≥50% of task duration (10). Therefore, if the judgement of the user is that exposure on the back torso is "unlikely", then this body part will not contribute to the exposure. In contrast, when the user chooses "almost constantly" as the probability of deposition, then this will contribute with a factor of 10. The final outcome is a numerical estimate for the dermal exposure level encountered by workers performing a certain task or job (categorized into the levels zero, low, moderate, high, very high and extremely high).

As presented in Figure 14, the tool offers exposure results in several steps, finally resulting in the "total actual dermal exposure estimated at job level". This value results by weighting the actual exposure estimates for each body part for all three transport mechanisms by its body surface factor, further multiplying the sum for all nine body parts with

task-related factors and finally time-weighting the task to be able to compare the contributions of several tasks.

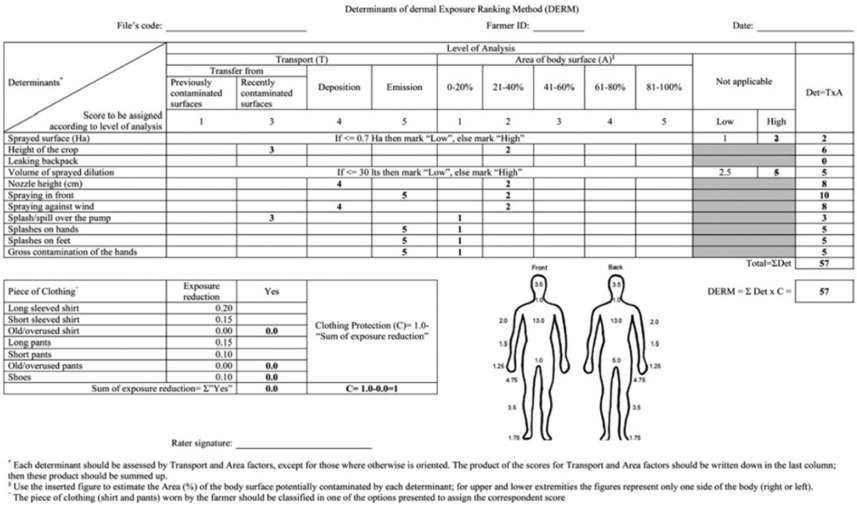
6.2.1.3 Validation status

Two subsequent papers by these authors illustrated the repeatability of the assessment (van Wendel de Joode et al., 2005a) and the accuracy of the methods (van Wendel de Joode et al., 2005b). The authors concluded that the DREAM method was suitable for groups of workers with considerable contrast in dermal exposure levels and when the output in a rough category (no, low, moderate, high, very high or extremely high exposure) is sufficient in a first estimate to get an idea about the extent of possible exposure. Nevertheless, for scenarios with less contrasting exposure levels, analytical methodologies for obtaining quantitative dermal exposure measures would be preferable.

6.2.2 DERM

6.2.2.1 General description and scope of application

The Dermal Exposure Ranking Method (DERM) was developed by Blanco et al. (2008). In analogy to DREAM, it is based on the conceptual model described by Schneider et al. (1999) (see section 3.1). As a main objective, DERM was intended to be a practical, easy-to-use tool, taking into consideration the economic and technical potential of developing countries in relation to dermal exposure assessment. Its intention is to identify the most probable determinants responsible for dermal exposure in a group of subsistence farmers, relating predominantly to occupational pesticide application in developing countries (see section A3.2 in Appendix 3). The authors intend to shift the emphasis from measuring exposure to show compliance with regulations to understanding the determinants of exposure and orienting control efforts towards those determinants identified as most relevant. Thus, DERM is intended to support the design of monitoring and preventive programmes or to aid the prioritization of the most adequate measurement strategies. In addition, the authors propose that the DERM evaluation form is a useful tool in combination with fluorescent tracer measurements (see section 5.1.3.1) in educational programmes addressed to diminish exposure or eliminate risky work



Determinants of dermal Exposure Ranking Method (DERM)

File's code: _____ Farmer ID: _____ Date: _____

Determinants*	Level of Analysis											
	Transport (T)				Area of body surface (A)§					Not applicable		Det=TxA
	Transfer from		Deposition	Emission	0-20%	21-40%	41-60%	61-80%	81-100%			
	Previously contaminated surfaces	Recently contaminated surfaces										
Score to be assigned according to level of analysis	1	3	4	5	1	2	3	4	5	Low	High	
Sprayed surface (Ha)	If <= 0.7 Ha then mark "Low", else mark "High"									1	**2**	**2**
Height of the crop		**3**				**2**						**6**
Leaking backpack												**0**
Volume of sprayed dilution	If <= 30 lts then mark "Low", else mark "High"									2.5	**5**	**5**
Nozzle height (cm)			**4**			**2**						**8**
Spraying in front				**5**		**2**						**10**
Spraying against wind			**4**			**2**						**8**
Splash/spill over the pump		**3**			**1**							**3**
Splashes on hands				**5**	**1**							**5**
Splashes on feet				**5**	**1**							**5**
Gross contamination of the hands				**5**	**1**							**5**
											Total=ΣDet	**57**

Piece of Clothing*	Exposure reduction	Yes	
Long sleeved shirt	0.20		Clothing Protection (C)= 1.0- "Sum of exposure reduction"
Short sleeved shirt	0.15		
Old/overused shirt	0.00	**0.0**	
Long pants	0.15		
Short pants	0.10		
Old/overused pants	0.00	**0.0**	
Shoes	0.10	**0.0**	
Sum of exposure reduction= Σ"Yes"		**0.0**	**C= 1.0-0.0=1**

Front Back

5.0 5.0 2.0 13.0 13.0 2.0 1.5 1.0 9.0 1.5 1.25 4.75 4.75 1.25 3.5 3.5 1.75 1.75

DERM = Σ Det x C = **57**

Rater signature: _____

* Each determinant should be assessed by Transport and Area factors, except for those where otherwise is oriented. The product of the scores for Transport and Area factors should be written down in the last column; then these product should be summed up.
§ Use the inserted figure to estimate the Area (%) of the body surface potentially contaminated by each determinant; for upper and lower extremities the figures represent only one side of the body (right or left).
* The piece of clothing (shirt and pants) worn by the farmer should be classified in one of the options presented to assign the correspondent score

Fig. 15. The DERM evaluation form (Blanco et al., 2008).

Reprinted from L.E. Blanco, A. Aragón, I. Lundberg, C. Wesseling & G. Nise, The determinants of dermal exposure ranking method (DERM): a pesticide exposure assessment approach for developing countries, Annals of Occupational Hygiene, 2008, volume 52, issue 6, pages 535–544, by permission of Oxford University Press.

practices. As the output is provided on an arbitrary scale (dimensionless), the results are difficult to use for risk assessment.

6.2.2.2 *Underlying data basis, concept and derivation of dermal exposure estimates*

DERM is based on a paper form using determinants of dermal exposure in a combination of checklists and expert rating assessments (see Fig. 15). For this, the tool relies on an assessment of three key factors as observed by the assessor: the dermal exposure surface area (A), the mechanism by which a pesticide could be transported to the skin (T) and the protective effect of clothing (C). The determinants for these key factors are (see also Fig. 15):

- sprayed surface (ha)
- height of the crop (cm)
- leaking backpack
- volume of sprayed solution (l)

- nozzle height (cm)
- spraying with nozzle directed in front
- spraying against wind
- splashing/spilling spray solution over the pump
- splashes on the hands
- splashes on the feet
- gross contamination of the hands by blocking a hose leakage, repairing nozzle or entering hand into tank
- wearing long-sleeved shirt
- wearing an old/overused/torn shirt
- wearing long pants
- wearing old/overused/torn pants
- wearing shoes.

The determinants for each key factor are to be categorized and scored by the user (see Fig. 15). Scores for the key factor transport process (T) are defined assuming that general transfer processes lead to low exposure (score of 1), deposition processes and transfer from recently contaminated/splashed/sprayed surfaces or clothing lead to medium exposure (score of 3 or 4, respectively) and emission of the pesticide directly onto the skin leads to high exposure (score of 5). In the same manner, the area of the body surface expected to be contaminated (A) is ranked from 1 to 5 in relation to percentage ranges of the total body surface (i.e. 0–20%, 21–40%, etc.). The authors state that the ranges and scores were defined arbitrarily, with the only assumption being that the level of exposure is approximately the same within a category. Finally, the user has to define a clothing protection factor (C), which is the complement of the reduction in the exposure level (1 – exposure reduction) that occurred because of the clothing worn. The maximum protection that it is assumed can be provided by clothing is 50% (long-sleeved shirt and long trousers: $C = 1 – 0.5$), whereas old, overused or torn shirts or trousers or being barefoot are assumed to provide no protection.

The transport process (T) and the area of the body surface (A) are assumed to be directly proportional to the exposure and act independently. Both factors are scored by independent evaluation for each determinant using ordinal numbers increasing proportionally to the intensity of exposure. Afterwards, the sum of the score of transport process (T) and body surface area (A) is multiplied by the clothing

protection factor (C) to estimate the final DERM score—that is, a numerical estimate for the dermal exposure level. The algorithm is clearly described in Blanco et al. (2008), along with an example.

6.2.2.3 *Validation status*

Blanco et al. (2008) provided the results from a comparison of the DERM algorithm with two independent semiquantitative visual scoring systems based on fluorescent tracer. As DERM estimates were not normally distributed, Spearman's correlation coefficient was used, showing good correlation between the methods (0.69 and 0.67, respectively). Even though a good correlation was achieved, DERM estimated higher or lower exposure than the visual scoring systems for some applications. The authors found a relationship between exposure and the presence of water on the foliage due to morning dew or night rain and assumed that the soaked clothing allows a more intense permeation through clothing. Thus, they suggested that the effects of soaked clothes should be included in the modelling.

In conclusion, the authors suggested that DERM is a useful tool for identifying the key determinants responsible for high exposure. In relation to their study, these determinants were mainly related to the work practices (nozzle height, spraying against wind and splashes on the hands), worksite conditions (height of the crop) and equipment (leaking backpack). The authors argued that their results should be used for designing priorities for intervention programmes—for example, to induce modifications of the way in which the applicators pour water into the backpack sprayer tank when splashing on the hands has been identified as a key determinant for these farmers.

6.2.3 EASE

6.2.3.1 *General description and scope of application*

Estimation and Assessment of Substance Exposure (EASE) is a generic exposure estimation method developed in the early 1990s by the United Kingdom Health and Safety Executive (HSE) to predict workplace exposure to substances hazardous to health. The method was designed to be applicable to a wide range of substances and

circumstances of use (Cherrie et al., 2003). Simplified categories were established and assigned to measurement data in order to support risk assessment of notified, new and existing substances used in industry in accordance with European directives and regulations (EEC, 1967, 1993a; EC, 2003a). This legislation has been superseded by the REACH Regulation, and EASE is no longer recommended for use within this regulation. However, it is discussed here, as EASE is the predecessor of other current models, such as ECETOC TRA and MEASE. A software version of this tool was available only for a few years. Unfortunately, the exact process of model development and the derivation of output ranges from measurement data are not documented.

6.2.3.2 *Underlying data basis, concept and derivation of dermal exposure estimates*

The model predictions of the dermal part of EASE are derived from measured exposure data obtained from the USEPA (Cherrie et al., 2003). The data sets are not publicly available.

In the tool, the user is confronted with a series of logical criteria that are used to identify the appropriate exposure estimate (see the EASE determination scheme in Fig. A3.1 in Appendix 3.3; EC, 2003a). EASE is designed as a decision-tree, and the corresponding values of four determinants can be chosen. The four determinants implemented in EASE to predict dermal exposure are:

1) the physical state: solid, liquid, gas/vapour
2) the pattern of use: closed system, inclusion into matrix, non-dispersive use and wide dispersive use
3) the pattern of control: direct or non-direct handling
4) the level of contact per day: none, incidental, intermittent and extensive.

The predictions are potential exposure of the hands and forearms, expressed as a mass per unit area of exposed skin per day ($mg \cdot cm^{-2} \cdot d^{-1}$), and dermal exposure loading per day, in five exposure ranges, from very low to 5–15 $mg \cdot cm^{-2} \cdot d^{-1}$. The effect of handwashing, evaporation or any other loss from the skin and the use of PPE are

not considered (Cherrie et al., 2003). It is also assumed that dermal exposure to gases and vapours is very low.

6.2.3.3 *Validation status*

In comparison with measured exposure estimates, the EASE tool appears to overestimate exposure in most cases. Several publications can be found; however, as the EASE tool is no longer recommended for use or publicly available, these are not further discussed here (Lansink et al., 1998; Bredendiek-Kämper, 2001; Hughson & Cherrie, 2005; Johnston et al., 2005; Kindler & Winteler, 2010).

6.2.4 MEASE

6.2.4.1 *General description and scope of application*

The Metals' EASE (MEASE) was developed in 2007 by EBRC Consulting, supported by Eurometaux (i.e. the EU association of the non-ferrous metals industry), in order to estimate exposure to metals and other inorganic substances (EBRC, 2007, 2010a). The tool was intended to be a screening tool for use under the REACH Regulation to counter perceived limitations of the ECETOC TRA tool (which focuses mainly on organic chemicals; see section 6.2.5) and EASE (which overestimates exposure; see section 6.2.3). General information on the development and the underlying data basis of MEASE is available (Hughson & Cherrie, 2003; EBRC, 2007, 2010a,b), yet the underlying algorithm has not been published.

6.2.4.2 *Underlying data basis, concept and derivation of dermal exposure estimates*

Available data on dermal exposure to a variety of zinc, lead, antimony and nickel compounds have been collated as part of the Health Risk Assessment Guidance for Metals project (EBRC, 2007). Dermal exposure assessment in MEASE is based on the categorization of the EASE model, but adapted to these measured data as a basis for the exposure estimates (see EBRC, 2007). The Health Risk Assessment Guidance for Metals fact sheet presents data on the likely upper limit of the loading range that can be achieved on the skin (EBRC, 2007).

Immersion of the hands of volunteers into zinc oxide dust resulted in very high skin loadings (approximately 700 $\mu g \cdot cm^{-2}$) (Hughson & Cherrie, 2003), which was considered to represent the worst possible case of exposure loading under workplace settings. Repeated contact of the hands with layers of zinc oxide on a work surface showed that the skin quickly becomes loaded with the material, and there was no significant increase in the dermal exposure loading with further contact. In contrast, contact with non-contaminated surfaces or washing before breaks might reduce the dermal loading over time.

In accordance with EASE, the physical form of the substance and the operational conditions are to be selected, including (see Fig. 16):

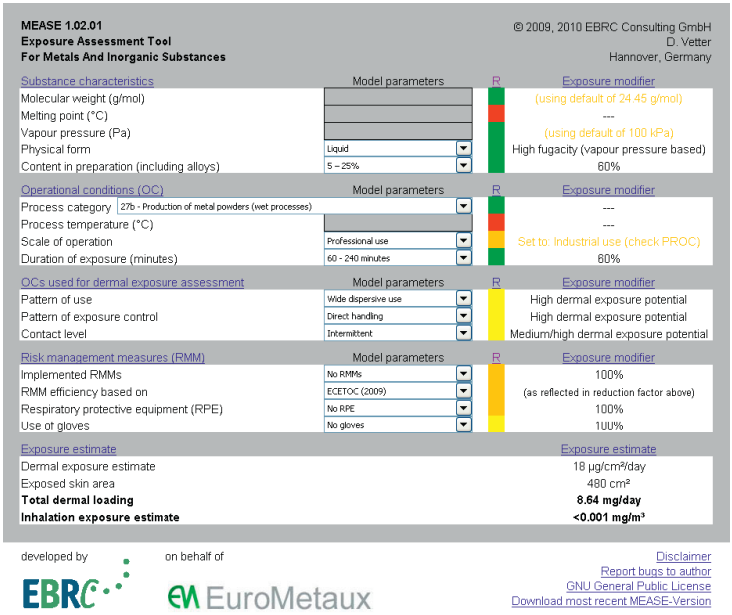


Fig. 16. Screenshot of the user interface of MEASE (column "R" gives the relevance indicator and shows in this example parameters in green[3] that are exclusively used for calculation of dermal exposure and in yellow the ones used for dermal as well as inhalation exposure outputs).

[1] The colour code is to be used with caution. For example, for liquids, the molecular weight and vapour pressure are relevant only for inhalation exposure, although it is indicated differently in the tool.

- physical form (options: massive, solid with ranges for dustiness, aqueous solution, liquid, gaseous)
- pattern of use (four options, ranging from "wide dispersive use" to "closed system without breaches")
- pattern of exposure control ("direct handling" or "non-direct handling")
- contact level (four options, ranging from "none" to "extensive", i.e. up to 10 events per day).

In contrast to the ECETOC TRA tool, the physical form gaseous can be selected, which leads to a lower loading rate. Each process category (PROC, according to chapter R.12 of *Guidance on information requirements and chemical safety assessment*; ECHA, 2010) is linked to a certain skin surface area. For the content in the preparation and the exposure duration, categorized exposure modifiers (ECHA, 2012b) are used to adapt the exposure estimate. Additionally, the use of gloves can be selected to adapt the exposure estimate. The glossary gives advice for the choice of (default) values, and the output is provided as "total dermal loading" for the specific exposed skin area, in milligrams per day (see Fig. 16).

6.2.4.3 *Validation status*

The MEASE tool has not been validated.

6.2.5 ECETOC TRA

6.2.5.1 *General description and scope of application*

In 2012, the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) developed the third version of the Targeted Risk Assessment (TRA) tool for exposure estimation as part of the REACH registration process (ECETOC, 2012). There are three TRA parts in an integrated version that allow the user to perform the assessments through a single interface: for occupational, consumer or environmental exposure assessment. Additionally, for consumers, there is a stand-alone version available. While the worker part integrates the dermal loading defaults of EASE, which were adapted by expert judgement to newer measurements if available, the consumer

part is mainly based on default values taken from fact sheets prepared by the Dutch National Institute for Public Health and the Environment (RIVM) (see below). The TRA tools are comprehensively described in the associated documentation (ECETOC, 2004, 2009, 2012). The underlying algorithm for the worker part is basically described, but not the derivation of the initial exposure values. The primary purpose of ECETOC TRA within REACH is to act as a screening tool to help identify which substances require a more detailed evaluation of exposure.

6.2.5.2 *ECETOC TRA tool for occupational dermal exposure (workers[1])*

The TRA tool for dermal exposure of workers (see Fig. 17) is based on the EASE concept (see section 6.2.3). Dermal exposure is given as a point estimate for several scenarios, as defined by task descriptions (process categories, i.e. PROCs; including PROCs 1–25) according to chapter R.12 of the REACH technical guidance document (ECHA, 2010). Each PROC is linked to a dermal exposure loading value derived by the EASE model (in $mg \cdot cm^{-2} \cdot d^{-1}$) if not adapted due to the experience of the model builders (expert judgement) or further available information (e.g. exposure to metals, as published in EBRC, 2007; see ECETOC, 2009). Furthermore, each PROC is assigned to a certain skin surface area depending on the body part that is considered relevant (ranging from 240 cm^2, i.e. palm of one hand, to 1980 cm^2, i.e. both hands and forearms).

In addition, further parameters can be selected that influence the exposure estimation. Similar to EASE, the presence of (local) exhaust ventilation (LEV) influences the dermal exposure estimate outcome (version 3 of TRA predicts LEV efficiencies ranging from 75% up to

[1] It should be noted that the term "worker" in the REACH context is used differently from its use in other regulatory environments (e.g. agricultural pesticide regulation in the EU, which differentiates between "worker" and "operator"; see section 6.2.11). Here, the term "workers" relates to any kind of occupational personnel and is further specified as "industrial users" or outside an industrial setting as "professional users" to reflect the typical conditions of use. For example, a worker undertaking spray painting in an automotive plant is termed an "industrial user", but a construction worker spray painting a bridge is termed a "professional user" (ECHA, 2012c).

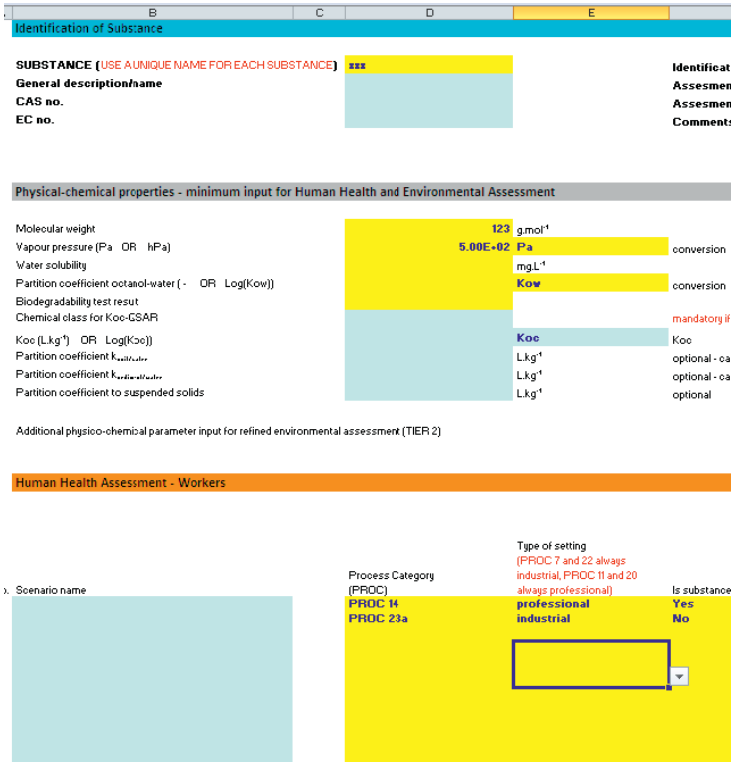


Fig. 17. Screenshot of the user interface of the TRA tool (version 3, integrated version for workers, consumers and the environment, worksheet tab “interface”).

95%; ECETOC, 2012). For the concentration of a substance and the process duration, non-linear exposure modifiers (ECHA, 2012b) are used to adapt the exposure estimate. For the dermal exposure model, the duration modifiers are applicable only to liquids of high or medium volatility and to non-dusty solids, as dusty solids and non-volatile liquids are assumed to stay on the skin, even after the source of exposure is no longer present. Because of the connection between duration and volatility, duration is also influenced by the vapour pressure of a liquid and the process temperature (ECETOC, 2012). In addition, the tool offers the possibility to refine exposure estimates by addressing PPE (e.g. gloves with a maximum efficiency of 95%; ECETOC, 2012).

The resulting dermal exposure mass is then converted into a systemic dose relating to a standard 70 kg person and assuming 100% dermal absorption (expressed in mg·(kg bw)$^{-1}$·d^{-1}; ECETOC, 2009). It should be noted that this resulting output is simply called "exposure" in the tool itself, as well as guidance reports.

The TRA tool for workers has not been validated. It is supposed to have some of the limitations of EASE (e.g. it is not possible to estimate exposure to mists or process fumes). A summary of exposure situations outside of the applicability domain of version 3 of TRA is published in ECETOC (2012).

6.2.5.3 *ECETOC TRA tool for dermal exposure of consumers*

The TRA dermal exposure tool for consumer exposure is based on a set of product categories (PC) and article categories (AC) that are described in chapter R.12 of the REACH technical guidance document (ECHA, 2010). Predetermined values (defaults) for each parameter are fixed in the tool, depending on the choice of the product or article (see below). Default values were taken from RIVM fact sheets (Delmaar et al., 2005) for various subcategories, which represent a further subdivision of the relatively broad PCs and ACs. Furthermore, the tool enables the user to create new subcategories, which can be used to adapt the ECETOC algorithm to specific products or articles that are not yet reflected by the implemented default values (ECETOC, 2012). In addition, the user is able to modify the fraction of the substance of interest in the product or article, together with the dermal exposure surface area. The user interface is shown in Figure 18.

The same basic algorithm is used for each scenario to calculate the potential dermal exposure. The resulting exposure is converted into a systemic dose (called "systemic exposure unit" by the tool) for a 60 kg person, expressed in milligrams per kilogram body weight per day (ECETOC, 2009). The model uses 100% dermal absorption as a default; however, if relevant information is available, this parameter can be adjusted by the user (in contrast to defined terminology in Appendix 1, this parameter for absorption is called "dermal transfer factor" in this tool; ECETOC, 2012). Thus, the potential dermal exposure is set equivalent to a worst-case assumption of a resulting

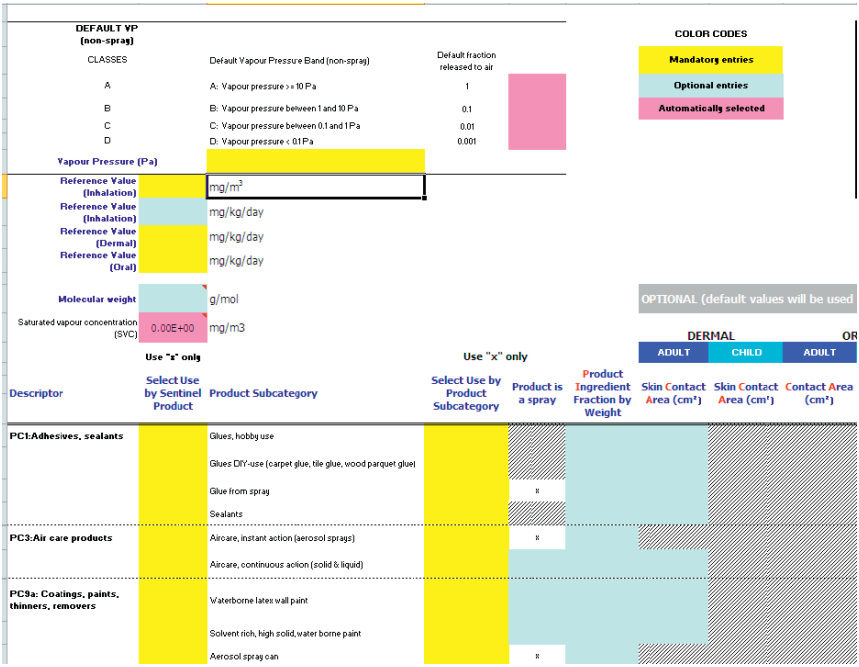


Fig. 18. Screenshot of the user interface of the TRA tool (version 3 for consumers, stand-alone version, worksheet tab “user input”).

systemic dermal dose. It should be noted that in the tool, these definitions are not differentiated, and the resulting value (worst-case systemic dose) is simply called “exposure” in the spreadsheets.

The dermal TRA tool for consumers has not been validated. However, because it is based on conservative assumptions, it is likely to overestimate actual exposure.

6.2.6 *RISKOFDERM*

6.2.6.1 *General description and scope of application*

Data on the RISKOFDERM project were used as the basis for the development of the tool RISKOFDERM for expert exposure assessors (this section) as well as a second tool, the RISKOFDERM Toolkit (see section 6.2.7.1), to provide advice to small and medium-sized companies (Auffarth et al., 2003; Goede et al., 2003; Oppl et al., 2003; Schuhmacher-Wolz et al., 2003; van Hemmen et al., 2003; Warren

et al., 2003, 2006; Oppl, 2004). The RISKOFDERM tool, including the complex algorithms, is provided, along with a detailed guidance document describing its use. The models of the tool are based on measurements, yet the estimation is not reproducible without the tool, nor is it comprehensible without extended expert knowledge (Warren et al., 2006).

6.2.6.2 *Underlying data basis, concept and derivation of dermal exposure estimates*

Within the RISKOFDERM project, the underlying data were obtained for tasks that make up a workday. This project involved the collection of dermal exposure measurements in five different European countries over the period 1996–2006 and includes more than 500 data sets for hand exposure and more than 600 data sets for body exposure. The data cover a wide range of industries and workplaces, which are listed in Warren et al. (2006) (e.g. mixing antifouling paint, loading zinc oxide, brush application of *N*-methyl-2-pyrrolidone, electroplating). It is assumed that dermal exposure can be extrapolated from one compound to another when it is task based (van Hemmen et al., 2003). Thus, tasks were assigned to one of six so-called dermal exposure operation (DEO) units, where each unit is a cluster of exposure scenarios (Marquart et al., 2006), judged to be more or less similar, and exposure routes for which similar relationships between potential dermal exposure and exposure determinants were expected (see section A3.2.1 and Table A3.7 in Appendix 3). The DEO units are presented in Table 30.

"Handling of contaminated objects" (original definition of DEO 1 in Warren et al., 2006) is clearly the most broadly defined within the six DEO units, and the predominant part of its available exposure data represents only a small subset of the included scenarios. Therefore, DEO 1 was renamed "mixing, filling, loading", as it presents only this subset.

Warren et al. (2006) described the development of the modelling tool for expert exposure assessors. They used the exposure data and adjusted the data in the form of mass or volume of product on skin per unit of time throughout the tasks. For this, they used the implicit

Table 30. Dermal exposure operation (DEO) units of RISKOFDERM[a,b]

DEO no.	DEO unit / generic DEO	Exposure route	Description / example tasks
1	Handling of contaminated objects / mixing, filling, loading[1]	Contact with contaminated objects and surfaces, but also aerosols; some direct contact or immersion may occur[2]	Transferring a product from one container to another: Weighing of powders, dumping of powders from bags or drums, pumping/pouring/ scooping of liquids or pastes, etc.[3]
2	Wiping[4]	Predominantly through direct contact, surface contact	Spreading product over the surface (tool without handle): Wiping surfaces with a liquid (preparation) using a sponge, cloth or rag[5]
3	Dispersion with hand-held tools	Mostly due to contact with contaminated surfaces; also some direct contact via splashing or dripping	Spreading product over the surface (tool with handle): Dispersion of products/substances using a brush, comb, rake or roller[6]
4	Spraying[7]	Aerosols and contact with contaminated surfaces are major sources of exposure[10]	Spray application: Spraying of products such as paints, glues, cleaning agents (hosing down with water using a normal water line under normal pressure is not included)[8]
5	Immersion	Direct contact and contaminated surfaces	Immersing objects: Exposure is to chemicals in which the object is immersed, not the ones coming from the object itself[9]

Table 30 (continued)

DEO no.	DEO unit / generic DEO	Exposure route	Description / example tasks
6	Mechanical treatment	Aerosols and contact with contaminated surfaces[10]	Treatment of solid objects: Emission of substances from objects due to treatment (e.g. wood dust) or to substances used in the process of treatment (e.g. metalworking fluids)[11]

[a] From Warren et al. (2006).

[b] Differences from the DEO units used in the tool BEAT (see section 6.2.8) are presented as well:

1 DEO unit (named in BEAT): Unsealed transfer of substances (in RISKOFDERM, the DEO 1 model is applicable only to hand exposures; Warren et al., 2006)

2 Exposure route (additionally): Exposure occurs through direct contact (splashing), aerosols not named (additionally named in BEAT to the ones above)

3 Description (additionally): Mixing, loading, filling (into bags, drums, small containers, etc.), pouring, diluting (additionally named in BEAT to the ones above), powders not named; excludes direct handing of a substance with the hands

4 DEO unit (named in BEAT): Handling of contaminated objects

5 Exposure route (additionally): Handling of contaminated containers or other objects (including manual transportation), direct handling of pellets or granules (additionally named in BEAT to the ones above)

6 Description (additionally): Sweeping, mopping, scrubbing (additionally named in BEAT to the ones above)

7 DEO unit (named in BEAT): Spray dispersion

8 Description in BEAT: Spraying, misting, fogging, showering; dusting, powder coating

9 Description in BEAT: Manual/semiautomated dipping, galvanizing

10 Exposure route: Deposition of dust or aerosol, surface contact

11 Description in BEAT: Cutting, drilling, sawing, edging, milling, grinding, abrading

assumptions that exposure increases linearly with time throughout the tasks and that the concentration of the hazardous substance within the product is proportional to the exposure; in other words, product exposure is estimated with RISKOFDERM, and later the weight percentage of the active substance can be considered manually by the user. The tool is designed to provide estimates for solids and liquids; however, due to the limitations of the underlying data sets, both aggregate states are not implemented for all DEO units (DEO units 2, 3 and 5 are applicable only for exposure to liquids).

Six separate models (equations) were established for each DEO unit. Within each, linear mixed effect statistical models were used to estimate the influence of a range of relevant exposure determinants (see section A3.2.1 in Appendix 3) and to estimate components of variance. The models are designed to predict median potential dermal exposure rate for the hands and for the remainder of the body from the values of these relevant exposure determinants. These rates are expressed as milligrams or millilitres of "in-use" product per minute. Using these median potential dermal exposure rates and an estimated geometric standard deviation allows a range of exposure percentiles to be calculated.

All are fitted to the measured exposure values corresponding to the specific DEO unit, which are included in the underlying database. For each of the determinants (α_n, called "fixed effects") within a DEO unit listed in Table 31, certain values are modelled, which represent the change of the mean log-transformed potential exposure α_0 induced by the corresponding determinant. Duration of exposure is implemented with a linear function between dermal exposure and duration. Viscosity for liquids is further subdivided into oil-like and syrup-like.

Depending on the DEO unit, different determinants are included in the calculation (see Table 31; a more detailed table, including the different options for a determinant, is presented in section A3.5 in Appendix 3; see also section A3.2.1 in Appendix 3). The different number of determinants is related to the varying number of underlying data sets for the different DEO units. For DEO 4 (spray dispersion model), the largest data sets (475 data covering 10 scenarios) were available; this model has the greatest number

Table 31. Exposure determinants and the DEO unit to which they apply in RISKOFDERM and BEAT[a]

Determinant	DEO unit (RISKOFDERM)	DEO unit (BEAT)
Physical state of formulation (in BEAT, further determinants are "particle size" and "particle wetness")	1, 4, 6	1, 2, 3, 4, 5, 6
Aerosol generation	1	1, 2, 3, 4, 5, 6
Viscosity	3	1, 2, 3, 5, 6
Volatility	4	4
Work environment (confined/restricted space)	4	2, 3, 4, 6
Automation	1	1, 5
Ventilation	1, 4, 5	1, 3, 4, 6
Liquid-based dust control	Not included	6
Kinetic energy	Not included	1, 6
Spray pressure	Not included	4
Segregation	4	4, 6
Surface area of contact	2, 3, 4, 5	2
Kind of skin contact	1	Not included
Level of contamination	Not included	2
Frequency of contact	1, 6	2
Application/use rate[b]	1, 2, 3, 4	1, 3, 4
Distance to source (proximity, length of tool handle)	3, 5	3, 4, 6
Orientation	3, 4	3, 4
Duration[b]	1, 2, 3, 4, 5, 6	1, 2, 3, 4, 5, 6

[a] From Warren et al. (2006); BEAT (2011).

[b] Application rate and duration are called "continuous parameters" in RISKOFDERM, and their ranges are presented in section A3.4 in Appendix 3.

of exposure determinants, with several having quite modest effects (Warren et al., 2006). In contrast, the immersion model (DEO 5) incorporates only the determinants "proximity" and "ventilation" (additionally to duration and application rate) and is as well the least satisfactory model, having large residual errors for both the hands and the body. Models that can predict both body and hand exposures could be developed only for DEOs 2–5; in DEO 6, for example, no potential

hand exposure measurements were available for modelling (Warren et al., 2006; see section A3.4 in Appendix 3).

It is possible to create an overview of the finished exposure assessment, including a summary of the input determinants and exposure results for different percentiles, in written and graphical form by using the button "overview results" (Fig. 19). Moreover, several "rules of thumb" were extracted from Warren et al. (2006), which are summarized in Table 32 and may give the user a better overview of the influence of the different determinants within the tool (see also section A3.2 in Appendix 3).

The tool clearly identifies the limitations of the range of input determinants, which reflect the underlying database that was analysed. It also highlights when outputs are likely to exceed what is credible (i.e. warnings will show up in the tool). In addition, the authors realize that the tool is based on relatively small data sets from a limited number of workplaces, with high correlation between many of the determinants. Moreover, the sampling methodology used to collect the basic data could not be standardized, for various reasons. For example, Hughson & Aitken (2004) used cotton gloves and patches to collect samples for their wiping tasks, whereas Fransman

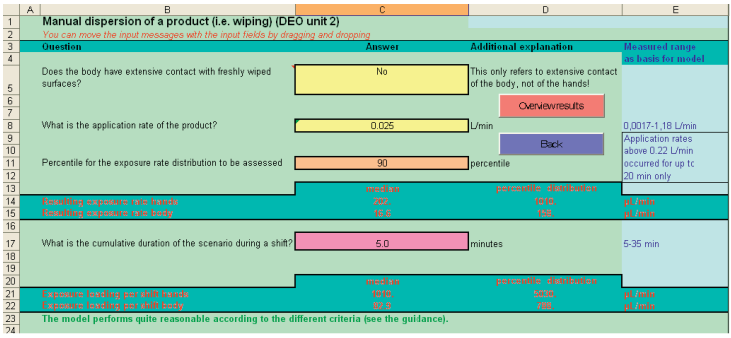


Fig. 19. Screenshot of the user interface of RISKOFDERM (wiping model)[1].

[1] The unit of the resulting "exposure loading per shift" should probably be given as "exposure volume per shift" in µl instead of µl·min^{-1}, assuming a programming error in the tool.

Table 32. Influence of different determinants

DEO unit	Determinant	Exposure change factor
1 Mixing, filling, loading	Solid → liquid Less dusty → highly dusty More than light contact → light contact More than rare contact → rare contact	~30 >7 ~2/3 ~2/3
2 Wiping	Ventilation Hand exposure → body exposure	No effect ~1/10
3 Dispersion using a hand-held tool	Hand exposure → body exposure Tool >30 cm in length → tool <30 cm in length	~10 ~3
4 Spraying	Hand exposure → body exposure Spray pressure	~5 No effect
5 Immersion	Hand exposure → body exposure Proximity 30–100 cm → proximity <30 cm Proximity 30–100 cm → proximity >100 cm LEV	~1/10 ~5 ~1/5 ~1/4
6 Mechanical treatment of objects	Liquid → solid LEV Viscosity	~7/100 No effect No effect

LEV, local exhaust ventilation

et al. (2004) used a mixture of handwashing, wiping, cotton pads and analysis of protective gloves as sampling methods in their study. The non-standard methodologies will have added unknown biases to the data set. Moreover, substances with high vapour pressures are not present in the database, so evaporation from the skin is not taken into account.

6.2.6.3 *Validation status*

The RISKOFDERM tool has not been validated. However, all available dermal exposure measurements and details for the exposure situations were incorporated into the tool. When situations are outside the range of the measured data sets, the user is warned. A small set of data points was used for a benchmark study that gave reasonable

results and was used for a comparison of the performance of the different (DEO-specific) models (TNO, 2006). Details of this study and valid ranges for continuous parameters (use rate and duration) are provided in section A3.4 in Appendix 3. Data points used for this benchmark study were later included in the database used for model fitting (TNO, 2006; Warren et al., 2006). Concerning the sizes of data sets for separate DEO units, limitations of each data set and the quality of performance, a detailed overview is provided in Warren et al. (2006) and TNO (2006).

6.2.7 Control banding tools based on the RISKOFDERM project

In order to provide small and medium-sized companies with a general ranking tool to classify and identify possible hazards, "control banding" approaches are available that focus mainly on risk prioritization and risk management measures. They centre around a series of questions about the substance and the way it is handled. Their output provides general advice in relation to the necessity for changing the working environment (the outcome may be "no action needed" or "stop working with the chemical") but does not provide quantitative estimates. Popular control banding tools are the United Kingdom's Control of Substances Hazardous to Health Regulations (COSHH) Essentials (Garrod & Rajan-Sithamparanadarajah, 2003; HSE, 2011a), the RISKOFDERM Toolkit (Oppl et al., 2003), Stoffenmanager (Dutch Ministry of Social Affairs and Employment, 2013) and the German workplace control scheme, or EMKG (BAuA, 2011b; Kahl et al., 2011).

In the following sections, the RISKOFDERM Toolkit and Stoffenmanager are briefly described, as both of these are based on the RISKOFDERM project. However, both use a very conservative approach, which suggests that exposures and risks are much higher than they are likely to be in practice. Further information considering control banding in general can be found in the review of Zalk & Nelson (2008) and other references (Jayjock et al., 2000; Hashimoto et al., 2007; ACGIH, 2008; Marquart et al., 2008; Paik et al., 2008; Zalk & Nelson, 2008; Bracker et al., 2009; E.G. Lee et al., 2009; Nelson & Zalk, 2011).

6.2.7.1 RISKOFDERM Toolkit

The RISKOFDERM Toolkit (version A 1.11 UK-03/2004) is designed to provide advice on risk management measures to non-experts (Oppl et al., 2003). It is implemented in a Microsoft Excel spreadsheet with associated supporting documentation and is freely available on the Internet (version A 1.11 is available on the Eurofins website: Eurofins, 2004). Although, like RISKOFDERM, it is based on data from the RISKOFDERM project and on the six DEO units (see above), the RISKOFDERM Toolkit uses modifiers based on incremental log scale instead of linear mixed effect models to estimate exposure, and its structure of use differs in many respects from that of RISKOFDERM (e.g. skin areas other than hands, time is categorized) (Cherrie et al., 1996).

The user has to provide information about the hazard of the substance (R-phrases), the exposure loading rates ($mg \cdot cm^{-2} \cdot h^{-1}$) for a given DEO unit as described by Warren et al. (2003), the dermal exposure period and the dermal exposure surface area. Separate algorithms, both relying on initial exposure values and a set of modifiers (e.g. for clothing, duration of activity), are provided for local and systemic effects from chemicals (Goede et al., 2003; Oppl et al., 2003). Finally, the tool provides a categorical output on a 10-point scale, coded from 1 (= no action needed) and 2 (= no special measures to be taken—basic skin care) through to 10 (= substitute and stop working with the chemical).

The developers recognized the limitations of their approach and the uncertainty associated with the input data and therefore the output. As a consequence, they had aimed to provide "a rough estimate of dermal risk in very broad categories". The tool is not recommended for chemicals that constitute a severe hazard (i.e. R45 = May cause cancer and R46 = May cause heritable genetic damage). No validation of the toolkit has been published.

6.2.7.2 Stoffenmanager

Stoffenmanager (version 5.0, 2013) is a Dutch control banding tool that has been developed to provide advice for small and medium-sized companies. Stoffenmanager is a web-based tool (Zalk & Nelson, 2008;

Dutch Ministry of Social Affairs and Employment, 2013). Moreover, an instruction film is provided in an attempt to make the tool accessible to anyone interested in using it.

The core of this module is the RISKOFDERM Toolkit (see section 6.2.7.1). The tool is designed to use categorical estimates of exposure (in categories from 1 for "negligible" to 6 for "extreme") and hazard (in categories from A for "low" to E for "extreme") to provide the final outcome as one of three risk categories, from "low" to "high". For this, the tool asks for basic information about the toxicity of the substance, which of the RISKOFDERM DEO units the task falls within (see sections above), the work, the size of the work environment and the presence of any protective clothing. No validation of this tool has been published.

6.2.8 BEAT

6.2.8.1 General description and scope of application

The Bayesian Exposure Assessment Tool (BEAT) was originally developed in 2002 by the United Kingdom's HSE for experienced assessors undertaking regulatory risk assessments carried out in connection with the European Biocidal Products Directive (EC, 1998a), as recommended in the Technical Notes for Guidance (TNsG) on Human Exposure to Biocidal Products (TNsG, 2007; BEAT, 2011). BEAT provides the option to search for appropriate generic data (suitable indicative exposure estimates) based on (task) analogy with measured exposure data. In addition, the software offers a hierarchical Bayesian model for probabilistic predictions by using various analogous data sets in a single exposure distribution. In addition, if sufficient data for an analysis are available, BEAT offers further statistical tools (e.g. Markov Chain Monte Carlo analysis). A feature of BEAT is that users are not restricted to using exposure values extracted from the measurement database; instead, the user may insert other data. Moreover, BEAT provides a visualization of the spatial distribution of dermal exposure of the body using three-dimensional mapping (IGHRC, 2010). General information about the development and the underlying concept are provided in the help files integrated in the tool, but details about the underlying algorithm are not publicly available.

6.2.8.2 *Underlying data basis, concept and derivation of dermal exposure estimates*

The BEAT database contains measured exposure data for a wide range of occupational exposure scenarios relevant to biocides (for definition, see Appendix 1), including full contextual information on every measurement (TNsG, 2007). Many of the underlying measurements in BEAT are the same as those underpinning the 2002 TNsG; however, their treatment differs, and significant errors have been omitted (e.g. excluding outliers from the data) (Warren, 2009). Further data included in the database were HSE biocide data, RISKOFDERM data, some data from the Dutch Organization for Applied Scientific Research (TNO) and an Austrian wood preservative study. The implemented data were selected based on the tool builders' expertise; for example, EUROPOEM (see section 6.2.11.5) mixing and loading of agricultural studies were excluded (Warren, 2009).

The user may choose from an existing worked example of the database or create an individual exposure scenario by inputting information on product characteristics, task-specific exposure information and details about the work environment and control measures (refer to a more detailed table providing all selectable options per determinant in section A3.5 in Appendix 3). BEAT accordingly groups this scenario description in one of the six generic task groups (DEO units)—that is, general categories of tasks reflecting the potential for exposure. Although the DEOs were devised as part of the RISKOFDERM project (van Hemmen et al., 2003), modifications concerning the naming of some DEOs as well as the inclusion of a slightly wider range of tasks have been defined for BEAT (see Table 30 in section 6.2.6).

In order to search the database for analogous exposure data, the program compares the information provided with existing scenarios in the database by the use of a task-based search algorithm.

BEAT uses a five-stage hierarchical algorithm for assessing the degree of analogy (explained in more detail in the following paragraphs; for further information, see section A3.7 in Appendix 3):

1) discarding all measurements of a different physical state;
2) assigning uncertainty factors (UFs) to differences in each of the relevant exposure determinants (see Tables A3.8 and A3.11 in Appendix 3) based on an internal rule base developed from a survey of the opinions of occupational hygienists and experts in dermal exposure assessment;
3) combining the UFs into an overall UF for each measurement, taking into account the time spent on different tasks;
4) taking the overall UF as the arithmetic mean of the UFs for all measurements within the data, rounded to the nearest integer;
5) providing the five most analogous data sets with UFs less than 50.

An example is the UF for the determinant "contamination of objects", related to DEO 2. When, for the scenario to be assessed, a "dry contamination surface" is chosen in contrast to a "damp contamination surface" provided in the scenario of the database, a UF of 10 (for the body) is assigned. This value would increase correspondingly if the determinants decreased in similarity (e.g. a UF of 50 for the difference between "touching a dry contamination surface" and "touching a wet or saturated contamination surface"). Thus, a UF of 10 does not represent the belief that exposures are expected to be 10 times higher or lower; rather, it represents how likely it is that scenarios will be different due to a different determinant. In other words, a UF of 10 represents the belief that exposures are not likely (90% confidence) to differ by more than a factor of 10 when this determinant is changed.

According to steps 3 and 4, UFs are combined into an overall score when scenarios differ in more than a single determinant, also considering differences in the time spent on tasks between scenarios. By default, the search algorithm displays a maximum of five analogous scenarios from the database, ranked according to their similarity (step 5 above). The strength of analogy is indicated by the UF. The authors advise the user to keep in mind that a UF reflects scenario uncertainty only and does not incorporate the statistical uncertainty determined by the sample size. A larger but less analogous data set may be preferable to higher-ranked but smaller data sets. In addition, the authors claim that the current algorithms do not take account of the toxicity of the products handled or differentiate between the sampling (measurement) techniques on which the data are based.

For each of the five analogous scenarios from the database, further information is available to support the user in choosing an adequate scenario (e.g. reference, photographs or scenario description details). Percentiles of the indicative potential exposure estimates (measurements) for hands or body exposure of the selected scenario are presented as parametric estimates (in $mg \cdot min^{-1}$) based upon a fitted lognormal distribution. In addition, non-parametric estimates may be derived from the displayed list of measured exposures (see Fig. 20). BEAT advises the user as to which percentile should be used and offers the option of generating a summary report, including a calculated systemic body dose, exported in Microsoft Excel format.

Additionally, the software offers a hierarchical Bayesian model to integrate the various analogous data sets into a single exposure

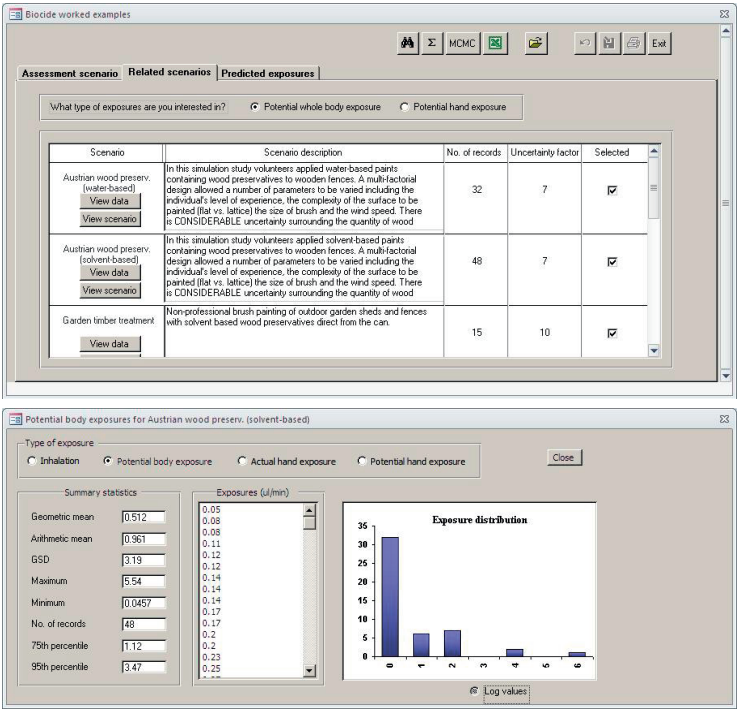


Fig. 20. BEAT's proposal for related scenarios for "Disinfection using a mop" (above) from which the user can choose and potential body exposure for selected scenario "Austrian wood preserv. (solvent-based)" (BEAT, 2011).

distribution instead of picking an indicative exposure estimate based on the best analogous data set (as described above). For this, the user may select or dismiss several of the analogous data sets for the exposure assessment, which may exert a strong influence on the final output (and thus should be applied with care). The most appropriate distribution for the assessment scenario is shown in relation to the indicative distribution approach of Phillips & Garrod (2001) (see section A3.6 in Appendix 3; the 50th, 75th or 95th percentile). When better-fitting data for dermal exposure estimates are available, the predicted potential dermal exposure estimates change correspondingly from the Phillips & Garrod (2001) values. In addition, advanced users may use an integrated Markov Chain Monte Carlo analysis tool, providing a full characterization of uncertainty for the geometric mean and geometric standard deviation. Another alternative is to pool two or more data sets and the percentiles of the combined data set to provide indicative exposure values (appropriate only if all data sets relate to very similar exposure scenarios).

6.2.8.3 *Validation status*

The BEAT dermal exposure tool has not been validated.

6.2.9 *ConsExpo*

6.2.9.1 *General description and scope of application*

The CONSumer EXPOsure tool (ConsExpo) was developed by RIVM. It allows users to estimate exposure to agents (chemicals) contained in consumer products for indoor uses. The first version that integrated dermal exposure was published in 2001 (version 3.0) The tool is recommended, for example, for use in connection with the European Biocidal Products Directive (EC, 1998a) (see Technical Notes for Guidance on Human Exposure to Biocidal Products; TNsG, 2007), the European REACH Regulation (ECHA, 2012a,b) and the Canadian Environmental Protection Act, 1999 (Government of Canada, 1999). The models integrated in ConsExpo assume task-based direct contact of a product with the skin, depending on the type of the application/exposure. ConsExpo offers deterministic or probabilistic exposure assessments. Background information about the algorithms used and the default values is provided

in the user guidance manuals and several RIVM fact sheets (van Veen, 2001; Bremmer & van Veen, 2002; Delmaar et al., 2005; Bremmer et al., 2006a,b,c; Prud'homme de Lodder et al., 2006a,b; Bremmer & van Engelen, 2007; ter Burg et al., 2007).

6.2.9.2 *Underlying data basis, concept and derivation of dermal exposure estimates*

In ConsExpo, direct dermal contact with a product is assumed. The implemented models are based on the concept of mass balance and comprise a set of five different dermal loading scenarios from which the user can choose (Delmaar et al., 2005). These are:

1) instant application of product to the skin;
2) constant rate of application to the skin;
3) transfer from surfaces by rubbing off;
4) migration[1] from a surface in contact with the skin;
5) diffusion from a surface in contact with the skin.

The instant application (1) and constant rate of application (2) scenarios rely on the assumption that the total content of a product is loaded on the skin, either as a single event (1) or as continuous action (2). The transfer by rubbing off scenario (3) is used for treated surfaces and is based on the idea that a certain amount of the applied product is rubbed off by direct contact with the surface. The migration scenario (4) describes the transfer of a substance from a product to the skin due to dermal contact (e.g. exposure to dyes in clothing that may leach onto the skin). The diffusion scenario (5) describes the situation where a viscous product is applied to the skin and the substance of interest subsequently diffuses through the product to the skin. The equations for the dermal exposure loading of each scenario are presented in detail in the manual of the tool. However, further detail about the development and the background of the algorithms for modelling (e.g. if actual measured data have been used) is not documented.

[1] The definition in ConsExpo is different from the general terminology used in this document, which differentiates between "transfer" (= transfer to skin) and "migration" (= possible amount on surface that is available for transfer, for example, due to leaching out of the product); see section 5.2.

Depending on the chosen scenario (model), the input of specific exposure parameters is required. A parameter that needs to be defined for all modes is the surface area of the skin that is exposed to the product. In other cases, very specific data can be required that may be difficult to obtain. For such circumstances, the tool is equipped with a database of default products for which exposure scenarios have been defined, and default values for the model input have been compiled from the literature (see Fig. 21). A judgement about the quality of the provided default parameters is provided by the tool builders, and the quality of each value is described by four categories (from "good quality data, parameter value reliable" to "no relevant data, parameter value only based on expert judgment").

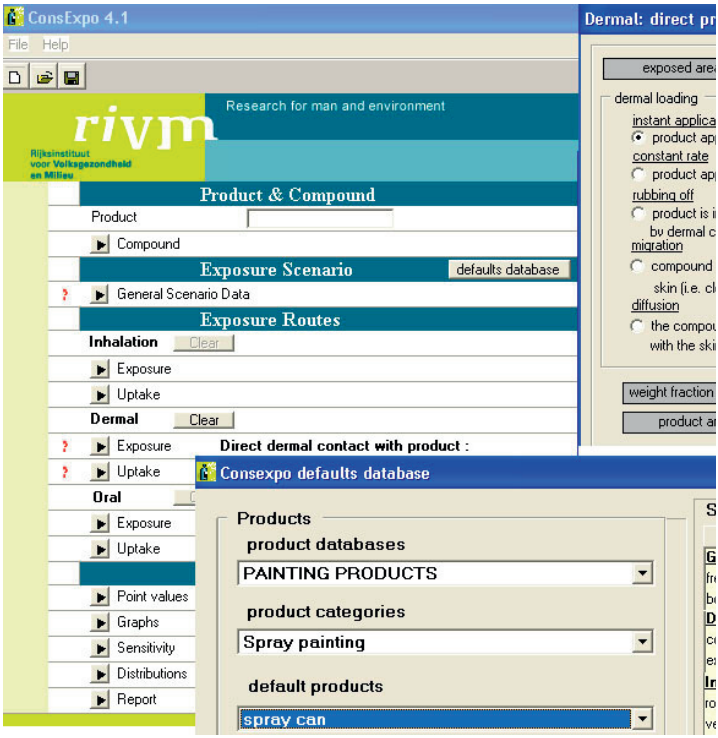


Fig. 21. Screenshots of the user interface of ConsExpo.

This database should be considered as a starting point for the exposure assessment, as the applicability (domain) and source of the provided defaults are not apparent. As these may be substance specific and based on specific data (e.g. limited to compounds in aqueous solutions), the user is asked to verify the choice for provided defaults by looking up the information in the manual and fact sheets. In addition, the user should keep in mind that the tool is based on specific scenarios that have been defined for the use of paints, pest control products, toys, cosmetics, cleaning products and disinfectants.

A more specific assessment can be performed using more relevant data (if available), providing the user with flexibility in terms of changing the default values. In contrast, the inexperienced user may have difficulty in choosing the appropriate values, if fixed values are not available. Moreover, ConsExpo enables the user to perform either deterministic or probabilistic exposure assessments, in the latter case with the user selecting one of four alternative distributions.

6.2.9.3 *Validation status*

The ConsExpo dermal exposure models are simple valid representations of the relevant exposure processes. There is no published assessment of the validity of the dermal exposure models.

6.2.10 *SprayExpo*

6.2.10.1 *General description and scope of application*

The SprayExpo tool is based on a model to predict exposure to products during spray application of a non-volatile active substance dissolved or dispersed in a volatile solvent (Koch, 2004). It was originally developed by the Fraunhofer Institute for Toxicology and Experimental Medicine (Germany) for the German Federal Institute for Occupational Safety and Health (BAuA) for the evaluation of biocidal products (see definition in Appendix 1). SprayExpo calculates the airborne concentration of spray aerosols in indoor environments and then estimates the dermal exposure by calculating the deposition onto the body. The model is clearly described in the documentation

(Koch et al., 2012), although the calculations made by the software tool are complex.

6.2.10.2 *Underlying data basis, concept and derivation of dermal exposure estimates*

SprayExpo is based on a simulation of the motion of released droplets, taking into account gravitational settling, turbulent mixing with the surrounding air and solvent evaporation. A droplet deposition module is incorporated for surface treatment by spraying, which calculates the fraction of non-impacting droplets that are relevant for human exposure (BAuA, 2012a). SprayExpo has been recently revised to incorporate an improved droplet impaction module for calculating the overspray during spraying onto a surface (i.e. the fraction of droplets that are not deposited onto the surface) (Koch et al., 2012). The main input parameters are the released droplet spectrum, the release rate, the concentration of the active substance, the spatial and temporal patterns of the release process, the vapour pressure of the liquid, the size of the room and the ventilation rate (see Fig. 22; BAuA, 2012a). In version 2.0, simple process parameters (e.g. spraying pressure) and the primary droplet distributions are provided in a database from which they can be retrieved by selecting a common spraying technique. In addition, the path of the sprayer can be explicitly included in the model by selecting different release patterns with detailed information about the target of the spraying process and the sprayer's position (spraying along a line on a wall, spraying a wall area, spraying a ceiling, spraying the floor or room spraying; see "application pattern" in Fig. 22; BAuA, 2012a).

Dermal exposure is provided as total mass of sprayed aerosol deposited on the body (mg) per application (spraying event) at a specific point in time by sedimentation (it is assumed that 10% of the body surface is horizontal) and by turbulent diffusion using the calculated air concentration. In addition, SprayExpo provides an assessment report in which the deposition rate is presented graphically as a function of time. Additional presented outputs are the average dermal exposure mass deposition rate ($mg \cdot s^{-1}$) per application as well as the total dermal deposition mass over time. However, in the tool itself, the total dermal exposure mass is called "dermal dose". As these values

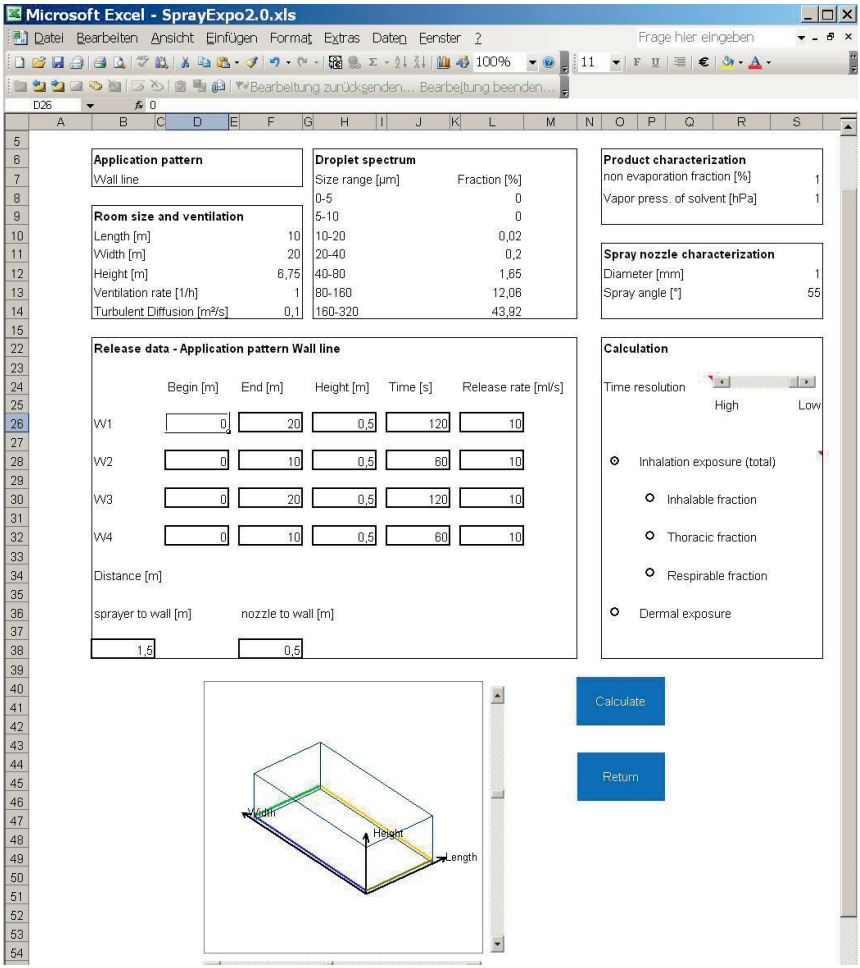


Fig. 22. Screenshot of the user interface of SprayExpo 2.0.

depend on the aerosol concentration in the air and the deposition onto the body, they are directly correlated to the application pattern.

6.2.10.3 *Validation status*

The model was recently evaluated by a sensitivity analysis (e.g. influence of vapour pressure of solvent, distance of nozzle from wall)

and by comparison with measured values when applying different spraying techniques (Koch et al., 2012). For dermal exposures, the model can take into account the deposition of the active substance on the body surface only by aerosol settling (sedimentation flow of the airborne droplets), but does not include accidentally occurring splashes. As a result, dermal exposure at the workplace is in most cases underestimated by the SprayExpo model. In contrast, the comparison of modelled predictions with measured values at real workplaces demonstrates that SprayExpo is appropriate for assessing exposure during indoor spraying processes. It is acknowledged, however, that the model must be used by those possessing the necessary technical expertise. In addition, it should be noted that the models used in SprayExpo have been developed for spraying processes using products containing non-evaporating substances in indoor environments only and that long-term emissions of vapours from walls and other surfaces are not included.

6.2.11 Pesticide operator models

The implementation of authorization procedures for pesticides has also triggered the development of exposure models and tools. The term "pesticide" refers to any substance intended for preventing, destroying, attracting, repelling or controlling any pest. In the EU, the term pesticide relates to two regulatory authorization frameworks, one for non-agricultural pesticides (biocides) and the other for agricultural pesticides (plant protection products) (for terminology, see Appendix 1). In this section, models and tools relating to agricultural uses of pesticides regulated by the authorization procedures of the USA and the EU are presented.

Different groups of the population can be exposed before, during and after the application of pesticides. In relation to pesticides (plant protection products), a distinction is made between the following population groups (DG SANCO, 2006; EFSA, 2008):

- *operators*: persons involved in activities relating to the application of pesticides (mixing/loading, application, repair and maintenance);
- *workers*: persons who, as part of their employment, enter an area or handle a crop that has been treated (re-entry; tasks include,

for example, harvesting and/or pruning/thinning of orchard fruit, grapes, vegetables or ornamentals). The different definition of "worker" here (compared with the definition used in models and tools presented previously in this document) should be noted;

- *bystanders*: persons who are located in/next to an area where applications are taking place;
- *residents*: persons who live or work adjacent to an area that has been treated.

For assessing operator (handler) exposure to pesticides, most of the tools involve the use of databases and rely on measured exposure data from various studies. The basic assumption is that exposures are not a function of the specific physicochemical properties of the active ingredient, but rather a function of the use conditions (i.e. work activity, application equipment, formulation type, packaging type, level of clothing, total amount of active ingredient handled and individual work practices) (Krieger, 2001). Thus, measured dermal exposures from a given set of studies on surrogate active ingredients are used to approximate exposures to a given active ingredient under similar use conditions (Krieger, 2001).

To assess the exposure of operators when applying pesticides as sprays, three models are mainly used within the EU: the United Kingdom Predictive Operator Exposure Model (POEM), the German model and the Dutch model (EFSA, 2008). These different predictive exposure models were developed almost completely independently in the early 1990s. Comprehensive descriptions and comparisons of the various predictive models are published elsewhere (van Hemmen, 1993; Kangas & Sihvonen, 1996; EFSA, 2008). To avoid the limitations of generic databases that are based on broad generic default values, the scenario-specific exposure database EUROPOEM was developed, presenting applicability to European conditions (Krieger, 2001). However, EUROPOEM was not formally adopted by the EU member states for assessment of operator exposures under Directive 91/414/EEC (EEC, 1991); thus, registration is still based largely on the United Kingdom's POEM and the German model (Krieger, 2001). Another widely used model is the United States Pesticide Handlers Exposure Database (PHED); however, this model is awaiting further development and adoption of a replacement (EFSA, 2008). These models are described further below.

6.2.11.1 The German model

The German operator exposure model (or the BBA model, where "BBA" is the abbreviation for the German Federal Biological Research Centre for Agriculture and Forestry) has a straightforward structure and is simple to use (EFSA, 2008; HSE, 2012a). The basis of the model is the assumption that dermal exposure for operators is proportional to the amount of pesticide applied. The underlying database of exposures is presented in Lundehn et al. (1992). The studies in the database were carried out by industry for registration purposes; however, the model is described only at the database level, and not at the level of the studies (EFSA, 2008). The size of the database varies and is relatively small (mixing/loading) for two of three formulations and for downward applications made with tractor-mounted equipment (van Hemmen & van der Jagt, 2005; EFSA, 2008). Exposure estimates can be calculated for four application methods, with default values being used for the area treated per day (20 ha for field crops, 8 ha for high crops sprayed with a broadcast air-assisted sprayer and 1 ha for backpack spraying). Estimates are provided separately for mixing and loading (hands only) and application (separately for the hands, head and body of the applicator, who is assumed to be dressed; half of the upper arms, forearms and lower legs are unprotected). The tool also offers a range of PPE to be specified—for example, chemical protective gloves (reduces dermal exposure of the hands by 99%) or broad-brimmed headwear (reduces dermal exposure of the head by 50%). It is available as a Microsoft Excel spreadsheet, which can be downloaded online (HSE, 2012a). The German model has not been validated.

6.2.11.2 The Dutch model

In the 1990s, the Dutch authorities developed a predictive exposure model based on exposure information available in the published literature (EFSA, 2008). The exposure data were categorized according to formulation type and application technique (van Hemmen & van der Jagt, 2005; EFSA, 2008). The 90th percentile of the distributions of the exposure estimates was selected, as the available data were generally drawn from relatively small data sets that had relatively high variability in the data. Also, because of the limited availability of data on the

mass of pesticide used, the tool uses the amount (mass) of exposure per unit of time as the exposure unit (EFSA, 2008). These indicative exposure mass rates are provided for mixing/loading of liquids and solids and for four application methods (either as grams of formulated product per hour or as millilitres of product sprayed per hour). Although the exposure estimates may be adjusted to allow for reductions for operators wearing PPE, the tool does not contain data on appropriate reduction factors (EFSA, 2008).

According to EFSA (2008), the tool is rather conservative, in view of the choice of the 90th percentile. It is based on literature data that are almost completely taken from surveillance studies, rather than from studies carried out for registration purposes (van Hemmen & van der Jagt, 2005; EFSA, 2008). For Dutch national authorizations, data on mixing/loading from the Dutch model are used, but otherwise POEM or the German model is used, as they are considered to be better predictors of exposure (van Hemmen & van der Jagt, 2005; EFSA, 2008). The Dutch model is not publicly available and has not been validated.

6.2.11.3 *PHED*

The Pesticide Handlers Exposure Database (PHED) was developed in 1992 jointly by the USEPA, Health Canada, the California Department of Pesticide Regulation and member companies of the American Crop Protection Association. It represents a database tool in North America used in developing estimates of mixer/loader and applicator exposures for some types of application equipment. For other types of application equipment, more recent data are currently being developed by the registrant task force, the Agricultural Handlers Exposure Task Force (AHETF) (Lunchick et al., 1994; USEPA, 1995, 1998, 2012a; Krieger, 2001; Beauvais et al., 2007). In PHED, the exposure while handling pesticides is estimated based on different exposure conditions, the handling and application process, the application method, packaging type, clothing and formulation (van Hemmen & van der Jagt, 2005; EFSA, 2008). PHED is a generic database containing exposure data (more than 1700 monitored exposure events submitted on a voluntary basis) describing operators mixing/loading and/or applying pesticides in the field (EFSA, 2008). The grading criteria for the studies are based on laboratory recovery, storage stability and

field recovery (EFSA, 2008). The actual PHED computer program was developed in a database language that is no longer technically supported. Nevertheless, the principles of PHED are presented below, as the USEPA and PMRA (Canada) prepared surrogate exposure tables containing a series of standard unit exposure values compiled in reference documents (PMRA, 2002; USEPA, 2013b).

6.2.11.4 POEM

The United Kingdom Predictive Operator Exposure Model (POEM), which was developed in the late 1980s, has a straightforward structure and is simple to use; however, not all of the required information is publicly available. For example, the data sets are not described at the study level, and exposure data are available only in classes (Joint Medical Panel, 1986; Hamey, 1992; Lunchick et al., 1994; van Hemmen & van der Jagt, 2005; EFSA, 2008; HSE, 2012b,c,d). POEM is based on limited generic monitoring data on the exposure of pesticide spray operators in the United Kingdom (Krieger, 2001; EFSA, 2008). The underlying data for POEM were obtained from research studies in which exposure was measured using interception samplers (patches), and so the model predicts dermal exposure mass in terms of this (analytical) measurement methodology. Data from the German model and EUROPOEM or PHED to estimate exposure during mixing and loading were included (e.g. for wettable powders or water dispersible granule formulations) (HSE, 2012e). Hand pouring data for non-certified users of mixing/loading products have recently been added, including the main types of container and measuring devices for concentrate products supplied to the home garden market (van Hemmen & van der Jagt, 2005; EFSA, 2008). POEM is discussed thoroughly in Joint Medical Panel (1986), Martin (1990) and Hamey (1992).

POEM is based on several variables (default values) in order to predict daily exposure from spraying applications (see Table A3.11 in section A3.8 in Appendix 3). The user can choose between two spreadsheets in order to calculate exposure for liquid or solid concentrate formulations (HSE, 2012b). Default values for key parameters, concerning the application method, formulation type, packaging information and PPE, are provided and are to be selected from lists (pull-down menus) by the user (Joint Medical Panel, 1986). Further information,

such as concentration of active substance, dermal absorption, dose of product and application volume, is to be added in text format.

POEM divides the exposure estimation into the mixing and loading step and the application of the pesticide formulation itself. For exposures during the mixing and loading step, POEM assumes that only the hands are contaminated and that the magnitude of exposure depends on the volume applied and the neck aperture width of the container used for dilution of the concentrated active ingredient (Krieger, 2001). However, this relationship between the chosen container volume and the resulting dermal exposure estimate, "hand contamination per operation", is not further described, nor is the data basis provided. In addition, the algorithms of the tool are not publicly available.

The final output of the tool is provided for a variety of parameters; these include "actual dermal exposure volume to the dilute pesticide formulation" ($ml \cdot d^{-1}$) and, by multiplying this value by the concentration of the active substance in the formulation, "dermal exposure mass of active substance per day" ($mg \cdot d^{-1}$), as well as further corresponding outputs in relation to systemic exposure. POEM combines the dermal absorbed dose and the inhalation exposure to obtain a total absorbed dose based on a 60 kg adult body weight in milligrams per kilogram body weight per day. The upper-bounding value of the 75th percentile of the evaluated exposure data is expressed as final "operator exposure" ($mg \cdot (kg\ bw)^{-1} \cdot d^{-1}$).

The POEM tool can be used only in a limited number of spraying application scenarios, and only gloves can be included as PPE, worn during mixing and loading (90% reduction in hand exposure for solvent-based formulations and 95% for water-based formulations) and/or application (for all spraying, a 90% reduction in hand exposure is assumed). POEM has not been validated (HSE, 2012e).

6.2.11.5 *EUROPOEM*

As a result of harmonization efforts in relation to the authorization procedure for plant protection products in the EU according to Directive 91/414/EEC (EEC, 1991), the European Commission funded a project (AIR3 CT931370) to establish a database including

a model for occupational exposure estimation (AIR, 1996; van Hemmen, 2001; EUROPOEM, 2012). Data obtained in representative field studies, including proprietary studies, were incorporated in the database. Studies were considered based on quality of documentation, study design, adequate methodology, number of replicates per person, analytical chemistry, and quality assurance and quality control elements for each individual study according to an Organisation for Economic Co-operation and Development (OECD) guidance document (OECD, 1997; van Hemmen, 2001). Data obtained included exposure data on boom sprayers, backpack sprayers and air blast sprayers, measured by patch techniques, whole-body dosimeters, personal air pumps or fixed-site air collectors (EUROPOEM, 2012). Each study was summarized in a standardized generic format for EUROPOEM (Krieger, 2001). Data were distinguished with respect to mixing/loading activities, application activities by the operator and consecutive mixing, loading and application by the same person. Other criteria were the formulation type (powders, granules and liquids), upward versus downward spraying direction and tractor-driven versus hand-held equipment (van Hemmen, 2001).

The structure of the database is similar to that of PHED, and the database was built by considering POEM, the German model and the Dutch model; as well, an Excel spreadsheet was available, similar to POEM (Krieger, 2001; van Hemmen, 2001). In part because of the high variability in the surrogate exposure data between different studies for a given use scenario, a single statistical value between the 75th percentile and the rounded maximum exposure is selected as the surrogate exposure value (Krieger, 2001). The exposure estimate is given per amount of active substance handled or as the amount of formulation or spray volume per unit of time. This conservatism in exposure estimation was implemented considering the highly variable conditions throughout the EU (e.g. equipment used, climatic conditions and work habits) (Krieger, 2001). Thus, the resulting point value exposure estimate is typically the 75th percentile of the exposure data when a large number of data points (e.g. 50–100) are available from at least 10 studies that represent a wide range of active substances, uses and climatic conditions (Krieger, 2001).

The exposure assessment is performed according to a tiered approach. The first tier reflects the most conservative estimate by

using reasonable worst-case assumptions for relevant variables. If the first-tier assessment fails, the exposure-reducing effect of PPE is considered, with reduction factors.

Although the development, maintenance and dissemination of EUROPOEM were expected to be accomplished by 1996 (CORDIS, 2012), the tool is not publicly available at the moment.

6.2.12 Pesticide models for post-application

Re-entry worker exposure is primarily to dry pesticide deposits, and most pesticides are relatively non-volatile. Therefore, dermal exposure is considered to be the most significant route of exposure for post-application workers (EFSA, 2008). The models developed for this type of exposure follow the assumption that the application of pesticides will leave residues on the foliage. During re-entry activities, these residues on treated surfaces (mostly plant materials/crops) may be transferred[1] to the skin or clothing of the worker. This process is determined mainly by two factors: the dislodgeability (magnitude of available exposure to substance or product at/from plant) and the transfer coefficient (driven by the intensity of the contact of the worker with the plant). The transfer coefficient replaces the formerly used term, "transfer factor" (EFSA, 2008).

The dislodgeable foliar residue (DFR) is expressed as mass per unit area of residue on foliage that can be dislodged during re-entry tasks. In contrast to DFR, transfer coefficients are not chemical specific, but relate to a given activity and crop (see also section 5.2). Transfer coefficients are expressed as the area of contact per unit of time for a specific task ($cm^2 \cdot h^{-1}$) and are derived by making concurrent measurements of dermal exposure ($\mu g \cdot h^{-1}$) and DFR ($\mu g \cdot cm^{-2}$) and plotting the former as a function of the latter; thus, transfer coefficients are inversely proportional to DFR (EFSA, 2008). The transfer coefficient is estimated via the equivalent area of treated surfaces (foliage) that a worker contacts while performing a given activity on a given

[1] This report differentiates between "transfer" (= transfer to skin) and migration (= possible amount on surface that is available for transfer, for example, due to leaching out of the product); see section 5.2.

crop (EFSA, 2008). Furthermore, dermal exposure depends on factors such as application rate, the efficiency of application procedures, task duration and the type of task involved (Hoernicke et al., 1998; Krebs et al., 2000; EFSA, 2008; BROWSE, 2011b). Additionally, a factor can be used to account for penetration through protective clothing.

6.2.12.1 EUROPOEM II

The approach of the German BBA model was further developed during the EUROPOEM II project between 1997 and 2000 (BROWSE, 2011b; EU FAIR, 2012; see concepts presented in section A3.2.3 in Appendix 3). For this purpose, a database was developed for exposure of workers re-entering areas where crops have previously been treated with plant protection products.

Although knowledge of DFR is essential in predicting exposure for re-entry workers, an accurate measure of DFR is often not available, and generic values must be used (EFSA, 2008). EFSA (2008) referred to EUROPOEM II and recommended a worst-case default value of 1 or 3 $\mu g \cdot cm^{-2} \cdot (kg\ active\ ingredient)^{-1} \cdot ha^{-1}$ multiplied by the application rate (kg active ingredient$\cdot ha^{-1}$) to give a DFR value with the units of micrograms per square centimetre ($\mu g \cdot cm^{-2}$). According to EUROPOEM II, defaults for transfer coefficients range from 2500 $cm^2 \cdot h^{-1}$ for vegetables up to 5000 $cm^2 \cdot h^{-1}$ for ornamentals. However, experimental data vary from around 50 to 30 000 $cm^2 \cdot h^{-1}$ for some harvesting tasks; thus, a worst-case default value of 30 000 $cm^2 \cdot ha^{-1}$ is suggested (EFSA, 2008; BROWSE, 2011b).

As only one worst-case default value for DFR is provided and indicative transfer coefficient values are available only for the manual harvest of a limited number of crop groups, the use of the model for estimating worker exposure remains very limited (EFSA, 2008; BROWSE, 2011b). EFSA (2008) found varying results when comparing predicted exposures with measured ones and gave as a reason the limitations of the model, but also inconsistencies in the approaches taken to measure dermal exposure.

Unfortunately, EUROPOEM is not publicly available. The official home page of the project (http://www.enduser.co.uk/europoem/) was last updated in 2003.

6.2.12.2 ARTF

The United States Agricultural Reentry Task Force (ARTF) combined re-entry activities into groups of crops/activities that involve similar contact with crop foliage (and thus similar exposure and transfer coefficients). Information was gathered on exposure monitoring studies, including hand labour activities, in a variety of crops, resulting in a database with generic transfer coefficient values according to crop/activity group. However, this database is not publicly available (EFSA, 2008; BROWSE, 2011b).

6.2.13 Bystander and resident exposure

Bystander and resident exposure refers to the exposure of persons who are located next to an area where pesticide applications are or have been taking place. Predominantly exposure to spray or vapour drift is considered; however, exposure due to contact with contaminated surfaces following drift fallout in adjacent areas also occurs. The issue of third-party exposures has been little studied to date, and a scientifically robust collection of data on exposure of bystanders is not yet available to enable the establishment of a science-based model. Consequently, there are no widely established models for assessing bystander and resident exposure. Nevertheless, EFSA (2008) suggests using the following models or tools:

- United Kingdom POEM, EUROPOEM and/or German model: modelling direct contact with airborne spray using spray drift data (EFSA, 2008; Martin et al., 2008);
- Dutch model for exposure from treated turf: modelling indirect contact with spray drift fallout using spray drift data in combination with models for estimating children's exposure from contact with turf treated or contaminated with lawn pesticides (EFSA, 2008; Prud'homme de Lodder et al., 2009);
- Pesticides Safety Directorate guideline/United Kingdom model;
- Bystander and Resident Exposure Assessment Model (BREAM).

These models share common approaches and are partly based on the same limited data on spray drift that were predominantly generated

in the 1980s with spraying practices that may no longer be representative (United Kingdom POEM, EUROPOEM and German model). The Pesticides Safety Directorate of the United Kingdom assesses exposure from contact with contaminated materials by employing the spray drift fallout values used for aquatic risk assessment purposes (Rautmann et al., 2001) as well as the children's exposure approach used by the USEPA for contact with treated lawns (Ross et al., 1990, 1991; Hurto & Prinster, 1993; USEPA, 1999a,b, 2012a,b; EFSA, 2008). All resulting algorithms are equivalent to the one presented previously for worker re-entry exposure, being dependent on information about transfer processes (see section 5.2.2). In addition, the United Kingdom BREAM project aims to develop a computational spray drift model for airborne concentrations and ground deposits to predict the potential exposure to pesticides for bystanders and residents in the countryside, relevant for United Kingdom applications (Butler Ellis & Miller, 2010; Butler Ellis et al., 2010; Defra, 2010; BROWSE, 2011c; Teske et al., 2011; Kennedy et al., 2012). Further models (e.g. contact with contaminated soils) are presented in, for example, Health Canada (2012).

6.2.14 Pesticide multipathway exposure models

As a consequence of the Federal Environmental Pesticide Control Act of 1972 in the USA (USFWS, 1972), the use of multipathway models is required for assessing exposure of the general population to pesticides. The so-called "receptor-oriented" or "calendar-based" models include all sources of exposure to a single chemical by various routes and pathways (here called "aggregate" exposure) and exposure to all chemicals with the same mechanism of toxicity (here called "cumulative" exposure). Special attention is given to subpopulations and special periods of life, such as children and women of childbearing age (USEPA, 2001, 2002, 2012d,e; Price et al., 2003; IGHRC, 2004; Fryer et al., 2006; Glen et al., 2012; see definitions provided in Appendix 1).

The basis of these models is the generation of populations of simulated individuals designed to be representative of the required target population, combining information on pesticide usage, human activity, environmental residues and environmental concentrations by

considering temporal, spatial and demographic variation among pesticide uses (Fryer et al., 2006). This is done by calculating daily exposures for each simulated individual on the basis of the individual's characteristics and behaviour, including information such as age, sex, race, income, region, ethnicity and birthplace, as well as how the individual grows, how the individual moves from home to home and from region to region of the USA and the individual's daily activity patterns. These simulated individuals' exposures are then estimated as a function of factors related to pesticide use, including the time-based integration of both residential and dietary exposures to pesticides (e.g. by food, drinking-water, hand-to-mouth activity, dermal exposure, inhalation or previous or concurrent applications of a product containing that compound). Further, models can compute application and chemical characteristics such as the probability of pesticide application, timing of exposure, season, location, surface area or chemical degradation (FIFRA SAP, 2000; Petersen et al., 2000; Price et al., 2000, 2002; IGHRC, 2004; Fryer et al., 2006; Exponent, 2009; Glen et al., 2012; USEPA, 2012c,d).

In order to be able to incorporate all interindividual variability and characteristics, most tools are self-contained database simulation programs drawing on data from a number of different sources, including journal articles, public databases on chemical/product-specific factors, survey data, product use data or labels, market share information, exposure studies and publicly available toxicity data. In some cases, data that are not publicly available (e.g. registrant studies) are integrated in the tool as well (e.g. Calendex). In general, input parameters used in the models can be based on point estimates (deterministic) or probabilistic estimates (i.e. derived from mathematical distributions representative of measured data or drawn at random from a file of relevant data points) (Petersen et al., 2000; Exponent, 2009; USEPA, 2012d). Probabilistic assessments adopt a Monte Carlo simulation technique to generate time series of exposure (1 day to a year or more) for simulated individuals (i.e. stochastically created synthetic persons) (Glen et al., 2012). To make the population representative of the population in the USA, individual exposures can be combined to produce exposure distributions (Glen et al., 2012). In addition to simulations for the general population in the USA, calculations for specified subpopulations can be performed, defined by age, sex, race/ethnicity or geographical region of residence

(IGHRC, 2004). Finally, when toxicity data are available, the tools provide risk estimations for the simulated exposure scenarios. Furthermore, the outputs of, for example, the SHEDS-Residential model (see section 6.2.14.4) can be used as inputs to physiologically based pharmacokinetic models (Glen et al., 2012).

The implemented algorithms for dermal exposure rely predominantly on approaches found in the USEPA's standard operating procedures for conducting residential exposure assessments for pesticides in various scenarios (USEPA, 1997a, 1999a, 2007a), although they vary in terms of specific features (including built-in data sources and population characteristics and ability to conduct probabilistic analyses) and presentation of the outputs. The user has to keep in mind that all the presented tools were developed in order to tackle specific regulatory needs and thus have methodological limitations due to their initial scope. Their applicability is limited mainly to pesticides and the population in the USA, as they are based on demographic data for the USA, some of which cannot be adjusted. An extensive array of input parameters or specific information might be required (e.g. residential use, physicochemical properties, frequency and probability of occurrences, dermal absorption, application rates, decline of the dislodgeable residues over time). Thus, significant professional judgement is necessary in order to use the appropriate algorithms and input data. Moreover, in order to ensure that the models maintain their representativeness, there is a need to periodically update the underlying databases (FIFRA SAP, 2000).

6.2.14.1 *Calendex™*

Calendex was originally developed by Novigen, Inc. and Durango Software LLC (now Exponent, Inc.) for estimating exposures of the population in the USA to pesticides in the residential environment: pesticides in food, air and water and chemical ingredients in formulated products (Exponent, 2009). Version 3.3 (2009) is licensed and made available on a fee basis through Exponent, Inc. (Petersen et al., 2000; Exponent, 2009). Additionally, an evaluation version is made freely available to the public by the USEPA for testing, along with a user manual (USEPA, 2012d).

Calendex does not utilize a fixed equation to estimate dermal exposure, but offers a library of equations. Users determine the most appropriate equations and parameters or define algorithms themselves (IGHRC, 2004). In addition to parameters already provided by the data libraries, users have to enter chemical- or product-specific data that constitute the contact and residue functions (e.g. half-lives, contact parameters, degradation data, residue factors) (Petersen et al., 2000). The computer codes (copyrighted by Durango Software LCC, provided in Petersen et al., 2000) are intended (published) for use only by the USEPA Scientific Advisory Panel in reviewing the Calendex model. Exposure is expressed in milligrams per pound ($mg \cdot lb^{-1}$) active ingredient as a function of contact and residue (Petersen et al., 2000).

The following limitations of Calendex have been reported: lack of transparency, lack of tracking mechanisms to analyse contributions to the model output, ucertainty from extrapolations of short-term data to simulate long-term exposures, use of data that are not representative of the entire population in the USA, and the need for significant professional judgement in applying the model (FIFRA SAP, 2000; IGHRC, 2004; Canales & Leckie, 2006).

6.2.14.2 *CARES*

The Cumulative and Aggregate Risk Evaluation System (CARES, version 3.0 of 2008; version 4.0 of 2010 available for testing) was developed by the trade association CropLife America, with the involvement of government, industry and academia, for estimating the risk from dietary, residential and drinking-water exposure to pesticides. The software is currently distributed by the International Life Sciences Institute at no charge, along with a manual, further documentation and training materials (ILSI, 2008). The manual offers further guidance (e.g. advice for measurement procedures and references for standard values) (ILSI, 2008).

The tool differentiates between scenario-specific (e.g. application rate or area treated), method-specific (e.g. transfer coefficient, for post-application exposures) and product-specific parameters (e.g. amount of formulation applied). Additionally, the tool divides the resulting

dermal exposure mass by the body weight of an adult, leading to a systemic dose, assuming 100% dermal absorption (termed "dermal exposure" in the tool).

The tool has been criticized for using unrealistic activity patterns, for being inflexible and for not being transparent, and Canales & Leckie (2006) stated that it should not be used for scenarios other than residential exposure.

6.2.14.3 *LifeLine™*

LifeLine (version 5.0 of 2007) is maintained by the not-for-profit organization The LifeLine Group Inc. (LifeLine, 2007) to estimate exposures to pesticides through diet, home environments, drinking-water and tap water, and residential pesticide products. It is available online as freeware, along with the technical and user manuals (LifeLine, 2007).

Dermal exposure estimates are taken from PHED (see section 6.2.11.3) or by specifying dermal exposures as a percentage of the amount of active ingredient that is applied (default provided, but user may change values: in general, 10%, with the exception of pet collars, with 1%; LifeLine, 2002).

This tool is best used for residential exposures; it is not suited for estimating exposure events of less than 1 day. The user friendliness of the tool could also be improved (Canales & Leckie, 2006).

6.2.14.4 *SHEDS-Residential*

The Stochastic Human Exposure and Dose Simulation model (SHEDS-Multimedia, version 3 of 2007) is used by the USEPA for simulating multimedia, multipathway human exposures to a variety of environmental chemicals, such as pesticides, metals and persistent bioaccumulative toxins (Glen et al., 2012). In the meantime, a draft version 4 of 2010 is available. SHEDS-Residential is one module predicting dermal exposure to residues from touching contaminated surfaces in the residential environment over time

(Glen et al., 2012). In addition, other SHEDS models with similar approaches, but addressing different chemical classes and exposure scenarios, have been developed (exposures to particulate matter, SHEDS-PM; air toxics, SHEDS-ATOX; and wood, SHEDS-Wood). SHEDS-Residential is available at no charge, but is programmed in the statistical language SAS and thus requires access to that software for use (Glen et al., 2012). The annotated SHEDS SAS code, technical manual, graphical user interface and user guide are provided online (USEPA, 2012e).

In SHEDS-Residential, dermal exposure is determined by the amount of chemical moving from the environment onto the skin surface, which is influenced by both the human macroactivity pattern (location where time is spent, e.g. in residence, vehicle, other building, outside away from/near home) and the microactivity pattern (amount of "touching" of contaminated media) (Zartarian et al., 2010; Glen et al., 2012). For this, the model uses the parameter "transfer coefficient" to estimate exposure. The user is advised to derive this value, for example, by collecting the mass on a dosimeter worn by an individual during an application (Glen et al., 2012). Additionally, the model may calculate this parameter when the user provides the model with the fraction of chemical on a contacted surface area that is transferred onto the skin ("dermal transfer efficiency"), by multiplying this value by the skin surface area contacted per time (Zartarian et al., 2010; Glen et al., 2012).

SHEDS-Residential differentiates between two types of "dermal exposure": the additional amount of chemical transferred onto skin per day ("new exposure") and the amount of chemical already transferred onto the skin ("running exposure") (Zartarian et al., 2010; Glen et al., 2012). Running exposure is carried over from one exposure event to the next, which is reduced by competing removal processes and increased by the loading once per diary event (Glen et al., 2012). A chemical is assumed to be retained on the exposure surface until it is absorbed, washed off, transferred to another body part or otherwise eliminated (e.g. by brushing off or hand-to-mouth transfer), thus reducing the "running exposure". The tracking of loading and unloading of the skin distinguishes the dermal exposure estimation in SHEDS-Residential from that of most other tools. Further assumptions concerning dermal exposure are that bedding does not contain

chemicals (no dermal exposure during sleeping), hands are always uncovered and handlers are wearing shorts and short sleeves.

6.2.15 Other models or tools

Various other models or tools are available that can be used for dermal exposure assessment. They may include target groups (e.g. operators/handlers and bystanders), but predominantly such models or tools focus on very specific applications or situations of an exposure scenario. In the following, some examples are presented in a condensed manner, along with references for further information.

In 2011 and 2012, WHO published revised versions of the series *Generic risk assessment models*, which include specific assessment scenarios for pesticides being used to control vector-borne diseases such as dengue, chagas and malaria:

- for insecticide-treated nets (WHO, 2012);
- for insecticides used for larviciding[1] (WHO, 2011b);
- for indoor and outdoor space treatment[2] (WHO, 2011c);
- for residual spraying of pesticides (WHO, 2011d).

In addition to relevant operator (handler) scenarios, the models also consider resident, post-application or bystander situations (adults and children), such as touching contaminated surfaces in houses after spray treatment of the walls, ingesting contaminated foodstuffs or water and hand-to-mouth behaviour of toddlers. The models are based on the same algorithms and use default values from the USEPA's *Standard operating procedures (SOPs) for residential exposure assessments* (USEPA, 1997b) and *Exposure factors handbook* (USEPA, 2011a), data from the EUROPOEM II database and the modelling approach of the United Kingdom POEM. The defaults were adapted to present a realistic case scenario (e.g. only light clothing covering the trunk

[1] Insecticides are used for larviciding in order to control immature stages of vectors living in permanent or semipermanent water, often in urban or other densely populated areas (e.g. including refugee camps) or extensively irrigated farms (Najera & Zaim, 2002; WHO, 2011c).

[2] Space spraying is the dissemination of small particles (<30 µm) that will remain airborne sufficiently long to make contact with flying target species to control the emerging adult populations (WHO, 2011c).

due to tropical climate). Other variations are adaptations to application techniques and expected equipment quality (e.g. using high spraying pressures or the existence of leakages during washing and maintenance of the equipment). In contrast to other models, no personal protection is intended at all in lax-standard scenarios, but guideline case scenarios including PPE may be used as well. Defaults for all determinants are presented along with the algorithms of the model for indoor residual spraying of pesticides in section A3.2.3.20 in Appendix 3.

The International Association for Soaps, Detergents and Maintenance Products (AISE) developed the Reach Exposure Assessment Consumer Tool (REACT; AISE, 2012a) to support this industry sector's efforts to assess dermal exposure of consumers to substances in soaps, detergents and maintenance products when preparing REACH registration dossiers (AISE, 2009a,b). This includes products (preparations) used by consumers, such as fabric washers, dish cleaners and hard surface cleaners (AISE, 2012b). The tool provides a set of product categories (PCs) specific for this industry sector based on HERA (2012), which can be used for refining an ECETOC TRA assessment.

Another tool focusing on a specific application is the Swimmer Exposure Assessment Model (SWIMODEL, version 3.0 of 2003), which was developed by the USEPA to act as a screening tool for pesticides found in indoor swimming pools and spas. The model is a modification of a study by Beech (1980) for estimating exposure to trihalomethanes in swimming pools (USEPA, 2003). The assessor has the option of using the default values available within the model or entering other available values (i.e. body weights, skin surface area and physicochemical data) (USEPA, 2003, 2012f). The final outputs are worst-case intake assumptions for swimmers, expressed as mass per event or lifetime average daily dose ($mg \cdot (kg\ bw)^{-1} \cdot d^{-1}$), considering the absorption and converting exposure into systemic doses (see section 3.6.1 and Appendix 1).

Additional models are available for specific applications concerning particular conditions of agricultural pesticide use (e.g. the Dutch greenhouse model, the Southern European Glasshouse Model, the SeedTropex exposure model for operators using seed treatment products). Descriptions of these models as well as comparative case-studies between various models and tools are published elsewhere

(Hamey, 1995; van Hemmen & van der Jagt, 2005; IGHRC, 2010; Wicke, 2010; Young et al., 2012; HSE, 2012f). A comprehensive overview is presented by EFSA (2008).

Finally, it should be mentioned that an Agricultural Handlers Exposure Database (AHED) is in development to replace PHED, which might rectify the deficiencies of EUROPOEM, as it is proposed to contain exclusively data that regulators have deemed appropriate for use in a generic database (AHETF, 2008; EFSA, 2008; USEPA, 2011b,c).

6.3 Overview of exposure estimation tools

In Table 33, general information about the models and tools is provided in a comparative and condensed form. Further information (e.g. terminology of abbreviations used in this list, default values, units of determinants, underlying algorithms) can be found in section A3.2 of Appendix 3.

6.4 Considerations for selecting and using suitable models/tools

No general advice can be provided to potential users as to which model or tool should be selected, as they all have different applicability. Section 6.3 provides an overview of all models and tools described above. Some general aspects on choosing a suitable model or tool are presented below.

The regulatory context can be an important issue, as several tools have been developed within the scope of specific regulatory contexts, and their use may be requested or recommended by the respective authorities.

6.4.1 Complexity

According to their complexity, the models or tools may be categorized as Tier 1, Tier 2, etc., models. With increasing tiers, the complexity and presumably also the accuracy of the predictions increase.

Table 33. Overview of models/tools for dermal exposure assessment

(a) DREAM and DERM

	DREAM	DERM
General information		
(Full) name	Dermal Exposure Assessment Method	Dermal Exposure Ranking Method
Version and year	Version 1 of 2003	Version 1 of 2008
Target group	Occupational exposure	Occupational exposure
Implemented model	Categorization of dermal exposure influencing processes by preassigned factors that are summed in a subsequent evaluation scheme	Preassigned grading system for transfer condition, exposed body surface and clothing
Substances	Pesticides	Pesticides
Task/process/event	All applications of pesticides	All applications of pesticides (aimed for use in developing countries)
Underlying data basis	Based on literature and expert judgement	Expert judgement
Acceptance in regulatory context	No	No
Software specification	Paper form (publication)	Paper form/evaluation in form of checklist
Publicly available	Yes (if access to scientific journal)	Yes (if access to scientific journal)
Dermal exposure estimation		
Parameters (inputs/exposure determinants) used for exposure estimation (see section A3.2.3)		– A_i – T_i – $F_{cloth\ pen}$

Table 33 (continued)

	DREAM	DERM
Final tool output (unit)	Semiquantitative categorized levels: zero, low, moderate, high, very high and extremely high exposure	Semiquantitative score
Validation available	Studies on repeatability and accuracy available	Correlation studies available
Transparency (documentation provided)		
Of model/algorithm development	Partly provided	Partly provided
Of exposure estimation (algorithm itself)	Provided	Provided
Of underlying data (origin and applicability)[a]	Partly provided	Partly provided
Of default values (origin and applicability)[a]	Partly provided	Not provided
Calculation reproducible without tool?	Yes	Yes
Miscellaneous		
Specific characteristics	—	Simple to use (paper evaluation form)

[a] For measurements: e.g. including measurement circumstances (exposure scenario descriptions); for expert judgements: e.g. including explanatory statements/arguments.

Table 33 (continued)

(b) EASE, MEASE and ECETOC TRA

	EASE	MEASE	ECETOC TRA (worker or consumer)[a]
General information			
(Full) name	Estimation and Assessment of Substance Exposure	Metals' EASE	ECETOC Targeted Risk Assessment
Version and year	Version 2 of 2003	Version 1.02.01 of 2010	TRAV3 of 2012
Target group	Occupational exposure	Occupational exposure	Occupational and non-occupational exposure (two independent tools presented)
Implemented model	Categorization of exposure conditions (type of skin contact)	Categorization of exposure conditions (type of skin contact, EASE related)	Worker: categorization of exposure conditions (based on EASE, but process/task related) Consumer: thickness layer model
Substances	Not specified	Metals/inorganic substances	Focusing on organic chemicals; no fibres, liquid aerosols or emissions from hot processes (e.g. fumes)
Task/process/event	Not specified	Not specified	Worker: 27 different tasks/processes (PROCs) Consumer: product- and article-related contact (PCs & ACs) (according to REACH)
Underlying data basis (were measured values used for modelling?)	Data on liquids and expert judgement	Data on various metals and expert judgement	Worker: dermal exposure loading values of EASE adjusted by expert judgement Consumer: none used

Table 33 (continued)

	EASE	MEASE	ECETOC TRA (worker or consumer)[a]
Acceptance in regulatory context	Not any more (only supporting tool)	Yes; REACH (screening)	Yes; REACH (screening)
Software specification	Not a software program (only briefly available), but scheme of logic criteria to choose from	Excel spreadsheet for Windows	Excel spreadsheet for Windows
Publicly available	No (withdrawn)	Yes: free of charge (see section A3.1)	Yes: free of charge (see section A3.1)
Dermal exposure estimation			
Parameters (inputs/exposure determinants) used for exposure estimation (see section A3.2.3)	– $F_{cont\ pat}$ – $F_{s\ char}$ – $F_{use\ pat}$ – n_{appl}	– $DLR_{s\ default}$ – A_{skin} – $F_{cloth\ pen}$ – $F_{s\ char}$ – m_f – t_{exp} – $F_{use\ pat}$ – $F_{cont\ pat}$ – n_{appl}	worker: – $DLR_{s\ default}$ ($F_{use\ pat}$) – A_{skin} ($F_{use\ pat}$) – m_f – t_{exp} ($F_{s\ char}$) – $F_{cloth\ pen}$ – F_{LEV} ($F_{op\ cond}$) consumer: – A_{skin} – m_f – n_{appl} – TH – ρ_{prod}
Final tool output (unit) (according to tool terminology)	"Dermal exposure" ($mg \cdot cm^{-2} \cdot d^{-1}$) Provided ranges: 0–0.1, 1–5, 5–15 $mg \cdot cm^{-2} \cdot d^{-1}$	"Total dermal loading" ($mg \cdot d^{-1}$)	"Dermal exposure" ($mg \cdot (kg\ bw)^{-1} \cdot d^{-1}$) (assuming 100% absorption)

Table 33 (continued)

	EASE	MEASE	ECETOC TRA (worker or consumer)[a]
Type of estimated dermal exposure (unit) (according to terminology defined in this document)	Potential dermal exposure loading rate to a specific skin surface area (hands and forearms) per day (DLR_s, $mg \cdot cm^{-2} \cdot d^{-1}$)	Actual dermal exposure mass rate (DMR_s, $mg \cdot d^{-1}$) (in contrast to the unit, the output relates to a specific skin surface area; thus, the output relates to a dermal exposure loading rate, DLR_s, $mg \cdot cm^{-2} \cdot d^{-1}$)	Potential (consumer) / actual (worker) dermal exposure mass rate (DMRs, $mg \cdot d^{-1}$) (in contrast to the unit, the output relates to a specific skin surface area per day; thus, the output relates to a dermal exposure loading rate, DLR_s, $mg \cdot cm^{-2} \cdot d^{-1}$)
Overestimation/ underestimation of exposure	Mostly overestimates exposure	Likely to be conservative	Likely to be conservative
Validation available	Not available	Not available	Not available
Transparency (documentation provided)			
Of model/algorithm development	Not available	Based on EASE, EASE estimates, adapted to Health Risk Assessment Guidance for Metals fact sheets	Worker: partly provided (based on EASE) Consumer: partly provided
Of exposure estimation (algorithm itself)	No algorithm, but categorization approach	Not available	Worker: not available Consumer: provided

Table 33 (continued)

	EASE	MEASE	ECETOC TRA (worker or consumer)[a]
Of underlying data (origin and applicability)[b]	Not available	Results of quantitative measurements, but no further details (e.g. measurement circumstances) available	Worker: not provided (based on EASE) Consumer: none used
Of default values (origin and applicability)[b]	Not available	Partly provided in documentation and/or glossary of tool	Worker: not provided (based on EASE refinements) Consumer: partly provided in RIVM fact sheets
Calculation reproducible without tool?	Tool no longer available	No	Yes
Miscellaneous			
Specific characteristics	Not available or recommended for use	Parameters influencing the final output are indicated	Files can be saved, and reports with used parameters in calculation can be stored/printed

[a] Worker as defined by REACH; see text.

[b] For measurements: e.g. including measurement circumstances (exposure scenario descriptions); for expert judgements: e.g. including explanatory statements/arguments.

Table 33 (continued)

(c) RISKOFDERM and BEAT

	RISKOFDERM	BEAT
General information		
(Full) name	—	Bayesian Exposure Assessment Tool
Version and year	Version 2.1 of 2008	Version 1.72 of 2008
Target group	Occupational exposure	Occupational exposure
Implemented model	Measurement data sets, fitted by linear mixed effect models	A database of task-related exposure measurements plus a hierarchical Bayesian model for predictions if various analogous data sets are available
Substances	Liquids and solids No substances with high vapour pressure in database No fumes	Liquids and solids
Task/process/event	Tasks assigned to one of six DEO units Sometimes restrictions due to original data set (“only on manual tasks for powders”)	Mainly intended for biocide uses (in Europe) Based on specified DEO units and product types used in biocide regulation
Underlying data basis (were measured values used for modelling?)	Measurements of wide range of industries/ workplaces	Measurements for wide range of scenarios (related to occupational biocide use)
Acceptance in regulatory context	Yes: REACH (in Europe)	Yes: biocides (in Europe)
Software specification	Excel spreadsheet for Windows	Microsoft Access for Windows
Publicly available	Yes: free of charge (see section A3.1)	Yes: free of charge (see section A3.1)

Table 33 (continued)

	RISKOFDERM	BEAT
Dermal exposure estimation		
Parameters (inputs/exposure determinants) used for exposure estimation (see section A3.2.3)	25 different determinants based on the underlying database; number of determinants varies between DEOs; below, DEO 1 (for others, see section A3.5): – $F_{emission}$ – $F_{op\ cond}$ – F_{LEV} – $F_{cont\ pat}$ – t_{exp} – $MR_{s\ appl}$ – $F_{fraction}$	Exposure not calculated, but database with values offered, no information about statistical modelling (see section on transparency below)
Final tool output (unit) (according to tool terminology)	"Exposure loading" per shift ($\mu g \cdot (8\ h)^{-1}$)	"Potential dermal exposure to body or hands" ($mg \cdot min^{-1}$)
Type of estimated dermal exposure (unit) (according to terminology defined in this document)	"Potential dermal exposure volume rate" ($mg \cdot d^{-1}$) (in contrast to the unit, the output is provided for a specific skin surface area [body and/or hands] for a typical occupational day of 8 h exposure duration; thus, the output relates to a potential dermal exposure loading rate, $mg \cdot cm^{-2} \cdot d^{-1}$)	"Potential dermal exposure mass rate" ($mg \cdot min^{-1}$) (in contrast to the unit, the output is provided for a specific skin surface area [body or hands]; thus, the output relates to a potential dermal exposure loading rate, $mg \cdot cm^{-2} \cdot d^{-1}$)
Overestimation/underestimation of exposure	Assessment likely to be conservative	Assessment likely to be conservative
Validation available	Comparison (benchmark study) available	Not validated

Table 33 (continued)

	RISKOFDERM	BEAT
Transparency (documentation provided)		
Of model/algorithm development	Yes	Partly provided
Of exposure estimation (algorithm itself)	Yes	Partly provided (search for analogous data) (not using Bayesian model for distribution approach)
Calculation reproducible without tool?	No	Partly
Of underlying data (origin and applicability)[a]	Yes	Yes
Of default values (origin and applicability)[a]	Not applicable	Yes
Miscellaneous		
Specific characteristics	Overview and summary report of inputs available Estimates of the percentile of the exposure distribution provided Provides information if outputs are likely to exceed applicability domain of database Possible to present mean exposure/different percentiles	Contains a module to incorporate additional measurement data Further statistical tools (e.g. Markov Chain Monte Carlo analysis) available Visualization of distribution of exposure to body provided

[a] For measurements: e.g. including measurement circumstances (exposure scenario descriptions); for expert judgements: e.g. including explanatory statements/arguments.

Table 33 (continued)

(d) ConsExpo and SprayExpo

	ConsExpo	SprayExpo
General information		
(Full) name	Consumer exposure tool	—
Version and year	Version 4.1 of 2010	Version 2 of 2012
Target group	Non-occupational exposure	Occupational and non-occupational exposure
Implemented model	Five transfer concepts for dermal loading	Deposition of sprayed substances onto skin after modelling the air room concentration, including sedimentation and turbulent diffusion dimensions
Substances	Products: paints, pest control products, toys, cosmetics, cleaning products and disinfectants	Non-volatile active substance dissolved or dispersed in a volatile solvent
Task/process/event	Not specified; five different dermal loading concepts	Spray applications
Underlying data basis (were measured values used for modelling?)	See below in section on transparency	See below in section on transparency
Acceptance in regulatory context	Yes: REACH and biocides (in Europe)	Yes: biocides (in Europe)
Software specification	Stand-alone package on Windows	Excel spreadsheet for Windows
Publicly available	Yes: free of charge (see section A3.1)	Yes: free of charge (see section A3.1)

Table 33 (continued)

	ConsExpo	SprayExpo
Dermal exposure estimation		
Parameters (inputs/exposure determinants) used for exposure estimation (see section A3.2.3)	Depending on scenario: – A_{skin} – $A_{skin\ rub}$ – $c_s(x,t)$ – $F_{trans\ fraction\ p}$ – $F_{trans\ fraction\ s}$ – $L_{s\ trans}$ – m_f – $M_{prod\ skin}$ – $MR_{prod\ appl\ skin}$ – t_{exp}	– $A_{skin\ hori}$ – $A_{skin\ vert}$ – c_{air} – $MR_{s\ dep}$ (t) – t_{exp} – υ_{dep} – υ_{set} Additional input parameters for calculation of air concentration in room (c_{air}), which is basis for dermal exposure output: – released droplet spectrum – release rate – spatial and temporal pattern of release process – vapour pressure – size of room – ventilation rate
Final tool output (unit) (according to tool terminology)	"Dermal load" ($mg \cdot cm^{-2}$)	"Dermal dose" (mg), i.e. total dermal deposition from air; average deposition rate ($mg \cdot s^{-1}$), i.e. mass deposited per second
Type of estimated dermal exposure (unit) (according to terminology defined in this document)	Potential dermal exposure loading per application/event (DL_s, $mg \cdot cm^{-2}$) (in contrast to the unit, the output is provided per day, assuming one application per day; thus, the output relates to a dermal exposure loading rate, DLR_s, $mg \cdot cm^{-2} \cdot d^{-1}$)	Potential dermal exposure mass (DM_s, mg) or mass rate (DMR_s, $mg \cdot s^{-1}$) (in contrast to the unit, the output is provided for a specific skin surface area per day, assuming one application per day; thus, the output relates to a dermal exposure loading rate; DLR_s, $mg \cdot cm^{-2} \cdot d^{-1}$)

Table 33 (continued)

	ConsExpo	SprayExpo
Overestimation/ underestimation of exposure	No information	Assumed to underestimate dermal exposure (only covers deposition from air, not, for example, accidentally occurring splashes)
Validation available	Not available	Sensitivity and comparison study available
Transparency (documentation provided)		
Of model/algorithm development	Partly provided (in former manuals and publications)	Provided
Of exposure estimation (algorithm itself)	Provided for most application scenarios (not for diffusion)	Provided
Of underlying data (origin and applicability)[a]	Partly provided (in former manuals and publications)	Algorithm very complex and not reproducible without the tool
Of default values (origin and applicability)[a]	Origins (partly) provided in database/fact sheets Compiled from literature or expert knowledge	Application pattern (e.g. spraying ceiling versus floor) and sprayer's position included in modelling
Calculation reproducible without tool?	Yes (not for diffusion)	No
Miscellaneous		
Specific characteristics	User must be/is able to change/insert (specific) input parameters Quality ranking of default values provided	—

[a] For measurements: e.g. including measurement circumstances (exposure scenario descriptions); for expert judgements: e.g. including explanatory statements/arguments.

Table 33 (continued)

(e) German BBA model, Dutch model, PHED, POEM, EUROPOEM and EUROPOEM II

	German BBA model	Dutch model	PHED	POEM	EUROPOEM	EUROPOEM II
General information						
(Full) name	German Operator Exposure Model	Dutch Operator Exposure Model	Pesticide Handlers Exposure Database	Predictive Operator Exposure Model	European Predictive Operator Exposure Model (Database Project)	European Predictive Operator Exposure Model II
Version and year of tool	Version 2003	Not available	Surrogate Exposure Guide of 2013	Version 2007	Not available	No tool available
Development of model / release date	1992	1990s	1992	Late 1980s	1996	1997–1998
Target group	Occupational exposure	Occupational exposure	Occupational exposure	Occupational exposure	Occupational exposure	Occupational (post-application) and non-occupational (bystander) exposure
Substances	Agricultural pesticides	Agricultural pesticides	Agricultural pesticides	Agricultural pesticides	Agricultural pesticides	Agricultural pesticides
Implemented model	Categorization of exposure conditions (task related)	Categorization of exposure conditions (task related)	Categorization of exposure conditions (task related) plus distributional fit test on measurement data	Categorization of exposure conditions (task related)	Data combined according to comparable use	Data combined according to comparable use

Table 33 (continued)

	German BBA model	Dutch model	PHED	POEM	EUROPOEM	EUROPOEM II
Task/process/ event	Spraying	Application	Mixing and loading Application	Spraying	Spraying	Re-entry worker: exposure to dry (non-volatile) pesticides Bystander: drift after pesticide application
Output	Quantitative	Quantitative	Quantitative	Quantitative	Quantitative	Quantitative
Underlying data basis (were measured values used for modelling?)	No information	Data almost completely from surveillance studies and publicly available literature	>1700 monitored exposure events under actual field conditions (not publicly available)	Limited generic monitoring data (no information on study level and not publicly available)	Data on field studies (not publicly available)	Data on field studies (not publicly available)
Acceptance in regulatory context	Pesticides (plant protection products: in EU)	Pesticides (plant protection products: in EU)	Pesticides (plant protection products: North America, i.e. USEPA, Health Canada)	Pesticides (plant protection products: in EU)	Pesticides (plant protection products: in EU)	No
Software specification	Microsoft Excel spreadsheet	Not available	Available only as pdf (Surrogate Exposure Guide)	Microsoft Excel spreadsheet	Microsoft Excel spreadsheet	Not available
Publicly available	Yes: free of charge (see section A3.1)	Not available generally	Only available as “Surrogate Exposure Guide” listing estimates	Yes: free of charge (see section A3.1)	Not available	Yes

Table 33 (continued)

	German BBA model	Dutch model	PHED	POEM	EUROPOEM	EUROPOEM II
Dermal exposure estimation						
Included parameters	– A_{appl} – $DM_{s\ per\ mass\ handled\ EXP}$ – $L_{s\ appl}$	No information	– Application rate – Formulation type – Packaging type – Operational conditions – Equipment – Clothing/ protective equipment	Mixing & loading: – $c_{s\ in\ product}$ – $F_{cloth\ pen}$ – n_{appl} – $DV_{prod\ M\&L}$ – $DVR_{prod\ M\&L\ hands}$ Application: – $c_{s\ in\ dilution}$ – $F_{cloth\ pen\ i}$ – $F_{op\ equip}$ – $F_{trans\ fraction\ p}$ – t_{exp} – $DVR_{prod\ appl}$ – $DVR_{prod\ appl\ i}$ – $DVR_{prod\ appl\ tot}$ Additionally according to literature: – Area treated per day – Volume of product applied – Formulation type – Container size – Distribution of contamination	According to literature: – Application rate – Total amount handled – Concentration of active substance	– $L_{s\ appl}$ – $L_{s\ trans}$ – TC_s – $t_{exp\ day}$ – $F_{cloth\ pen\ i}$

Table 33 (continued)

	German BBA model	Dutch model	PHED	POEM	EUROPOEM	EUROPOEM II
Data criteria (for implementation of study in database)	No information	No information	Sample size, duration, body regions, clothing scenarios, laboratory recovery, storage stability, field recovery	Exclusively based on analytical quality assurance procedures	Adequacy of experimental design, quality assurance procedures, extent of documentation, number of replicates	No information
Statistical value used for exposure estimate	Geometric mean	90th percentile	Geometric mean, median or arithmetic mean	75th percentile	75th percentile	75th percentile
Default values provided (see section A3.2.3)	Yes	Yes	Yes	Yes	No information	Yes
Final tool output (unit) (according to tool terminology)	"Dermal exposure" per application and for specific duration ($mg \cdot kg^{-1} \cdot d^{-1}$)	No information (unit: mass of formulated product per time unit, or volume of spray per time unit)	"Unit exposure" (mass per mass active ingredient handled)	"Dermal exposure mass of active substance handled per day" ($mg \cdot d^{-1}$) (for mixing and loading to the hands)	No information	"Dermal exposure" ($\mu g \cdot d^{-1}$)

Table 33 (continued)

	German BBA model	Dutch model	PHED	POEM	EUROPOEM	EUROPOEM II
				or “dermal exposure volume of spray (diluted product) per day” ($ml \cdot d^{-1}$) (for spray application)		
Type of estimated dermal exposure (unit) (according to terminology defined in this document)	Potential dermal exposure mass rate per mass handled	No information	Actual dermal exposure mass rate per mass handled	Actual dermal exposure mass rate ($mg \cdot d^{-1}$) (for mixing and loading: in contrast to the unit, the output is provided for a specific skin surface area (hands); thus, the output relates to an actual dermal exposure loading rate, $mg \cdot cm^{-2} \cdot d^{-1}$)	No information	Potential dermal exposure mass rate ($\mu g \cdot d^{-1}$)

Table 33 (continued)

	German BBA model	Dutch model	PHED	POEM	EUROPOEM	EUROPOEM II
Overestimation/ underestimation of exposure	Likely to be conservative	Likely to be conservative	Likely to be conservative	Likely to be conservative	Likely to be conservative	Likely to be conservative
Transparency (documentation provided)						
Of underlying data (origin and applicability)[a]	No	No	No	Limited available	No	No
Of default values (origin and applicability)[a]	No	No	No	No	No	No
Calculation reproducible without tool? (algorithm of tool available)	No	Not applicable	Not applicable	No	Not applicable	Not applicable

Table 33 (continued)

	German BBA model	Dutch model	PHED	POEM	EUROPOEM	EUROPOEM II
Miscellaneous						
Specific characteristics	Relatively small database	—	High variability in data subsets Some study replicates not generally applicable (too short duration)	Limited number of application scenarios Databases are not described at the study level, and exposure data are available only in classes Only unprotected operator scenarios in combined scenarios/events	High variability in data	—

[a] For measurements: e.g. including measurement circumstances (exposure scenario descriptions); for expert judgements: e.g. including explanatory statements/arguments.

Tier 1 models or tools are easy to use and are designed to overestimate the exposure[1] for screening purposes. Under REACH, ECETOC TRA is one of the models recommended for this purpose. Another example would be DERM, which is an easy-to-use tool to educate farmers in developing countries in relation to their specific working behaviour and environment.

Tier 2 and higher-tier models or tools are designed to provide more realistic quantitative estimates of dermal exposure. They may include complex algorithms in order to reflect the influences of the various complex transport processes and substance- or application-specific determinants and/or are based on large databases (e.g. ConsExpo or BEAT). Generally, including more relevant parameters in the algorithm of a model should improve predictions (e.g. the physical mechanisms of drying of surfaces in contrast to assuming continuously wet surfaces). However, a fairly complex algorithm does not necessarily provide a more realistic exposure assessment (see section A3.2 in Appendix 3).

6.4.2 Applicability domain

6.4.2.1 Target population

An important aspect is the scenario to be covered. Models can be distinguished with respect to the target population (e.g. workers or consumers); more specifically, in the case of pesticides, there is a differentiation between operators, workers, bystanders and residents. Most of the models are intended primarily for determination of occupational exposure (professional workers, operators, handlers). Exceptions are ECETOC TRA, AISE REACT, ConsExpo, SWIMODEL and models for bystander exposure to pesticides that include consumer exposure.

[1] "Screening" or "Tier 1" assessments typically refer to conservative scenario descriptions and a summation of deterministic estimates. These assessments address a range of somewhat similar uses with limited numbers of parameters based on measured or modelled data, or both, to serve as a basis for comparison with a measure of hazard to determine whether further assessment is necessary (Meek et al., 2011).

6.4.2.2 Task

Some models or tools are suitable only for specific tasks (e.g. SprayExpo explicitly for spraying applications), whereas others cover a wide variety of tasks and may be further adapted by the user for specific questions (e.g. ConsExpo). Generally, a comprehensive task description is desirable for an exposure assessment, but at least the determinants used in the model or adjustable in the tool have to be available (see section 3.3 and section A3.2 in Appendix 3). In the following, some points are presented that should be considered in relation to the task descriptions.

Wording or clustering of task uses between the tools may be different, which may be due to a specific regulatory context. For instance, the exposure tasks in BEAT are assigned according to the "product types" as they are defined by the European Biocidal Products Directive (EC, 1998a). In contrast, the user has to identify task descriptions for occupational users (workers) in ECETOC TRA according to the concept of "process categories" (PROCs), which have been developed in the context of the European REACH framework. Stoffenmanager uses "handling categories", and in the RISKOFDERM project, "dermal exposure operation (DEO) units" were assigned to cluster exposure scenarios in relation to the data basis. All these categories or clusters were designed to enable more or less structured description of uses. However, the definitions between the tools might vary (e.g. the DEOs of RISKOFDERM and BEAT; see section 6.2.6), and users not accustomed to these terms and definitions may be unable to handle them correctly.

6.4.2.3 Transferability of measured data

If modelling is based on measurement data, the type of substance with its physicochemical properties has to be considered. Even if a broad database for estimates or default values exists and is publicly available, these data can be limited to specific substances or applications (e.g. pesticides). A generalization of the underlying data in the model or tool might falsify the exposure estimation (e.g. when a single value for one substance is used to represent a whole group of potential exposure agents with a wide range of physicochemical properties).

Other parameters that affect data transferability are the circumstances of the measurement (scenario, task descriptions, analytical method of measurement). Further, the task description or assumptions for modelling may include operational conditions (e.g. national occupational guidelines or regulations, work equipment, automation, exhaust ventilation, climate), personal work practices (e.g. pouring liquids slowly and with caution), different use of protective equipment and different hygiene habits, such as washing of hands. In developing countries, work equipment used may be out of date or broken due to financial constraints, resulting in increased exposure potential (e.g. using leaky sprayer equipment or repairing equipment themselves by touching contaminated parts with their bare hands) (van Wendel de Joode et al., 1996; Aragón et al., 2001; Blanco et al., 2008). Thus, using models or tools that do not include these relevant aspects may underestimate exposure in these cases.

Dermal exposure estimates are often presented as mass per unit of time (e.g. RISKOFDERM and BEAT), for which it is implicitly assumed that dermal exposure is linearly related to the duration of work. However, this (measured) indicative rate is valid only for the scenario from which it has been obtained and is thus dependent on this specific applicability domain of the underlying measurement scenario, including its duration or the frequency of applications. For example, with repeated contact between the hands and layers of zinc oxide on a work surface, the skin quickly became loaded with the material, so that there was no significant increase in dermal exposure with further contact (IGHRC, 2010). Thus, some models or tools imply that the total amount of a substance is transferred within one event (e.g. thickness layer model, see models using "TH" in section A3.2.4 in Appendix 3). Consequently, the model or tool must clearly state whether estimates according to the conditions of the underlying measurement study apply for only a single task or for several repetitions, for only a few minutes or for the whole work shift.

Accordingly, due to the underlying analytical methodology, final modelling outputs are often expressed as mass per surface area (i.e. dermal exposure loading; see section 3.6.1 and Appendix 1). To do so, the variation in exposure mass between specific areas of the skin is averaged over the relatively large area assessed (e.g. half a hand or more) (Schaafsma et al., 2011). However, using the exposure mass

of a skin region with a high probability of exposure (e.g. hands) is unsuitable for averaging over the whole body area, as it would lead to an overestimation.

6.4.2.4 *Transferability of defaults based on expert judgement*

Some models are composed of a set of mass balance equations, in which some determinants were derived from expert judgement (e.g. EASE, ECETOC TRA, DREAM or DERM; see section A3.2.3 in Appendix 3).

Tools often represent a mixed approach, as they might rely on some set of measurements as well as determinants (default values) derived by empirical rules or generic conceptual considerations. One has to keep in mind that default values can represent (reasonable) worst-case estimations or simplifications of distributions (mean or 95%) or might be defined in accordance with a regulatory context. In order to provide information about the reliability of default values, a ranking system can be implemented (e.g. ConsExpo).

6.4.3 *Terminology and presentation of the output*

The final exposure output and its terminology are presented differently in the various models and tools. In most cases, estimates in terms of the mass of the substance in question are provided. However, it is not always clearly stated whether this represents the mass of the active substance or the mass of the in-use product. In addition, the output is often called exposure, although absorption (uptake) has been included, resulting in a systemic dose (see Appendix 1). For comparing exposure estimates between different pathways of exposure, so-called "exposure units" are sometimes defined—that is, normalizing exposure by dividing the exposure mass by the amount of active substance handled, by unit area of skin, per event, by unit of time or by body weight (EFSA, 2008). For example, BEAT values are generally presented as "milligrams deposition of in-use product per minute of task", in contrast to the provided exposure estimate of POEM, in the form of "active substance per kilogram of active substance handled". The different units chosen for an estimate reflect the different focus of the

tools (IGHRC, 2010). Thus, users should inform themselves about the definitions and units of the final output independently of the wording chosen by the model or tool builders.

6.4.4 Current developments

EFSA (2008) reviewed available agricultural pesticide models used in the EU (e.g. German model, United Kingdom POEM, PHED, EUROPOEM) and other models used for the regulation of non-agricultural pesticides (biocides) (e.g. ConsExpo; see section 6.2.9). The following limitations and deficiencies were identified (EFSA, 2008; Hart et al., 2011):

- poor quality of data basis (limited, old, not compliant with good laboratory practice and not validated);
- a limited number of exposure scenarios;
- dissimilar ways of normalization;
- different default values for a determinant (see section A3.2.3 in Appendix 3);
- different statistical point estimates used for defaults;
- overestimation of exposures (linear extrapolation if larger quantities handled);
- missing information on operator practices (e.g. use of controls and protective equipment);
- lack of resident and bystander models.

In Europe, two projects are currently (from 2011 to 2013) being performed to overcome some of these restrictions and limitations: the project BROWSE (Bystanders, Residents, Operators and WorkerS Exposure models for plant protection products) and the project eteam (Evaluation of Tier 1 Exposure Assessment Models under Reach).

BROWSE is supposed to develop a single, new and improved modelling framework for operator exposure as well as models for worker, resident and bystander exposure and to ensure the sustainable use of pesticides. It is aimed at integrating all available exposure data to replace the diversity of different models currently used, implementing a user-friendly software program and testing it with end users in order to provide tools and guidance in support of Regulation

(EC) No 1107/2009 replacing 91/414/EEC (EEC, 1991; EFSA, 2008; EC, 2009b; Hart et al., 2011). The project is supposed to cover all different regions of the EU, to expand the range of crops and tasks, to add other important exposure factors (e.g. degradation of the residue), to integrate all available relevant data and to gather missing information (e.g. realistic task durations, behaviour of operators in relation to use of protective equipment) by conducting a worker survey carried out in the United Kingdom, Italy and Greece (Ngoc et al., 2011; Charistou et al., 2012).

The eteam project, sponsored by BAuA, aims to compare and contrast the different REACH Tier 1 exposure assessment models. The overall aim of this project is to evaluate the generic first-tier exposure tools that are currently widely used for chemical safety assessments under REACH in order to determine or confirm the applicability domains of the models and to achieve more confidence in the accuracy and reliability of the model predictions. Furthermore, the project will review the user-friendliness of the tools to assess their practical usage (BAuA, 2012b). The tools in the project that contain a model to estimate dermal exposure are ECETOC TRA, MEASE and RISKOFDERM.

7. SKIN DISEASES ASSOCIATED WITH DERMAL EXPOSURE

Dermal exposure to chemical or physical agents may lead to skin disease. This chapter gives a brief overview of the spectrum of diseases resulting from dermal exposure to chemicals at the workplace, as well as illnesses and adverse reactions associated with dermal exposure to consumer products. Its intention is to provide a basic understanding of the types of dermal diseases, their extent, affected occupations and associated costs. Direct skin effects, such as irritation and irritant contact dermatitis, as well as examples of diseases caused by immunological reactions after systemic delivery of allergens are discussed. Specific, but not comprehensive, examples of skin diseases and their causes, potential aggravating factors and complications are provided for illustrative purposes. Methods for skin protection and the prevention of dermal diseases are discussed in chapter 8. The following reviews have been used for this chapter, if not otherwise stated: NZ OSH, 1995; Kanerva et al., 2000; LaDou, 2006; Sithamparanadarajah, 2008; Zhai et al., 2008; CCOHS, 2012; HSE, 2012g,h; NIOSH, 2012; NLM, 2012; WebMD, 2012; Safe Work Australia, 2013).

Dermal exposure to chemical agents may also lead to systemic uptake and systemic disease. As these diseases are not specific to dermal exposure, they are not covered in this EHC.

7.1 General types of skin disease

The skin plays an essential role in protecting the body against external threats, and its ability to act as a barrier is particularly important for the prevention of occupational and environmental skin diseases. Occupational skin diseases encompass any abnormality of the skin caused or aggravated by the work environment.

The skin can be exposed by direct contact with an offending agent, which may result in skin disease. Furthermore, exposure by air may cause skin disease, as has been shown for contact allergens (e.g. plants or epoxy resins; Taïeb & Ducombs, 1996) or irritants (e.g. fibres, dust

particle, sprays, vapours; Lachapelle, 2000). In addition to, or together with, the above, physical influences (UV light, ionizing radiation, thermal conditions) may act as pathogens.

There are three general types of chemical–skin interactions that can take place during dermal exposures:

1) An agent can remain on the skin surface and induce local effects, ranging from irritation through burns or skin barrier degradation.
2) An agent can provoke allergic skin reactions at the point of contact and/or other remote sites of the body.
3) An agent may pass through the skin and contribute to the systemic dose (i.e. dermal uptake/absorption; see Appendix 1; IPCS, 2006).

Combinations of the above effects can also occur.

Thus, dermal contact with harmful agents can produce either local or systemic effects after the agents cross the skin barrier. Many exposure scenarios include interactions between these modes of action; for example, an irritant can damage the skin surface, leading to increased percutaneous penetration of the same or other chemicals. Localized harmful effects can range from irritation, burning and urticaria to cancer and can include allergies, phototoxicity and infections. A systemic effect can be observed in other organs or parts of the body after the chemicals penetrate through the skin and enter the bloodstream. A well-known example is systemic (haematogenic) allergic contact dermatitis, where the allergen has entered the bloodstream (after dermal penetration, but also after ingestion or inhalation) and encounters the memory T cells in the skin, thus giving rise to an eczematous reaction. For most chemicals, however, the relationship between dermal uptake and health effects observed elsewhere in the body is still poorly understood. Therefore, the following discussion will focus primarily on localized adverse skin effects, which include contact urticaria, acnes, cancers, leukoderma (vitiligo) and phototoxicity.

In cases where the offending agent can be avoided, the prognosis is quite good; in other cases, where the disease has taken a chronic course (e.g. chronic irritant contact dermatitis) or is complicated by a residual state (e.g. sensitization to a contact allergen), the prognosis is uncertain.

7.2 Contact dermatitis

Dermatitis, or eczema, is a localized inflammation of the skin that affects millions of people worldwide. In general, inflammation refers to a condition in which the body is trying to react to a localized tissue injury. Signs of inflammation can include redness, heat, swelling and pain. Contact dermatitis is one of the most common skin diseases associated with exposure to external irritants or allergens.

Contact dermatitis is caused by direct skin contact, often occurring at the workplace, and may be irritant (irritant contact dermatitis), allergic (allergic contact dermatitis) or both. Owing to similarities in clinical manifestation, histology and immunohistology, the exact distinction between irritant contact dermatitis and allergic contact dermatitis is not always easy, especially in cases of chronic disease. Therefore, diagnostic patch testing is indispensable to exclude underlying sensitization for the identification of irritant contact dermatitis. In addition, a significant proportion of contact dermatitis is caused by the combined effects of both irritation and allergy, where irritation (also due to barrier disruption) plays an important triggering role for sensitization ("danger model"). Overall, more than 80% of all work-related cases are attributed to irritant contact dermatitis, although allergic contact dermatitis prevails in certain occupations (e.g. for dental technicians or painters), and a significant number of work-related contact dermatitis cases are caused by the combined effects of both irritation and allergy (Sithamparanadarajah, 2008). In the majority of these cases, the hands are affected.

7.2.1 Irritant contact dermatitis

Irritant contact dermatitis is a local inflammatory reaction of the skin caused by intense single exposure to or repeated dermal contact with a chemical agent or wet work (see section 4.1.3), which damages skin structures in a direct, non-allergic way (Frosch & John, 2011). As such, irritant contact dermatitis is a nonspecific response of the skin to direct chemical damage associated with the release of inflammation mediators from the epidermal cells. The clinical picture is extremely variable and ranges from chemical burns to chronic irritant forms; thus, it is often indistinguishable from allergic contact dermatitis or strong corrosive agents causing the immediate death of

epidermal cells (chemical burns/skin ulcers; Frosch & John, 2011). It may be a diagnosis by exclusion after careful patch testing (Frosch & John, 2011).

A wide range of chemicals are capable of acting as cutaneous irritants (see Table 34); however, the most frequent origin of irritant contact dermatitis is the repeated exposure of the hands to soaps, cleansers and solvents. High-risk professions are nursing, hairdressing, food processing, construction and handling of plants (Frosch & John, 2011).

Table 34. Examples of skin irritants and allergens and occupations where they occur

Occupations	Irritants	Allergens
Agricultural workers	Plants, fertilizers, pesticides, cleaning products, disinfectants, solvents, dust, fuels and oils, wet work	Rubber, oats, barley, animal feed, veterinary medications, cement, plants, pesticides, wood preservatives
Artists	Solvents, clay, plaster	Turpentine, pigments, dyes, colophony, epoxy resin
Automobile and aircraft industry workers	Solvents, cutting oils, paints, hand cleansers	Chromates, nickel, cobalt, rubber, epoxy and dimethacrylate resins
Bakers and confectioners	Acids, flour, detergents, wet work	Flavours and spices, orange, lemon, essential oils, dyes, ammonium persulfate and benzoyl peroxide
Bartenders	Detergents, disinfectants, scale removers, wet work	Orange, lemon, lime, flavours
Bookbinders	Solvents, glues	Glues, resins, leathers
Butchers	Acids and alkalis, detergents, waste products, wet work	Nickel, sawdust
Cabinet makers, carpenters	Detergents, glues, solvents, thinners, wood dust, wood preservatives	Stains, glues, woods, turpentine, varnishes, colophony, dyes, fungicides
Cleaners	Detergents, other cleaning products, solvents, wet work	Rubber gloves
Coal miners	Dust, wet work	Rubber boots and masks

Table 34 (continued)

Occupations	Irritants	Allergens
Construction workers	Cement, dusts, solvents, sand, wet work, building materials	Chromates, cobalt, rubber and leather gloves, epoxy resins (glues and filling material), woods
Cooks and caterers	Acids and alkalis, bleaching agents, detergents, vegetable juices, wet work	Foods, onions, garlic, spices, flavours, rubber gloves, sodium metabisulfite, lauryl and octyl gallate, formaldehyde
Dentists/dental staff	Disinfectants, detergents, hand cleansers, wet work	Local anaesthetics, mercury, methacrylates, eugenol and other fragrances, disinfectants, rubber, dental impression material
Electricians	Fibre glass, soldering fluxes	Fluxes, resins, rubber
Electroplaters	Acids, alkalis	Nickel, chromium, cobalt
Floor layers	Solvents	Cement (chromates), resins, woods, varnish
Florists and gardeners	Compost, fertilizers, pesticides, wet work, soil, preservatives, manure	Plants, pesticides, rubber gloves, nickel
Foundry workers	Dust, sand	Phenol–formaldehyde and urea–formaldehyde resins, colophony
Hairdressers/ beauticians	Bleaching agents, dusts, dyes, acetone, permanent wave solutions, shampoos, disinfectants, wet work	Hair dyes, persulfates, rubber gloves, formaldehyde, perfumes
Homemakers	Detergents, cleansers, food, wet work	Rubber gloves, foods, spices, flavours, nickel, chromates, polishes, glues
Jewellers	Detergents, solvents	Epoxy resin, metals, soldering fluxes
Hospital workers/ medical personnel/ veterinarians	Detergents, disinfectants, wet work	Latex/rubber gloves, anaesthetics, antibiotics and antiseptics, formaldehyde, glutaraldehyde, phenothiazines, liquid chloroxylenol, hand creams and liquid soaps containing biocides and fragrances

Table 34 (continued)

Occupations	Irritants	Allergens
Mechanics	Cleaners and aggressive hand cleaning products, fuels, greases, oils, paints, solvents, diesel fuel	Rubber gloves, chromates, epoxy resin, antifreeze, cobalt, nickel
Metalworkers	Cutting oils/fluids, solvents, metal shavings/dusts	Nickel, chromates, additives (industrial biocides) in water-based cutting fluids
Office workers	Solvents, photocopiers, adhesives	Rubber, nickel, glue
Painters	Aggressive hand cleaners, solvents, thinners, wallpaper adhesives, including antibacterial/antimould agents	Turpentine, thinners, cobalt, chromates, polyester resins, formaldehyde, epoxy resin, adhesives, biocides in water-based paints
Plastic workers	Solvents, acids, styrene, oxidizing agents	Hardeners, phenolic resins, polyurethanes, acrylics, plasticizers
Printers/ photographers	Solvents, wet work	Nickel, chromates, cobalt, colophony, formaldehyde, turpentine, biocides
Rubber workers	Solvents, talc, uncured rubber, zinc stearate	Rubber, dyes, colophony
Shoemakers	Solvents	Glues, leather, rubber, turpentine, epoxy resins
Tannery workers	Acids, alkalis, reducing and oxidizing agents, wet work	Chromates, formaldehyde, tanning agents, fungicides, dyes
Textile workers	Fibres, bleaching agents, solvents	Formaldehyde resins, dyes, chromates, nickel

[a] Summarized from Cronin (1980); Fregert (1981); Bruze & Emmett (1990); Adams (1999); CCOHS (2008a,b); Frosch & John (2011); HSE (2011b).

Most irritants are believed to cause dermatitis by gradually overwhelming the skin's repair capacity. Mild irritants such as detergents are able to stimulate an inflammatory response of the skin by releasing proinflammatory cytokines and chemokines. Washing out the lipids contained in the stratum corneum may also play a role. Stronger

irritants can produce immediate direct damage to the keratinocytes. Dermatitis induced by mild irritants is often referred to as chronic or cumulative irritant contact dermatitis. Other types of irritant contact dermatitis include acute, acute cumulative, traumatic, pustular, non-erythematous and subjective. Until recently, irritant contact dermatitis associated with exposure to chemicals was considered an entirely non-immunological reaction caused solely by damage to the upper horny skin layer. There is some evidence, however, that chemicals may activate several types of protein after passing through the upper skin layer, suggesting that the immune system may also play a role in the development of irritant contact dermatitis.

7.2.2 Allergic contact dermatitis

Allergic contact dermatitis is a delayed type of induced sensitivity (a type IV hypersensitivity reaction) resulting from dermal contact with an allergen to which an individual has developed a specific sensitivity. Similar to other allergies, allergic contact dermatitis develops in two phases, operationally defined as induction and elicitation. Exposure to an allergen in a sufficient amount can induce skin sensitization. Subsequent exposure to a much lesser amount of allergen at the same or a different site of the skin leads to a secondary immune response in the form of a cutaneous inflammatory reaction, clinically defined as allergic contact dermatitis.

There is an inverse relationship between induction dose and elicitation dose. Individuals sensitized through high doses will react to (very) low doses on re-exposure (Hostýnek & Maibach, 2004). Hence, there is a need to reduce the exposure dose as much as possible in cases where exposure cannot be avoided.

Most chemicals capable of inducing allergic contact dermatitis are small molecules (molecular weight <1000 g/mol; some authors specify molecular weight <500 g/mol) that readily penetrate the skin. These chemicals are referred to as haptens and become immunogenic by conjugation to a carrier such as a protein. Hapten–protein complexes are internalized and processed by Langerhans cells located in the suprabasilar layer of the epidermis. Langerhans cells are dendritic cells that can subsequently migrate to the nearby lymph

nodes and interact with another type of immune cells (CD4+ T cells, also called helper T cells), provoking a primary immune response that results in sensitization. Thus, sensitization to a chemical requires intact lymphatic pathways. The allergen-specific T cells produce "memory cells" that are carried with the systemic circulation and can recognize a future invasion of the sensitizer. Subsequent contact with the sensitizer causes the release of cytokines and histamine, which bring the typical signs of inflammation. Figure 23 shows a simplified schema of the described mechanisms (see also Rustemeyer et al., 2011).

In addition to the above mechanisms, systemic contact dermatitis can occur in individuals with a history of contact allergy after systemic exposure to an allergen—for example, by means of oral, intravenous or intranasal application. Similarly, airborne contact dermatitis (e.g. ragweed dermatitis, which occurs mainly on the face) is caused by airborne allergens.

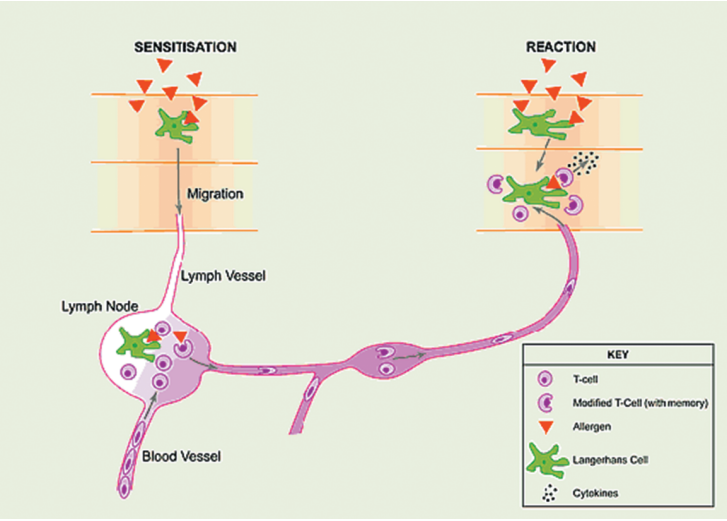


Fig. 23. A simplified schema of development of allergic contact dermatitis (Sithamparanadarajah, 2008).

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Important factors affecting the development of allergic contact dermatitis are duration and type of exposure, concentration and potency of the allergen, genetic susceptibility as well as existing polysensitization to contact allergens (Schnuch et al., 2008, 2011b). For a strong contact allergen such as poison ivy, the initial sensitization typically takes 10–14 days, and the process of sensitization produces no visible change in the skin. In contrast, sensitivity to chromate can develop after years of low-level exposure to wet cement, which is associated with chronic irritant contact dermatitis due to its alkaline nature.

Once sensitized, an individual is likely to remain with the allergy for his or her lifetime. The first step in treatment of allergic contact dermatitis is avoidance of the responsible agent. Avoiding further contact with the sensitizer may gradually reduce the level of sensitivity, but the sensitivity will not completely disappear. In most cases, medical therapy is needed, despite management measures such as avoidance of the offending allergen.

Diagnosis of allergic contact dermatitis involves assessment of the dermatitis pattern and the patient's exposure history. Allergic contact dermatitis is confirmed by a diagnostic "patch test" in which small non-irritating amounts of the test chemicals are placed on discs attached to a tape (a patch) and fixed onto the back of a patient. After 48 hours, the tests are removed and "read", and the patient usually returns for a further reading after another 2–3 days.

Further examples of skin allergens and occupations in which they occur are summarized above in Table 34 (see section 7.2.1). A comprehensive list of individual chemicals and chemical classes causing occupational allergic contact dermatitis can be found in the database Haz-Map (Relational Database of Hazardous Chemicals and Occupational Diseases) of the United States National Library of Medicine (NLM, 2012). Table 35 shows the results of patch testing with collectives of more than 1000 patients in dermatological clinics or in the general population. The consumer products that are shown as sources of exposure in this table demonstrate the relevance of allergic contact dermatitis for the general population. Nickel sulfate is the most important allergen, induced by nickel in jewellery. The prevalence (all individuals affected by the disease; see section 7.8), however, has

Table 35. Examples of frequent contact allergens and their sources

Source	Description	Examples	Prevalence (individuals affected, %)	
			Patients[a]	General population[b]
Costume jewellery, cement	Metallic salts	Nickel sulfate	15–25	0.7–28
		Cobalt chloride	5–6	—
		Potassium dichromate	2–5	0–1.1
Perfumes, perfumed products	—	Balsam of Peru	5–12	0–2.3
		Fragrance mix I (geraniol, hydroxycitronellal, α-amylcinnamaldehyde, eugenol, cinnamaldehyde, cinnamyl alcohol, isoeugenol, oakmoss)	5–12	0–3.4
		Fragrance mix II (Lyral™, citral, citronellol, farnesol, coumarin, hexyl cinnamic aldehyde)	2–5	—
Rubber	Antidegradant rubber	Mercaptobenzothiazole	0.5–1	—
		Mercapto mix	0.4–1.2	0–0.9
		Thiuram mix	1.6–4	0–1.7
		N-Isopropyl-*N*′-phenyl-*p*-phenylenediamine	0.3–1	—
Adhesives, pine	Rosin	Colophony	2–4	0–2.3
Hairdressing	Dying	4-Phenylenediamine	3.2–5	0–1.3
	Perming solution	Glyceryl monothioglycolate	2	—
	Bleach	Ammonium persulfate	0–1	—
Clothes	Dyes	Basic Red 46	—	—
	Wool	Lanolin	1–3	0–0.9
Shampoo, cleansers, household products, paints	Preservatives	Formaldehyde	1–9	0–1.7
		Methyldibromoglutaronitrile/phenoxyethanol	1–3	—
		Methylchloroisothiazolinone/methylisothiazolinone	2–4	0–0.6
		Quaternium-15	1–2	0–0.6
Drugs	—	Bufexamac	1	—
		Neomycein	1–10	—
		Bacitracin	9	—

[a] Prevalence in patients from dermatological clinics. Data from Germany (Geier et al., 2011), Australia (Cahill et al., 2012), different regions in Europe (Uter et al., 2009) and North America (Zug et al., 2009).

[b] Nielsen et al. (2001); Thyssen et al. (2007).

declined in recent years (Geier et al., 2011). Sensitization to cobalt is often secondary to either nickel sulfate or potassium dichromate sensitization (Geier et al., 2011).

Other important sensitizers are fragrances (see section 4.2.2.1). Balsam of Peru is another compound with high sensitization rates. Other sensitizers include several constituents of rubber, components of hair dyes, preservatives and drugs. For the prevalence of sensitization to drugs, there are major differences between countries; the prevalence of sensitization is considerably lower in Europe than in the USA (Uter et al., 2009; Zug et al., 2009).

Allergic contact dermatitis in children was previously considered to be a rare occurrence. However, there has been an increase in the number of case reports and cross-sectional studies in the last 30 years indicating that allergic contact dermatitis is highly relevant to children and that the frequency of allergic contact dermatitis in children is increasing. The most common allergens are nickel, cobalt, thimerosal and fragrances (Simonsen et al., 2011). Similarly, in Spain, the most frequent allergen, assessed by degree of relevance, was reported to be nickel, followed by cobalt, mercurials (thimerosal and metallic mercury), fragrances and rubber chemicals (naphthyl mix, mercapto mix, carba mix and *p*-phenylenediamine mix) (Romaguera & Vilaplana, 1998). In a study from Poland (Czarnobilska et al., 2012), preservatives, fragrances, propolis and balsam of Peru were also given as frequent allergens for children. The rates of contact sensitization in children reflect changes in their environment, and limitations imposed on the use of haptens with strong sensitizing properties may be an effective tool in the prevention of contact allergy. Children with moderate to severe allergic contact dermatitis have a high rate of contact allergy. Prevention is recommended through avoidance of exposure to the most frequent contact allergens, especially fragrances (Herro et al., 2011).

7.3 Contact urticaria

Contact urticaria is an immediate transient skin swelling surrounded by areas of redness (a condition commonly named wheal-and-flare) that occurs after direct contact with certain substances, such

Table 36. Examples of causes of contact urticaria and occupations where they occur[a]

Agents	Type of workers
Foods, spices, herbs	Cooks, food preparation workers, other kitchen workers
Food additives (e.g. cinnamic acid, benzaldehyde, benzoic acid, albumin)	Cooks, food preparation workers, other kitchen workers, bakers and millers
Animal hair	Animal husbandry worker, veterinarians, nurses, laboratory workers
Latex proteins	Health-care workers, animal husbandry workers, veterinarians, laboratory workers
Topical drugs	Health-care workers, pharmaceutical workers
Disinfectants	Hairdressers, cleaners, kitchen staff
Resins	Construction workers, resin manufacturing workers, printers, nail technicians
Chemicals used in rubber production	Rubber processing workers

[a] From HSE (2011c).

as foods, preservatives, fragrances, plant and animal products, metals and rubber latex (Table 36). Contact urticaria should be distinguished from allergic contact dermatitis, in which a reaction develops hours to days after contact with the offending agent. Contact urticaria is probably more common than currently recognized, and it can arise from different mechanisms: immunological (allergic) contact urticaria and non-immunological contact urticaria. In addition, a large group of urticaria cases is considered to have unknown causes.

Non-immunological contact urticaria is an immediate reaction of the skin that occurs in exposed individuals without prior sensitization. The clinical symptoms may vary depending on the identity, concentration and vehicle of the substance, the site and mode of exposure, as well as other factors, such as scratching and rubbing. The mechanism of non-immunological contact urticaria is not completely understood. While earlier research implied that histamine release from the mast cells is responsible for eliciting a reaction, later evidence suggested the involvement of prostaglandins. Prostaglandins have been

demonstrated to mediate the reaction to methyl nicotinate and benzoic and ascorbic acids, and treatment with inhibitors of prostaglandin synthesis suppresses the reaction to these substances. Substances causing non-immunological contact urticaria are usually low molecular mass chemicals capable of crossing the skin barrier. Some commonly reported causes of non-immunological contact urticaria include balsam of Peru, benzoic acid, cinnamic alcohol, cinnamic aldehyde, sorbic acid and dimethylsulfoxide.

Immunological contact urticaria is a type I hypersensitivity reaction mediated by immunoglobulin E (IgE) antibodies specific to the eliciting substance. As with allergic contact dermatitis, prior sensitization is required that can be either at the cutaneous level or via the mucous membranes of the respiratory or gastrointestinal tract. Subsequent exposure causes a reaction between the sensitizer, IgE cells and the mast cells, leading to the release of histamine, exoglycosidases, neutral proteases and proteoglycans, which cause an immediate wheal-and-flare response. Agents responsible for immunological contact urticaria are predominantly proteins; however, there is some evidence that low molecular mass chemicals (haptens) may also cause IgE-mediated type I allergic reactions. In this case, the hapten binds to a protein or macromolecule that acts as the allergen. Immunological contact urticaria reactions may spread beyond the site of contact and progress to a generalized urticaria, which in severe cases may lead to anaphylactic shock. At present, natural rubber latex is the most important cause of occupational immunological contact urticaria. Other frequently reported causes include raw meat and fish, semen, many antibiotics, some metals (e.g. platinum, nickel), acrylic monomers, short-chain alcohols, benzoic and salicylic acids, parabens, polyethylene glycol, polysorbate and other chemicals.

7.4 Acne (oil acne, chloracne, coal tar acne)

Acne is an inflammatory disorder of the sebaceous glands caused by hyperproliferation of the glans acini, leading to a blockade of sebum excretion and its retention and accumulation in the follicle; the follicle passes through the stage of a comedo to a ruptured follicle,

leading to inflammation of the skin in the form of papules and pustules. Acne can result from exposures to various chemical and environmental factors (physical or mechanical), usually encountered at the workplace, but occasionally in non-occupational settings as well. Acne is regarded as one of the most frequent causes of work-related skin disease, second only to contact dermatitis (Ancona, 1986). The skin eruptions may be mild and localized to the exposed parts of the body or severe, involving most of the follicular orifices. Different forms of acne have been associated with exposure to petroleum and its derivatives (i.e. crude oil, metalworking and cutting oils), certain coal tar products and halogenated aromatic compounds (Table 37). Acne cosmetica is a medical condition common in actors and models who are required to wear heavy and greasy makeup regularly, whereas tropical acne may develop in hot and humid environments, as observed among soldiers stationed in tropical climates. Acne mechanica is another form of acne caused by heat, occlusion, constant pressure and repetitive friction against the skin.

Oil acne is perhaps the most common form of occupational acne. It is frequently observed in heavy machinery workers, mechanics, and refinery and rubber workers. Oil acne results from irritation of the hair follicle by mineral oils, and it occurs in the form of blisters and small spots on the forearms and thighs of machine tool operators where exposure to oil is heavy. Characteristic features of oil acne include darkening of the skin caused by excessive production of melanin and an abnormal skin reaction to sunlight. Where adequate control measures aimed at minimizing the use of neat cutting oils and improved handling methods for crude oil have been introduced, they have led to a decline in the incidence (number of new cases; see section 7.8) of oil acne (Sithamparanadarajah, 2008).

Coal tar products cause coal tar acne, and this has been known ever since doctors discovered that acne was an occupational hazard of chimney sweeps. Occupations at risk include coal tar plant workers, roofers, and construction and road maintenance workers. In general, coal tar acne clears rapidly, but in some cases it may be aggravated by phototoxic reactions due to concurrent sun or UV light exposure.

Table 37. Causes of acne in various occupations[a]

Type	Agent	Occupational group
Oil acne	Petroleum and its derivatives: crude oil and fractions, cutting oils	Machine tool operators, mechanics, workers exposed to petroleum and its derivatives
Coal tar acne	Coal tar products: coal tar oils, pitch, creosote	Coal tar plant workers, construction workers, roofers, asphalt paving workers, paper tube impregnation workers, conduit manufacturers, wood and cable preservation workers
Chloracne	Halogenated aromatic compounds: PCBs, dibenzofurans (PCDFs) and dibenzo-*p*-dioxins (e.g. TCDD), chloronaphthalenes, 3,4,3′,4′-tetrachloroazoxybenzene, 3,4,3′,4′-tetrachloroazobenzene	Chemical manufacturing workers, laboratory workers, maintenance workers, waste handling workers, workers in different industries using certain halogenated hydrocarbons
Acne cosmetica	Cosmetic ingredients: lanolin, petrolatum, vegetable oils, butyl stearate, lauryl alcohol, oleic acid	Actors, models and others in the entertainment industry
Acne mechanica	Heat, covered skin, constant local pressure and repetitive friction	Hospital and clean room workers, athletes wearing tight synthetic clothing, truck drivers, some musicians (violinists' neck)
Tropical acne	Heat	Soldiers in tropical countries, foundry workers

PCB, polychlorinated biphenyl; PCDF, polychlorinated dibenzofurans; TCDD, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin

[a] Adapted from CCOHS (2008c).

Exposure to various halogenated aromatic compounds causes chloracne (Table 37), which is a specific effect on the sebaceous follicle. It can be a relatively mild condition, confined to the face and neck, although severe cases also occur. There may be only small groups of open comedones (blackheads) in the cheek areas and one or two characteristic "blind" straw-coloured cysts behind the ears. Chloracnegenic substances show structural similarities (i.e. polarity, planar orientation), and the degree and position of halogen substitution appear to be critical for their activity. A decreasing incidence of chloracne is

largely attributed to the gradual reduction or elimination of the use of the above chemicals (Kokelj, 1992).

From an industrial hygiene perspective, it is important to detect and report even minor incidences of occupational acne because of the utility of occupational acne as an early indicator for possible systemic exposure to chloracnegens. Chloracne is considered a sensitive biomarker of exposure to these chemicals, independent of their exposure route. Current evidence suggests that the external dose required to cause chloracne is significantly lower than that needed to cause systemic disorders (changes in circulating blood lipid levels, porphyria or any form of neoplasia/tumour).

7.5 Pigmentary disorders

A variety of chemicals can disrupt the normal colour factors of the skin (chromophores such as oxyhaemoglobin, carotene and melanin), resulting in pigmentary changes. Melanosis denotes hyperpigmentation, whereas leukoderma refers to loss of pigmentation.

Occupationally induced hyperpigmentation is the most common work-related pigment change, and it refers to the increased production of melanin by existing or proliferated pigment-producing cells (melanocytes). Hyperpigmentation may result from inflammatory dermatosis, excessive exposure to sunlight, chemical photosensitivity and other physical agents (ionizing radiation, chemical and thermal burns). Prolonged exposure to heat from open flames can result in striking reticulate pigmentation called erythema ab igne. Affected are glass workers, welders, foundry workers, open field cooks, bakers and silversmiths, who can subsequently develop thermal keratoses, progressing in some cases to squamous cell carcinoma.

Consumers may encounter hyperpigmentation in a special type of allergic contact dermatitis. Important agents are fragrances and dyes (Nakayama, 2011).

Certain workplace chemicals can selectively destroy melanocytes, causing a reduction in melanin content. This condition is expressed as paler or completely white patches of skin compared

with the individuals' normal skin. Hypotheses regarding the selective destruction of melanocytes include cytotoxicity, disturbance of oxidant–antioxidant balance, an intrinsic defect of melanocytes and autoimmune or neural mechanisms. While leukoderma is a general term for any pigmentary dilution, chemical leukoderma is a depigmentation due to chemicals that suppress the production of melanin or have a specific toxic effect on melanocytes. Chemical leukoderma is reversible if exposure is discontinued shortly after the onset of disease; however, it may become permanent if exposure remains. Vitiligo is another form of acquired progressive pigmentary disorder of the skin and mucous membranes characterized by circumscribed depigmented macules and patches. Vitiligo affects 0.5–2% of the world population, and the average age of onset is 20 years.

About 1% of adults suffer from depigmentation, and most cases in the general population are of unknown cause. Alkyl catechols (e.g. tertiary butanol), quinones (e.g. hydroquinone), alkyl phenols (e.g. *p*-*tert*-butylphenol) and thiols (β-mercaptoethylamine hydrochloride) are some of the chemicals reported to have had this effect occupationally (Nakayama, 2011; Noury et al., 2012). Cases have been described in many occupational groups, including chemical workers, engineering workers (from oil), automobile workers (from adhesives) and even hospital personnel (from germicides).

Some cases of vitiligo have been reported from the clinical use of hydroquinone for depigmentation (Nakayama, 2011).

7.6 Phototoxicity and photoallergy

Some chemicals have the ability to become activated by light with wavelengths within the UV-A range (320–400 nm). They have at least one resonating double bond or an aromatic ring that can absorb radiant energy. The mechanism of skin response can be either irritant (toxic) or allergic, leading to the development of photoirritant (phototoxic) or photoallergic reactions, respectively. The term phototoxicity refers to chemically induced increased reactivity of the skin after exposure to UV and/or visible radiation that occurs through a non-immunological mechanism. In contrast, photoallergy is an acquired, immunologically mediated reaction to a chemical activated by light,

and a delay is required for the development of photoallergic contact dermatitis. Phototoxic reactions can be further grouped into those that require oxygen (photodynamic reactions) and those that do not (non-photodynamic reactions). Reactions induced by porphyrins, coal tar products and some drugs are photodynamic. The photosensitizing effects of psoralen are a prominent example of a non-photodynamic reaction.

In most phototoxic reactions, photoactivation of a chemical results in the excitation of electrons from a stable singlet state to an excited triplet state. Returning to a more stable configuration, triplet electrons transfer their energy to oxygen, leading to the formation of reactive oxygen intermediates, such as an oxygen singlet, superoxide anion and hydrogen peroxide, which can damage cell membranes and DNA. This leads to activation of signal transduction pathways, which causes the release of cytokines and arachidonic acid metabolites, resulting in an inflammatory response that has the clinical appearance of an exaggerated sunburn reaction. Some phototoxic agents include furanocoumarins such as 8-methoxypsoralen, PAHs (anthracene, acridine and phenanthrene), tetracyclines, phenothiazines and thiazides (Table 38).

Photoallergic reactions are cell-mediated responses of the immune system where the antigen is a molecule activated by light. Exposure to light facilitates the binding of a photosensitizer to carrier proteins in the skin, forming a complete antigen that subsequently migrates with antigen-presenting cells (e.g. Langerhans cells) to regional lymph nodes. The process is similar to the immune responses of the skin described above. In the lymph nodes, T cells are activated, proliferate and are transported back to the site of initial contact with the photoallergen. Subsequent topical or systemic exposure to the photoallergen initiates an inflammatory response of the skin. Photoallergens include some halogenated salicylanilides, sulfonamides, coumarin derivatives, sunscreen components (glycerol, *p*-aminobenzoic acid) and several plant products (Table 38).

In general, phototoxicity is more frequent than photoallergy, and most cases of photosensitivity are associated with outdoor activities. The clinical signs may include swelling, redness, blistering and, in certain cases, hyperpigmentation. Photosensitivity reactions are affected

Table 38. Characteristics of phototoxic/photoallergic reactions and examples of some photosensitizers[a]

Feature	Phototoxic reaction	Photoallergic reaction
Incidence (number of new cases)	High	Low
Amount required for photosensitivity	Large	Small
Onset of reaction after exposure	Minutes to hours	24–72 hours
Occurrence on first exposure	No	Yes
Localization	Sun-exposed skin only	Sun-exposed skin, may spread to unexposed areas
Cross-reactivity with other agents	Rare	Common
Clinical characteristics	Exaggerated sunburn reaction	Eczematous lesions, dermatitis
Immunologically mediated	No	Yes; type IV
Example chemicals	Acridine, anthracene, coal tar, fluoroquinolones, 5-methoxypsoralen, phenanthrene, phenothiazines, psoralen, sulfonamides, sulfonylureas, tetracyclines, xanthoxin	Benzocaine, benzophenones, chloro-2-phenylphenol, coumarins, dichlorophene, diphenhydramine, fentichlor, halogenated phenols, musk ambrette, optical brighteners, *p*-aminobenzoic acid, phenothiazines, pyridoxine hydrochloride, sandalwood oil

[a] From Elkeeb & Maibach (2012); Heydari et al. (2012); Zhang (2012).

by the amount of the chemical and skin location, characteristics of the activating radiation, thickness and pigmentation of the skin, as well as immunological status of the person. Typical phototoxic sensitizers are components of tar products, such as acridine, anthracene and benzopyrene, causing very distinctive reactions (the so-called "tar smarts") in exposed roofers. Another group of naturally occurring photosensitizers is furanocoumarins, found frequently in fruits and vegetables. "Phytophotodermatitis" is a condition commonly reported by farmers, cannery workers, grocery store clerks and chefs. Exposure to citrus

fruits, which contain significant amounts of furanocoumarins, is the most common cause of non-occupational phytophotodermatitis. Many prescription drugs are systemic phototoxic sensitizers, and there are instances in which health-care workers and farmers have developed contact photosensitivity after delivering medications to patients and animals.

7.7 Skin cancers

Skin cancer is the most common of all human cancers. In the United Kingdom, 20% (490 cases) of the skin disease cases reported within The Health and Occupation Reporting network surveillance programme in 2009 were skin cancers (HSE, 2011d). Skin tumours can result from exposure to ionizing radiation, some metals, arsenicals, PAHs, etc. Occupational skin cancers can be broadly defined as those induced by chemical and/or physical agents at the workplace, and they are more common than is generally recognized. In addition, exposure to a carcinogen can cause premalignant changes specific to the inducing carcinogen that may or may not develop into a true malignancy. The most widespread cause of skin cancer in light-skinned populations is exposure to sunlight, specifically to its UV component. Other causes and corresponding occupations are shown in Table 39.

The common types of skin cancer include malignant melanoma and non-melanoma skin cancers: basal cell carcinoma and squamous cell carcinoma. Non-melanoma skin cancers are the most common form of cancer, with roughly 80% attributed to basal cell carcinoma and the rest being squamous cell carcinoma. The latter cancer is the more invasive and accounts for most of the deaths attributable to these tumours. Although non-melanoma skin cancers have an overall low mortality rate, their social importance is steadily increasing because of increased morbidity rates and associated costs of treatment.

Malignant melanoma is a cancer of melanocytes, the pigment cells of the epidermis, and its etiology is still largely unclear. Increased risk of melanoma has been associated with occupational exposure to printing lights, welding torch lights and fluorescent lights. Chemicals such as PCBs and vinyl choride were also suspected, acting independently of UV irradiation (Rockley et al., 1994; Gallagher et al., 2011).

Table 39. Examples of agents that cause skin cancer and occupations where they occur[a]

Causative agents	Occupation/type of work
UV radiation	Outdoor work (e.g. agriculture, driving, fishing and construction); welding, laser exposure, certain printing processes
Ionizing radiation	Nuclear industry, diagnostic X-ray work, uranium mining, airline personnel
Coal tar and derivatives	Coal tar handling, coal gasification, coal tar distillation
PAHs	Petroleum refining, coal tar distillation, working with shale oil, creosote, asphalt and chimney soot
Arsenic	Metal ore handling, pesticide manufacturing and agricultural exposure, smelting of copper, lead and zinc, mining of arsenic
Coke	Coke processing
Soot	Chimney cleaning

PAH, polycyclic aromatic hydrocarbon

[a] Adapted from HSE (2011e).

Further risk factors include fair complexion, excessive childhood sunburns, use of indoor tanning devices (Gandini et al., 2011), an increased number of common and dysplastic moles, a family history of melanoma, the presence of a changing mole or evolving lesion on the skin and, importantly, older age. Only between 5% and 10% of all reported skin cancers are diagnosed as malignant melanomas, and they cause the greatest number of deaths related to skin cancer worldwide.

Basal cell carcinoma is a malignant tumour of the basal cells of the epidermis, which can affect the lower layer of the skin and invade through adjacent tissues. This type of cancer is believed to be caused by skin damage from the sun and is commonly diagnosed in outdoor workers. It rarely metastasizes. In most cases, the contribution of chemical exposure has been difficult to estimate due to daily co-exposure to sunlight. Additional sources of occupational exposure to UV radiation can be welding processes and UV tubes.

Squamous cell carcinoma is a malignant tumour of the keratinocytes that usually develops in people over the age of 55 years. This

type of cancer is 3 times more common in men than in women, and it is particularly dangerous because of its ability to penetrate the lymphatic circulation and metastasize. Squamous cell carcinoma is associated with exposure to sunlight or other sources of irradiation, including localized heat. Occupational squamous cell carcinoma is mainly caused by physical and chemical agents such as PAHs, unrefined mineral oils and sunlight (Table 39).

The best way to prevent skin cancer is the consistent application of sun protective practices. Further measures include improvements in industrial processes, reduction in the use of coal tar products and special care in the handling of sources of ionizing radiation.

7.8 Relevance of skin diseases

Common measures of the extent of diseases in a specified population are their prevalence (number of individuals affected by the disease at a certain point in time) and incidence (number of new cases during a particular period of time). Prevalence and incidence are frequently expressed as proportions (related to the population under risk, e.g. the total workforce in a country). The incidence rate is the number of new cases per unit of person-time. Prevalence is considered as a measure of the spread of a disease, whereas incidence is associated with the risk of contracting a disease.

The most important skin disease for the general population is allergic contact dermatitis (see section 7.2.2). Overall, in the general population in North America and western Europe, the prevalence of contact allergy to at least one allergen was 21.2%, according to a review of studies conducted from 1966 to 2007 (Thyssen et al., 2007). Thus, allergic contact dermatitis is a skin disease with high relevance for consumers.

Data on the prevalence and incidence of occupational skin diseases are rather heterogeneous. Sources of information include occupational disease registries, case-studies and cross-sectional studies in specific occupational groups. National disease registries provide incidence

data based on the notification of occupational skin diseases and usually combine all types of skin disease. The prevalence of occupational skin diseases is up to 19% (Shao et al., 2001; Schaefer et al., 2008). However, one has to consider that there is a high background for skin disease in the general population, as already indicated in section 7.2.2. Compared with the overall workforce, for occupations with high dermal exposure, such as hairdressers, printers and cleaners, the prevalence of occupational skin diseases is higher, lying between 14% and 65% (Perkins & Farrow, 2005; Sithamparanadarajah, 2008). Occupational skin disease represent about 10% of all occupational diseases in Europe and the USA (de Craecker et al., 2008; BLS, 2011; HSE, 2011d). The incidence rates for skin disease range from 5 to 134 per 100 000 workers per year in disease registries from different countries. In contrast to the pattern of skin disease in the general population, where allergy prevails, the most important occupational skin disease is irritant contact dermatitis, accounting for about 50–90% of the cases of skin disease (de Craecker et al., 2008; Schaefer et al., 2008). Skin cancer was detected in 0.009–19% of the cases (de Craecker et al., 2008; Schaefer et al., 2008). According to HSE (2011d), the high differences are due to the fact that skin cancer has a long latency. Therefore, the time of examination in relation to exposure is important. High figures come from dermatologists who also see workers after retirement.

In general, these data have to be treated with caution. Difficulties such as the lack of standard definitions of skin diseases suggest that the extent of skin diseases might be underestimated. National registries can be incomplete because of underdiagnoses and underreporting of milder cases of skin disease. As each country has its own system of notification and its own criteria for compensation, the extent of underreporting is likely to differ between countries. Furthermore, where respondents are suffering from more than one illness, prevalence estimates are often based on the illness they regard as most severe.

Occupational skin diseases can have a critical impact on public health. Patients with severe skin disease may become physically unable to work (absenteeism) and/or suffer impaired productivity and work efficiency (presenteeism). Both absenteeism and presenteeism contribute to the indirect costs and overall economic burden of skin disease.

Affected workers are frequently forced to change occupations and bear the costs of prequalification. In addition, many chronic skin diseases can have significant negative effects on a patient's quality of life. The visibility of dermatological diseases often leads to lowered self-esteem, rejection and social withdrawal, making skin diseases particularly socially devastating.

8. METHODS FOR EXPOSURE PREVENTION AND REDUCTION

Exposure to chemicals can present varying degrees of risk to human health. This chapter starts with a brief overview of legislative measures aimed at the protection of workers and consumers. This overview is followed by a presentation of general means of hazard identification, which enables the risks due to dermal exposure to be recognized and identified. Exposure prevention and reduction measures aim, on the one hand, to avoid the hazard by elimination or substitution where possible and, on the other hand, to minimize exposure by reducing dermal contact. Exposure control and risk management measures and their hierarchy in the workplace and for consumers are described. Although considered as ultimately a last resort, personal protective equipment (PPE) is widely accessible and one of the most common means of personal skin protection. This is particularly the case for protective gloves and skin protective products (creams). Thus, the factors influencing the effectiveness of PPE and principles for the adequate selection of PPE are discussed as well.

8.1 Legislation/regulatory requirements and approaches to exposure control and risk management

8.1.1 The occupational environment (workplace)

Employers are often required by law to protect their workers from being harmed in the workplace. In the following, legislation in both the EU and the USA is briefly discussed to show how workers' protection can be regulated by different authorities. Several other countries have regulations in place. It should be noted, however, that legislation varies from country to country.

8.1.1.1 European Union

In the EU, the entry into force of the Treaty of Nice, Article 137 (EU, 2001), served as the basis for the improvement of the working environment to protect workers' health and safety (Lauranson, 2010).

Table 40. Examples of EU directives introducing further measures aimed at improving the safety and health of workers in specific workplace environments

Directive	Subject matter	Reference(s)
Directive 89/654/EEC	Requirements for workplaces	EEC (1989b)
Directive 89/655/EEC amended by Directive 2001/45/EC	The use of work equipment	EEC (1989c); EC (2001c)
Directive 89/656/EEC	The use of personal protective equipment	EEC (1989d)
Directive 90/269/EEC	Manual handling of loads	EEC (1990a)
Directive 90/394/EEC	Exposure to carcinogens	EEC (1990b)
Directive 92/58/EEC	Provision of safety and health signs at work	EEC (1992a)
Directive 92/85/EEC	Pregnant workers	EEC (1992b)
Directive 98/24/EC amended by Directive 2000/39/EC	The protection of the health and safety of workers from the risks related to chemical agents at work	EC (1998b, 2000a)
Directive 2000/54/EC	The protection of workers from the risks related to exposure to biological agents at work	EC (2000b)
Directive 2004/37/EC	The protection of workers from the risks related to exposure to carcinogens or mutagens at work	EC (2004)

The subsequently released Directive 89/391/EEC (EEC, 1989a) is one of the cornerstones for health and safety in the workplace, with a particular focus on the culture of prevention (Lauranson, 2010). The directive served as the basis for further "daughter directives" (Table 40), providing a framework for the introduction of measures aimed at improving the safety and health of workers in specific workplace environments. These directives set out minimum requirements and fundamental principles, such as the principle of prevention and risk assessment at the workplace, as well as the responsibilities of employers and employees. European directives are legally binding and have to be transposed into national laws by member states. For further information, see the website of the EU OSHA (2013).

Table 41. Examples of EU policies concerning risk assessment and risk management[a]

Directive/Regulation	Subject matter	Reference
Directive 2001/95/EC	General Product Safety Directive	EC (2001b)
Regulation (EC) No 1907/2006	REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals)	EC (2006)
Directive 98/8/EC	Placing of biocidal products on the market	EC (1998a)
Directive 91/414/EEC	Placing of plant protection products on the market	EEC (1991)
Regulation (EC) No 1272/2008	Classification, labelling and packaging of substances and mixtures, introducing the Globally Harmonised System of Classification and Labelling of Chemicals (GHS)	EC (2008)

[a] From Bruinen de Bruin et al. (2007).

In addition, regulatory approaches to risk assessment and risk management are addressed by several policies (see Table 41). The implementation of the REACH Regulation (EC, 2006) aims to increase protection of the environment and the health of the population. It requires that information on chemicals be provided throughout the supply chain, including information on the risks posed by substances and how they should be handled. Key elements of the REACH strategy are the concepts "derived no-effect levels" (DNELs; ECHA, 2012d) and "exposure scenarios" (ECHA, 2012b), which describe conditions and risk management measures needed for the safe use of chemicals. An overview of risk management measures in the occupational environment and the hierarchy of exposure control measures is provided in section 8.3.

8.1.1.2 *United States of America*

In the USA, the primary agencies with regulatory authority over work establishments and workers are the Occupational Safety and Health Administration (OSHA), the USEPA and the USFDA. OSHA mandates the obligations of employers to ensure the safety of their workers and provides various information material on its website (OSHA, 2013a). Key regulatory statutes affecting occupational skin exposures are presented in Table 42 (OSHA, 2013c,d). In addition,

Table 42. Key regulatory statutes affecting occupational skin exposures in the USA[a]

Regulatory Act (Standard)[b]	Content
29 CFR 1910.1000 Table Z-1	Skin notations alert employer of additional hazard from skin absorption
29 CFR 1910.1001-29 / CFR 1910.1050 Substance-specific OSHA standards	Substance-specific standards include general requirements for hygiene facilities, protective clothing and medical surveillance
29 CFR 1910.120 Hazardous Waste Operations and Emergency Response	Provides general description and discussion of the levels of protection and protective gear when personnel are working to remediate hazardous waste sites
29 CFR 1910.132–138 Personal Protective Equipment Standard	To provide appropriate personal protective equipment, including protection of the skin
29 CFR 1910.141 General Industry Sanitation Standard	Employer shall provide adequate washing facilities for employees in industry
29 CFR 1928.110 Field Sanitation Standard	Employer shall provide adequate washing facilities in the field for hired farm workers
29 CFR 910.1926.51(f) Construction Industry Sanitation Standard	Employer shall provide adequate washing facilities for employees in construction
29 CFR 1900.1200 Hazard Communication Standard	To identify and communicate hazards to employees
40 CFR Part 170 Worker Protection Standard	Prescribes protective measures against pesticide exposures for agricultural workers
40 CFR, Part 721 Toxic Substances Control Act (TSCA)	Defines types of production and health effects data to be reported to USEPA
Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)	Requires submission of toxicological and exposure information necessary for risk/benefit assessments
General Duty Clause of the Occupational Safety and Health Act (Section 5(a)(1))	Employer provides a workplace free from serious recognized hazards

CFR, Code of Federal Regulations

[a] From Boeniger (2003a).

[b] Code of Federal Regulations available at http://www.archives.gov/federal-register/cfr/.

other non-mandatory guidelines for hazard assessment, PPE selection, training programmes and specific occupational environments are also available (OSHA, 2013a,b).

8.1.2 The non-occupational environment (consumer products)

Regulatory requirements for consumer products vary between countries in terms of their scope and impact. Often legislation focuses on a specific type of product, whereas others are excluded and may not be regulated at all. For instance, the Canada Consumer Product Safety Act (Government of Canada, 2010) applies to a wide variety of consumer products, including children's toys, household products and sporting goods, but excludes products such as motor vehicles, cosmetics, food or drugs, as these are regulated by other Canadian laws. Specific consumer products may be more tightly regulated than others (e.g. ingredients in children's toys). In fact, a substance that may be prohibited in the regulatory scope of one regulation may not be addressed in another type of consumer product.

On an international level, legislation and regulations also differ from one jurisdiction to another in terms of the requirements that consumer products must satisfy before they can be marketed. The safety and efficacy of the product may need to be proven before the product can be marketed (i.e. product authorization). In addition, legislation may define requirements concerning the product characteristics (e.g. child-proof containers) or product labelling (e.g. warning symbols and level of detail of instructions for use). For example, the key provisions of the Canada Consumer Product Safety Act are (Government of Canada, 2010):

- increased fines and penalties, including an administrative monetary penalties scheme;
- ability to require tests and studies necessary to verify compliance or prevent non-compliance;
- ability to order suppliers to carry out recalls and to take other corrective actions;
- "general prohibition" against the supply of consumer products that pose a danger to human health or safety;
- requirements for record-keeping to allow traceability of products within the distribution chain;

- requirement for industry to report an incident and recalls;
- requirements to provide inspectors carrying out their functions all reasonable assistance and information.

In the EU, the safety of consumers is assured by the General Product Safety Directive (Directive 2001/95/EC; EC, 2001b). In addition, the REACH Regulation not only affects workers (see section 8.1.1) but also requires the registrant to develop exposure scenarios and risk assessments to guarantee the safe use of a consumer product. However, REACH generally applies to chemical substances that are used in quantities of 10 tonnes or more per year. In the USA, the Toxic Substances Control Act (TSCA) provides the USEPA with the authority to require reporting, record keeping and testing requirements and restrictions relating to chemical substances and/or mixtures, and its inventory now exceeds 84 000 chemicals (USEPA, 2012g). The USEPA performs risk assessment; if there is a significant risk, appropriate risk reduction actions will be assessed. In addition, the USEPA aims to make health and safety information available to the public to the extent allowed by law (USEPA, 2012g).

8.2 Hazard identification

8.2.1 Classification and labelling: Globally Harmonized System

Legal requirements for information on chemical hazards and appropriate labelling exist in many countries. An international mandate for the need to develop harmonized hazard classification and labelling systems was concluded in Agenda 21 of the United Nations Conference on Environment and Development in Rio de Janeiro in 1992 (UN, 1993). In 2002, the United Nations adopted the Globally Harmonized System of Classification and Labelling of Chemicals (GHS), which provides harmonized criteria for the classification, packaging and labelling of dangerous substances and preparations and has been recently revised for the fourth time (UN, 2011).

Chemical health hazard information is communicated with risk phrases that include the prefix “H” followed by a specific number. Table 43 lists all phrases relating to systemic toxicity due to dermal

Table 43. Hazard (H) statements according to the United Nations GHS that are relevant in relation to skin exposure and former risk (R) phrases (as still in use), as well as precautionary measures (P)

Hazard statements			
EU Dangerous Substances Directive (old)		United Nations GHS (new)	
Systemic exposure via skin			
R21	Harmful in contact with skin	H310	Fatal in contact with skin
R24	Toxic in contact with skin	H311	Toxic in contact with skin
R27	Very toxic in contact with skin	H312	Harmful in contact with skin
		H313	May be harmful in contact with skin
Local effects due to exposure of skin			
R34	Causes burns	H314	Causes severe burns and eye damage
R35	Causes severe burns	H315	Causes skin irritation
R38	Irritating to the skin	H316	Causes mild skin irritation
R43	May cause sensitization by skin contact	H317	May cause an allergic skin reaction
R66	Repeated exposure may cause skin dryness or cracking	EUH066	Repeated exposure may cause skin dryness or cracking (only additionally in EU)

Precautionary statements	
P262	Do not get in eyes, on skin, or on clothing
P280	Wear protective gloves/protective clothing/eye protection/face protection
P281	Use personal protective equipment as required
P282	Wear cold insulating gloves/face shield/eye protection
P302+334	If on skin: Immerse in cool water/wrap in wet bandages
P302+350	If on skin: Gently wash with soap and water
P302+352	If on skin: Wash with plenty of soap and water
P303+361+353	If on skin (or hair): Remove/take off immediately all contaminated clothing. Rinse skin with water/shower
P332+313	If skin irritation occurs: Get medical advice/attention
P333+313	If skin irritation or rash occurs: Get medical advice/attention
P335+334	Brush off loose particles from skin. Immerse in cool water/wrap in wet bandages

exposure (followed by absorption), which is a major regulatory concern, as well as exposure resulting in local effects on the skin, such as irritation, burns and corrosion. In addition, safety phrases provide information about chemical-specific precautionary measures (using the prefix "P") to prevent or control exposure corresponding to the identified hazards. Safety data sheets should provide concise information describing the hazards associated with the use of chemicals and give information on handling, including appropriate exposure control measures, storage and emergency measures in case of accident.

So far, numerous countries have implemented or are in the process of implementing the GHS (see http://www.ghslegislation.com/tag/ghs-implementation-status/). However, the GHS is not legally binding, and many countries and regions have published their own regulations or standards to implement the GHS; the EU, for example, has published the Classification, Labelling and Packaging of Substances and Mixtures (Regulation EC No 1272/2008; see EC (2008) and additional hazard phrase for the EU in Table 43).

8.2.2 Skin notations (hazard designations) and classifications for irritating and sensitizing properties

The American Conference of Governmental Industrial Hygienists (ACGIH) first used skin notations (hazard designations) in 1961 as general risk indicators for risk communication (Boeniger, 2003b). Skin notations are designed to attract attention to the fact that dermal exposure followed by absorption can significantly contribute to the total systemic dose and/or that adverse health effects have been demonstrated under realistic exposure conditions. The increase in the systemic dose due to dermal contact is compared with the increase due to inhalation exposure. Thus, skin notations are often applied to chemicals with existing respiratory exposure limits, such as occupational exposure limits (OELs) and threshold limit values (TLVs), predominantly for the occupational environment. ACGIH assigns the notation "SKIN" to refer to the potential for significant chemical absorption and in addition "SEN" for agents producing sensitization, regardless of the exposure route (ACGIH, 2011). Moreover, OSHA in the USA publishes skin designations ("yes/no") along with its list of permissible (respiratory) exposure limits (PELs) for workers

(OSHA, 1999). The main difference is that OSHA exposure standards are enforceable as government regulations, whereas ACGIH standards are recommendations for use in the practice of industrial hygiene.

The Scientific Committee on Occupational Exposure in the EU and the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area of the German Research Foundation (DFG-MAK) also provide skin notations ("H") to highlight the potential of a chemical for significant uptake via the skin (Drexler, 1998; DFG, 2012).

Classifications for sensitizing properties are provided by the DFG-MAK Commission as well. These are indicated with "Sa" (may cause sensitization of the airways), "Sh" (may cause sensitization of the skin) or "Sah" (may cause sensitization of the airways and the skin). The lack of a notation does not necessarily imply that the substance has no sensitizing effect at all; rather, for example, the data in support of a sensitizing potential may be insufficient or the substance may be an insignificant occupational allergen (Lessmann et al., 2011). By 2010, the DFG-MAK Commission had evaluated more than 900 substances or groups of substances and had proposed notations and/or classifications for sensitizing properties for more than 240 substances (Lessmann et al., 2011).

The only approach that includes notations for chemicals with irritating and corrosive potential is the approach published by the National Institute for Occupational Safety and Health of the USA (NIOSH). Historically, NIOSH published skin notations in its *Pocket guide to chemical hazards* (NIOSH, 2010a). The new approach published in 2009 involves the assignment of multiple skin notations for distinguishing between systemic, direct and sensitizing effects caused by exposure of the skin (see Table 44; NIOSH, 2009, 2010b). Candidate chemicals may be assigned more than one skin notation when they are identified to cause multiple effects. In addition, subnotations can be used for further differentiation. An important component of the new strategy is the development of an effective review process and information management in order to prioritize chemicals of highest occupational concern (Sartorelli et al., 2007). So far, documents for 22 chemicals have been published (NIOSH, 2010b).

Table 44. NIOSH strategy of skin notations since 2009

Notation	Subnotation	Definition
SK		exposure of SKin
SK:SYS		SYStemic effect
	SK:SYS(FATAL)	Highly or extremely toxic and may be potentially lethal/life threatening via dermal route
SK:DIR		DIRect effect
	SK:DIR(IRR)	DIRect effect resulting in IRRitation
	SK:DIR(COR)	DIRect effect resulting in CORrosion
SK:SEN		SENsitizing effects (i.e. identified as causing or contributing to allergic contact dermatitis or other immune-mediated responses, such as airway hyperreactivity, i.e. asthma)

Screening relevant information resources, Dotson et al. (2007) identified more than 4000 candidate chemicals with information related to their health effects from dermal exposure and proposed a classification scheme to select a subset of 270 priority compounds based on their adverse health effects, OELs and potential exposure data. ACGIH lists about 190 chemicals with skin notations, whereas OSHA has labelled 147 chemicals (Boeniger, 2003b; ACGIH, 2011). However, the quantity of hazardous substances with the potential to cause skin damage or systemic toxicity that are regularly used in the workplace may far exceed the number indicated by skin notations (Klingner & Boeniger, 2002). Mansdorf (1998) identified a significant lack of available permeation data and found the advice for glove materials unacceptable in several cases where skin notations were available; for example, a recommendation for specific glove material was provided for only about 39% of the organic chemicals of the NIOSH *Pocket guide to hazardous chemicals* (NIOSH, 2010a) that were identified with the need to protect the skin.

In conclusion, skin notations should serve as an indicator of a potential dermal hazard, providing a qualitative measure, while not further specifying the risk (Nielsen & Grandjean, 2004; Sartorelli et al., 2007). With respect to numerous ongoing international efforts to improve skin notations, the need for their harmonization is obvious.

Finally, it should be noted that the absence of a skin notation does not automatically mean that the dermal route of exposure is not relevant or that there is no health risk from dermal exposure; rather, it could suggest that further knowledge on the issue is missing (McDougal & Boeniger, 2002; Lessmann et al., 2011).

8.2.3 Occupational exposure limits

Regulatory risk assessments evaluate the conditions under which chemicals may cause harm to individuals or populations. This can be done by comparing actual exposures with reference values developed by regulatory agencies and advisory bodies. For example, in relation to exposure of workers via inhalation, OELs, TLVs or PELs are recommended by several authoritative bodies. They represent concentrations and conditions under which it is believed that prolonged repeated exposures will not produce any adverse effects in the occupational environment. Several authors have also proposed the establishment of dermal occupational exposure limits (DOELs) (e.g. Fenske, 1993; Bos et al., 1998; Brouwer et al., 1998; McDougal & Boeniger, 2002). Accordingly, DOELs are intended as quantitative measures of maximum acceptable exposure during a work shift, and their calculation is based on extrapolating an internal OEL to an external limit value.

Several regulations already demand OELs for dermal exposure. For pesticides and biocides in the EU, dermal acceptable operator exposure levels (AOELs) are derived (DG SANCO, 2006; EC, 2009d, 2010a). Similarly, the REACH Regulation requires DNELs, both for the occupational situation and for consumers (ECHA, 2012d; see also Schaafsma et al., 2011). Local and systemic dermal DNELs are distinguished. AOELs and DNELs are provided in the units milligrams per kilogram body weight per day.

8.3 Hierarchy of exposure control and risk management measures in the occupational environment (workplace)

The main approaches to exposure control and risk management (sometimes referred to as the STOP principle; see Fig. 24 and Fig. A4.1 in Appendix 4) include 1) elimination/substitution of

especially hazardous substances, 2) engineering controls (technical measures), 3) administrative (organizational) measures and 4) individual/personal protective equipment (PPE).

"The best way to control a hazard is to eliminate it" (NYCOSH, 2013). In agreement with the classic paradigm for hazard control, substitution is preferred over engineering controls, which are preferred over administrative controls, which are preferred over PPE (see Fig. 24). A typical top-down approach for occupational risk management starts with selection of processes and chemicals with minimum hazard potential, continues with the design of a workplace and equipment to eliminate potential sources of exposure and ends with the introduction of control measures, such as the use of PPE. Nevertheless, PPE is considered as a "last resort" that does not always efficiently reduce exposure, as it is dependent on many factors and requirements, and the ability of regulatory bodies to enforce or monitor such requirements is limited. This is also laid down in Article

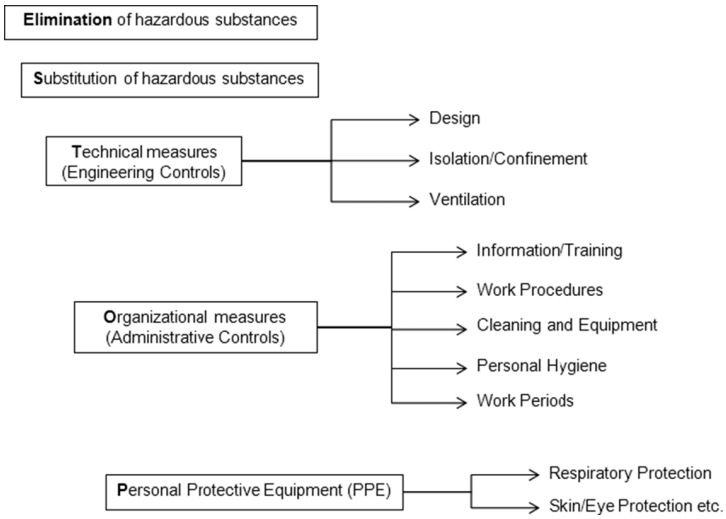

Fig. 24. Hierarchy of exposure control measures. In the context of elimination/substitution, "hazardous substances" are those of very high concern (i.e. carcinogenic, mutagenic or toxic to reproduction; persistent, bioaccumulative and toxic; and very persistent and very bioaccumulative) as well as substances affecting the hormone system (i.e. endocrine disruptors).

6(2) of the European Directive 98/24/EC (EC, 1998b), which states the following priority of control measures at the workplace:

- design of appropriate work processes and engineering controls;
- application of collective protection measures at the source of the risk;
- application of individual protection measures, including PPE.

8.3.1 Elimination or substitution with less hazardous materials or processes

Elimination and/or substitution of hazardous substances with less harmful or harmless materials has first priority above all other means of exposure control and is the most powerful risk management measure.

Elimination may be achieved by changing a process, thus avoiding the need for that chemical. Substitution means that one chemical is substituted by another. It must be ensured that the substitutes do not possess other, more harmful properties.

Accordingly, the European Directive 98/24/EC (EC, 1998b) specifies that:

> substitution shall by preference be undertaken, whereby the employer shall avoid the use of a hazardous chemical agent by replacing it with a chemical agent or process which, under its condition of use, is not hazardous or less hazardous to workers' safety and health, as the case may be.

"Hazardous" and "toxic" substances are defined as those chemicals present in the workplace that are capable of causing harm (OSHA, 2013b). According to Directive 98/24/EC (EC, 1998b), in the EU, any substance is "hazardous" that in the workplace presents a risk to the safety and health of workers, for example:

- by meeting the criteria for classification as a dangerous substance/preparation as defined in Directive 67/548/EEC (EEC, 1967; criteria of Annex VI) or 88/379/EEC (EEC, 1988; whether or not classified and listed under a directive); or

- because of its physicochemical, chemical or toxicological properties; or
- because of the way it is used or because it is present.

Generally, as noted above, it has to be ensured that the substitutes do not possess other, even more harmful properties. In addition, substitution should always be considered in relation to the use pattern of the new substance, as a resulting increase in exposure (due to a change in the use pattern) to a low-hazard chemical does not necessarily decrease the overall risk. A systematic process for substitution decisions is available within the "column model for chemical substitutes" (IFA, 2011), according to TRGS 600 (BAuA, 2008). In addition, information is available at the European Substitution Support Portal (SUBSPORT, 2013).

Examples of successful implementation of this strategy are the almost complete removal of chromate from most brands of the French liquid bleach "Eau de Javel" (Lachapelle et al., 1990) and the elimination of carcinogenic organic lead and aromatic hydrocarbon additives from motor fuels and petroleum products. Other preventive measures include the replacement of allergenic or corrosive products with less hazardous substances (e.g. replacement of propylene glycol in water-cooling systems with less sensitizing agents, such as zinc borate, or the addition of ferrous sulfate to cement in Denmark to reduce the sensitizing potential of chromate) (Brown, 2004). In the past, methylene chloride has been extensively used as a paint stripper, causing significant dermal and inhalation exposures among painters. More recently, substitution of methylene chloride with aqueous solutions of alkalis, such as potassium or sodium hydroxide and alkaline salts (caustic paint strippers), or mixtures of organic solvents, if necessary also containing acids or alkalis, is recommended (TRGS 612: BAuA, 2007).

8.3.2 Engineering controls

When substitution of hazardous chemicals or processes is not feasible, additional measures to control employee exposure need to be taken. Engineering controls eliminate or reduce exposure to a chemical or physical hazard using specifically designed machinery or equipment

or by changes in the production process. Examples include ventilation systems, such as a fume hood.

During the design of a workstation, special attention is given to controlling the process rather than the person (i.e. developing installations, processes and activities aimed at minimizing the workers' exposure). The specific use of technical measures to capture and isolate potential skin hazards depends largely on the physicochemical characteristics of the hazard and the nature of the exposure.

Frequently applied measures include:

- process change (change in manufacturing technology, e.g. wetting dust);
- source capture (for limiting airborne spread of contaminants from welding, cutting and spray metallization processes);
- source modification (e.g. paint dipping instead of spraying);
- design/redesign tools, equipment, machinery, materials, facility;
- enclose the hazards and isolate the equipment (complete enclosure of moving parts, using glove box operations);
- use barriers or isolation/separation of employees (e.g. perform process in special rooms, in areas away from workers, or use machine guarding);
- local exhaust ventilation (LEV).

A key factor in the risk assessment process is the evaluation of actual work practices. In fact, for example, process change may be costly and more difficult to implement than other control measures, such as exhaust ventilation or PPE. Frequently, there might be effective alternatives to particular hand manipulation or work tasks that are much less expensive and less difficult to implement than engineering controls. OSHA considers economic feasibility to be a major issue with respect to engineering controls and may permit PPE in lieu of engineering controls if there are no feasible administrative or work practice controls and if adequate PPE or devices are available.

However, the influence of engineering controls on the magnitude of dermal exposure is by far less examined than their influence on inhalation exposure. Unless dermal contact can be avoided entirely by

complete enclosure, it is difficult to assess the efficacy of engineering controls in a workplace risk assessment.

8.3.3 Organizational/administrative controls

While administrative (or work practice/organizational) means of control are not a substitute for design and engineering techniques, they provide an additional approach to limiting the occupational exposure risks when other methods have failed to achieve the expected control levels. Administrative controls can include:

- adjustments of work practices;
- reduction of duration, frequency or severity of exposure;
- changes in work safety policies or work schedules;
- warning and labelling management;
- education and training;
- medical surveillance programmes and environmental monitoring.

Administrative controls may include scheduling maintenance operations that involve toxic substances at night when the staff is not present, prohibiting working with ionizing radiation once a predetermined level of exposure is reached, rotating workers through various job assignments or specifying re-entry intervals for workers following crop treatment. An example of worker rotation is the distribution of the wet work (see section 4.1.3) at hairdressers' salons among several employees, which may help in limiting individual exposure to acceptable levels (Elsner, 2007). Another example is the rotation of workers in and out of a hot area, rather than having them spend 8 hours per day in the heat (NYCOSH, 2013). Schäferheinrich et al. (2012) concluded that dermal exposure to creosotes when impregnating wood is higher when the workers perform more tasks manually, handle still warm (freshly impregnated) wood or are in close proximity to the impregnation equipment. By proper arrangement and organization of working conditions and training of the workers, it was demonstrated that all these factors could be reduced. Another measure to enhance the perception of a potential hazard is the installation of warning signs. However, the use of warning signs instead of correcting a hazard is not an acceptable form of hazard control (NYCOSH, 2013).

An effective control and prevention programme requires the joint efforts of management, first-line supervisors and employees and starts with education about the workplace hazards and the measures available for their control. Education and training could focus on suitable working/application processes, maintenance of the equipment or personal hygiene. In addition to personal habits, programmes that provide a process of structuring the general workplace, equipment and work activities are essential. General cleanliness at the workplace supports the prevention of dermal exposure and skin diseases. It is important to provide adequate equipment (e.g. washing facilities, including a supply of warm water, soft cotton or paper towels and moisturizing creams) while at the same time ensuring that employees are integrating use of the equipment into their daily routines. Another example of an organizational measure is a skin protection plan, usually provided by manufacturers of occupational skin care products. These plans combine information and instructions for skin protection, skin cleaning and skin care with the suitable products. Medical programmes are designed to prevent occupational illness and injury and implement both examinations for pre-existing skin diseases as well as periodic biological monitoring. Monitoring of the work environment includes periodic sampling of the skin and/or work sites, providing further means for assessment of the effectiveness of the implemented control measures.

Although administrative controls can (and should) always be used as control measures, they are subject to human error and cannot be relied upon to reduce exposure all the time. Additionally, it is usually not possible to quantify the effectiveness of these measures, as the effect is dependent on the compliance of every worker. Extra control mechanisms, such as substitution of less hazardous materials/procedures, engineering controls and PPE, may be required to address the hazards adequately.

8.3.4 Personal protective equipment (PPE)

The use of PPE is essential if the implementation of engineering and administrative measures cannot sufficiently control the exposure to chemical, physical or biological hazards.

PPE is designed to create a barrier against (workplace) hazards and thus includes any equipment for the purpose of isolating parts of the body from direct contact with a potential hazard. PPE ranges in complexity and includes chemical protective clothing (i.e. gloves, boots, coveralls, aprons, jackets, full body suits) and any other kind of devices or accessories, including respiratory protection, protective headgear and eyewear (face shields or goggles), protective hearing devices (earplugs, muffs) as well as skin protective products (SPP) or barrier creams (EEC, 1989d; OSHA, 2003; ASTM, 2013a). The definitions of chemical protective clothing and PPE can be diverse between different countries or institutions. Chemical protective clothing is often used synonymously with clothes, although the general definition is more widely applicable, including gloves and boots as well. In the following, the general and widely used term PPE is used when discussing skin protection by protective clothing, gloves and barrier creams.

There are several reasons why PPE should be used against chemical hazards only as a "last resort" (Packham, 2006):

- PPE protects the wearer only and does not remove the contaminant.
- Some types of PPE are inconvenient and interfere with the way people work.
- Some types of PPE may constrain both sensory input and speech.
- Compliance has to be monitored.
- The extent of protection is dependent upon good fit and attention to detail.
- If PPE is used incorrectly or badly maintained, the wearer may receive no protection.
- PPE, if selected or worn incorrectly, may increase the overall risk to health.
- PPE itself can cause risks to workers by hazardous materials in the PPE or by wet work conditions (e.g. in moisture-resistant gloves).

It is important to emphasize that overprotection as well as underprotection can be hazardous and should be avoided. Thus, the selection and proper use of PPE will be discussed in detail in section 8.5.

8.4 Hierarchy of exposure control for consumers

Similar to workplaces, prevention of exposure to hazardous substances is also the ultimate goal for consumers.

Risk management measures are aimed at controlling, limiting or avoiding exposures, thus helping to ensure the safe use (or handling) of substances that are part of consumer products. They can be either of regulatory nature (i.e. limit values, marketing restrictions, etc.) or related to technical design and recommended usage characteristics that are implemented by manufacturers (Fig. 25).

Besides regulatory frameworks, risk management measures relevant for consumers include those inherent to product design (controllable) and those that are communicated to consumers as directions for use (non-controllable). Three general types of risk management measures are distinguished by Bruinen de Bruin et al. (2007):

1) product-integrated measures;
2) consumer measures (instructions or communication on safe use, PPE);
3) administrative measures.

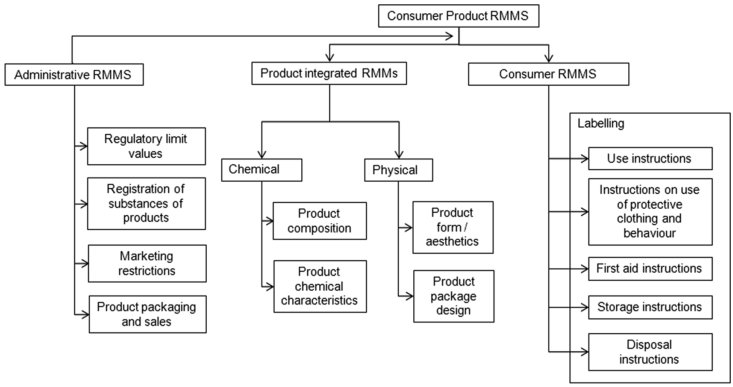

Fig. 25. Categorization concept for consumer product risk management measures (RMMs) (Bruinen de Bruin et al., 2007).

Product-integrated measures are usually the most effective risk management measures for consumers. Examples are changing the product's operational conditions or composition (e.g. maximum concentration used in the product), changing the product form (e.g. pellets or granules instead of powder, product forms that do not have to be unpacked or with a high viscosity, such as hair colourings that are like paste and provided in containers that facilitate mixing without skin contact), dye impregnation depth or maximum amount of product used (package size). Consumer exposure assessment must take into account reasonably foreseeable misuses. Thus, product-integrated risk management measures are preventive measures that are to be favoured, as they eliminate the possibility of misuse (e.g. by child-safe fastenings or limitation of content).

Consumer risk management measures rely on consumer compliance and thus are considered less effective. Consumer risk management measures based on instructions should be introduced only if it is shown that they are effective and well adhered to by consumers. For instance, PPE for consumer exposure can be considered only under limited circumstances, because it cannot be ensured that it will be used, even if recommended by the manufacturer and provided with the product (e.g. gloves with a hair dye). Moreover, consumers may not always read and follow the instructions for safe use (Kovacs et al., 1997). The type of product seems to have a substantial influence on the degree of compliance with the correct use of products. For instance, the same individuals acted differently when using either floor cleaners or impregnation sprays, demonstrating that consumers tend to pay more attention to use directions when the product is perceived as potentially dangerous or when the consumers are not familiar with the product (Heinemeyer et al., 2006).

Administrative risk management measures refer to organizational risk reduction and restriction strategies that are usually implemented by relevant authorities or industry (Bruinen de Bruin et al., 2007). These are related to the foreseeable uses and misuses of a product (e.g. regulatory limit values, registration of substances and products, marketing restrictions, labelling of protective clothing or product packaging and sales strategies). Administrative risk management measures are not expected to be developed by stakeholders across the

supply chain; however, they provide a key input that can be considered in the development of both product-integrated and consumer risk management measures.

Above all, suitable and comprehensive labelling of consumer products is essential. Obvious warning labels and instructions for use are mandatory for products containing specific ingredients. In addition, a comprehensive list of all ingredients is preferable, yet not always required by law.

It is especially desirable to provide sensitized individuals with the ability to avoid a product that includes substances with allergenic potential. Health Canada (2011) requires the following information on cosmetic labels in order to support consumers in making informed choices about the products they use and how to use them safely:

- an ingredient list;
- the identity of the product, in English and French;
- a statement of net quantity in metric units of measurement;
- the name and address of the manufacturer or distributor;
- directions, warnings or cautions, in English and French, where necessary for safe use of the product.

In addition, since 2003, the EU has an added requirement for any personal care product that contains 1 of 26 fragrance ingredients (Annex III of EU Cosmetics Directive 2003/15/EC; EC, 2003b). The presence of these fragrances in personal care products must be indicated in the list of ingredients when their concentration exceeds 0.001% in leave-on products or 0.01% in rinse-off products.

Nevertheless, appropriate labelling of products (information about ingredients and correct use) does not necessarily ensure that the consumer will adopt the appropriate behaviour. When assessing the effectiveness of labelling information for the process of paint stripping with methylene chloride, Riley et al. (2001) found that instructions such as the use of goggles frequently were not followed. Also, to ensure proper ventilation, it is important to provide concrete information on the label on how to achieve this. The instructions should be clearly visible in bold on the product label.

Manufacturers may additionally support the improvement of risk management measures by collecting data and providing further communication pathways to the consumers. Interactive websites or setting up of toll-free number services could provide the consumer with comprehensive information about the product ingredients or correct use and could as well provide the option for instant feedback or reporting if health problems arise during use (van Engelen et al., 2007). Finally, the marketing strategy of a consumer product must not downplay possible hazards, but should focus on the safe use of the consumer product and establishing consumer awareness of the benefits as well as the potential risks of the product.

In addition, several organizations and official authorities are aiming to protect consumers and reduce exposure using different initiatives, such as providing information and publishing data and encouraging manufacturers to revise their product portfolios (e.g. by providing lists of hazardous chemicals with the intention that manufacturers avoid their use or recall products from the market):

- SIN (Substitute It Now) List (International Chemical Secretariat, Sweden): List 2.1 consists of 626 chemicals that are identified as substances of very high concern based on the criteria established by REACH (ChemSec, 2013);
- PRIO (Swedish Chemicals Agency): Preventively reducing risks by supporting identification of the need for risk reduction and providing a guide for decision-making that can be used in setting risk reduction priorities (KEMI, 2013);
- OECD Global Recalls Portal: Brings together information on product recalls being issued around the world. The portal includes information on mandatory and voluntary consumer product recalls that were issued by a governmental body and were made publicly available (http://globalrecalls.oecd.org/);
- RAPEX (Rapid Alert System for non-food dangerous products) (EU): Alert system to facilitate the exchange of information if a product is found to be dangerous so that competent national authorities can withdraw the product from the market, recall it from consumers or issue warnings (EC, 2013b);
- Consumer Safety and Health Network (Organization of American States and Pan American Health Organization): A tool allowing consumers/authorities to exchange information and

experiences by, for example, collection, classification and permanent publication of alerts, regulations and relevant documents concerning the safety of the consumer (OAS, 2013).

Incident reports:

- CARREX (Caribbean Community Secretariat, Caricom): Consumer product incident reporting system, providing consumers with the ability to report to the authorities problems that prove to be dangerous to health (Caricom, 2013);
- CPSC (Consumer Product Safety Commission of the USA) public incident database: A tool allowing consumers, child service providers, health-care professionals, government officials and public safety entities to submit reports of harm involving consumer products. Manufacturers (including importers) and private labellers identified in reports will receive a copy of the report and have the opportunity to comment on them (http://www.SaferProducts.gov).

8.5 Selection and proper use of PPE

In the following, the general and widely used term PPE is used when discussing skin protection by protective clothing, gloves and skin protective creams. Sections 8.5.1, 8.5.2, 8.5.3 and 8.5.6 deal with general considerations on PPE, whereas gloves, as an especially important PPE, receive a separate section (section 8.5.4). Finally, some remarks are also provided on SPP (section 8.5.5).

Their effectiveness in protecting wearers from chemical exposure is the most important consideration for the selection of PPE. The basic expectation is that using suitable PPE prevents or controls the risk involved without increasing the overall risk, while being appropriate for the conditions where it is used. The process of selecting appropriate PPE includes:

1) *Identifying the nature or type of chemical hazard encountered*: An assessment of the potential adverse health effects from contact with the chemical includes considerations about general

hazards associated with the use of the chemical, systemic toxicity if there is the potential to penetrate the skin, as well as local effects on the skin (i.e. chemical burns, corrosion, staining and irritation). Generally, safety data sheets on chemicals with which contact is possible provide such information (see also section 8.1).

2) *Assessment of the pathway, route and magnitude of exposure*: Typical categories of exposure scenarios defining the type of exposure include surface contact, immersion, splash, spray and exposures to dust, mist or vapours. An analysis is essential to select suitable PPE material and, for example, the length of a glove and the predominant application step for which PPE should be used. Sometimes the analysis provides unexpected results. For example, Agostini et al. (2011) identified indirect exposure (i.e. the transfer from contaminated surfaces to the hands) as being the most important route of exposure for asphalt industry workers (see section 3.1.2 and chapter 6).

In addition, the following points need to be addressed:

3) material and chemical resistance (see section 8.5.1);
4) working conditions and environmental factors (see section 8.5.2);
5) the "human factor" (see section 8.5.3).

Additional information concerning the selection, use, care and maintenance of PPE (including gloves) is given by Klingner & Boeniger (2002), HSE (2006a,b, 2012i,j, 2013a,b,c), Mellström & Boman (2006), Sithamparanadarajah (2008), DGUV (2009), Watts (2010), BAuA (2011a), MRC (2011), BOHS et al. (2013), CCOHS (2013) and OSHA (2003).

8.5.1 Material and chemical resistance (testing standards)

Chemical resistance is the ability of the clothing or material to prevent or reduce exposure to chemicals. It is dependent on several technical characteristics of the PPE, such as material composition and thickness. It is often assessed by the use of a defined list of chemicals in a standardized test procedure, which in addition may define the labelling of the PPE product.

Among the many factors limiting the efficacy of PPE, permeation (diffusion/movement) through the intact protective materials and transfer of substances between the equipment surface and the skin (surface/internal contamination) are the most important (Schneider et al., 1999, 2000). Permeation represents the passage of a chemical through a barrier layer at a molecular level, involving the absorption of molecules into the contacted (outside) surface of a material, diffusion of the absorbed molecules in the material and desorption from the opposite (inside) surface of the material (EN 374:2003; Watts, 2010). In addition, penetration, where the chemical leaks through seams, zippers, pinholes and other imperfections in the material, may occur (CCOHS, 2009). The parameters most frequently assessed during the evaluation of PPE material, and specifically chemical permeation, are as follows (CCOHS, 2009; HSE, 2013d):

- *Measured breakthrough time (MBT) / breakthrough detection time (MBT/BDT)*: The time it takes the chemical to permeate through the protective material until it can be seen on the unexposed side of the material and reaches a specific flow rate.
- *Minimum detectable limit (MDL)*: The smallest amount of chemical detectable by an analytical system being used to measure permeation. The MDL qualifies the MBT as being the safest, most reliable information achievable.
- *(Steady-state) permeation rate*: Rate at which a chemical moves through a specific area of the material and reaches equilibrium with the glove material during a specified test period duration.
- *Degradation*: Indicator of the deterioration (getting harder, getting softer or swelling) of the material on contact with a specific chemical.

Consequently, using these parameters, the manufacturer may propose a "maximum wearing time", which is normally shorter than the MBT. All parameters are a function of the intensity and duration of skin exposure as well as being dependent on the material used, its thickness, the chemicals contacted, the type of work process and the temperature.

Such technical parameters are usually assessed in a series of standardized laboratory tests, such as defined by the American Society

for Testing and Materials (ASTM), the European Committee for Standardization (CEN) and the ISO. These standards list the minimum performance and address related issues, such as test specifications, test methods, practices, guides, terminology and classifications for PPE. In addition to technical characteristics, tests on supplementary information are also available (e.g. dealing with the comfort, fit, function and integrity of chemical protective clothing, such as ASTM F1154-11). Testing standards are often related to the labelling of the PPE, and both can be considered as a starting point for the selection (see Table A4.3 in Appendix 4). Thus, the need for standardized test methods for evaluation of the performance of PPE is obvious. A review of common in vitro and in vivo test methods for evaluation of the performance of protective gloves is provided in section A4.4 of Appendix 4.

Although in vitro tests are commonly used and provide valuable information on the protective properties of the barrier material, they are performed under tightly controlled laboratory conditions and may not always reflect the complexity of real-life workplace exposures (Gerritsen-Ebben et al., 2007). These empirical or conventional test methods do not consider variations of the working environment or conditions such as the joint action of multiple chemicals (further discussed for gloves in section 8.5.4.1), heat, humidity or mechanical stress (see sections 8.5.2 and 8.5.3). In addition, they do not consider the interaction between the material and the skin (i.e. the effect of occlusion) and possible metabolism. All these issues need to be more specifically considered through interlaboratory studies (Gerritsen-Ebben et al., 2007), and standard tests should aim to better reflect the performance of PPE under realistic working conditions, such as higher testing temperatures to simulate the conditions inside gloves in use (Evans et al., 2001; Klingner & Boeniger, 2002), or use in vivo tests to provide supplementary results.

8.5.2 Working conditions and environmental factors

It has frequently been emphasized that the effectiveness of PPE is largely affected by specific working conditions. Depending on the activity, the PPE selected must be adequately resistant for the specific intended use (i.e. adjusted to the specific workplace and operational/intended conditions of use). For instance, if a task involves

handling heavy, rough or sharp objects, then a protective glove must have high resistance to abrasion, cuts, snags, etc. ("physical stress"). When a chemical affects the PPE during use, the use duration has to be adapted. As a result of hand movement, a significant increase in permeation (decrease of MBT) through disposable nitrile gloves was observed, in contrast to the results of standard tests (Phalen & Wong, 2012). The circumstances of potential contact (incidental or extensive) also have to be considered. Table 45 provides a guide to the selection of PPE material in relation to possible hazards due to working conditions.

Environmental factors (e.g. high humidity, direct sunlight or other heat sources) and workplace conditions (e.g. long work days, infrequent rest breaks, no access to drinking-water) should also be considered (see also section 8.3.3). For instance, S.G. Lee et al. (2009) demonstrated in a case-study, when comparing laboratory and field

Table 45. Guide to the selection of skin protection in relation to working condition hazards[a]

Hazard due to working conditions	Degree of hazard	Protective material
Abrasion	Severe	Reinforced heavy rubber, staple-reinforced heavy leather
	Less severe	Rubber, plastic, leather, polyester, nylon, cotton
Sharp edges	Severe	Metal mesh, staple-reinforced heavy leather, aramid-steel mesh
	Less severe	Leather, terry cloth (aramid fibre)
	Mild with delicate work	Lightweight leather, polyester, nylon, cotton
Chemicals and fluids	Risk varies according to the chemical, its concentration and duration of contact, among other factors. Refer to the manufacturer or product material safety data sheet.	Dependent on chemical. Examples include natural rubber, neoprene, nitrile rubber, butyl rubber, polytetrafluoroethylene, polyvinyl chloride, polyvinyl alcohol
Cold	—	Leather, insulated plastic or rubber, wool, cotton

Table 45 (continued)

Hazard due to working conditions	Degree of hazard	Protective material
Heat	High (over 350 °C)	Asbestos
	Medium to high (up to 350 °C)	Neoprene-coated asbestos, heat-resistant leather with linings
	Warm (up to 200 °C)	Heat-resistant leather, terry cloth (aramid fibre)
	Less warm (up to 100 °C)	Chrome-tanned leather, terry cloth
General duty	—	Cotton, terry cloth, leather
Product contamination	—	Thin-film plastic, lightweight leather, cotton, polyester, nylon
Radiation	—	Lead-lined rubber, plastic or leather

[a] From CCOHS (2009).

data (hand spraying application of malathion for fly control), that chemical strength, duration of use, temperature, abrasion and work practices had a marked effect on the effectiveness of polyvinyl chloride gloves. Other factors may include duration and conditions of storage before actual use or the production of the PPE. For instance, gloves are manufactured by dipping procedures, punching and welding of plastic film sheets, knitting and sewing, and combinations of these processes. Such measures, however, can significantly affect the effectiveness of PPE. Significant differences in performance between glove materials of the same nominal composition from different manufacturers have been identified (Sansone & Tewari, 1980; Mickelsen & Hall, 1987), as well as significant variability between batch lots of a single manufacturer (Perkins & Pool, 1997).

8.5.3 The "human factor"

Workers' behaviour has been identified as an important determinant in controlling dermal exposure. It includes personal factors, motivation, training, individual working skills, proper pattern and period of use, ergonomics and correct fit, maintenance, acceptance of the wearer, the frequency of changing work clothes and laundering,

and personal hygiene (Kromhout & Vermeulen, 2001; Klingner & Boeniger, 2002; Geer & Buckley, 2006; Geer et al., 2007).

Personal factors influencing the efficiency of PPE can include the wearers' physical condition and health status, experience wearing PPE, hydration status and weight (i.e. underweight or overweight). Ergonomics is another important factor to consider when selecting PPE. The use of PPE adds weight and bulk to the wearer, thus increasing the discomfort during operations and creating significant hazards, such as heat and physical/psychological stress and impaired vision, mobility and communication. Such discomfort and the overall inconvenience of wearing PPE can create resistance to its conscientious use. Therefore, each item's benefit should be carefully evaluated for its potential to increase the overall risk.

Another important factor is proper application and maintenance, which can vary widely depending on conditions of use and differences between individual users (training, compliance). For instance, as most gloves are an effective barrier only for a limited time, it is important that they be changed at appropriate intervals. An additional consequence of the prolonged use of PPE is the increased humidity of the skin; the more hydrated the skin becomes, the less efficient is its barrier function. PPE that is internally contaminated may lead to a higher systemic dose, as the chemical is kept in contact with the skin longer (Rawson et al., 2005). Thus, proper glove donning and removal techniques must be used, for example, to prevent contamination of the glove interior in any event. Moreover, PPE should be regularly checked for evidence of physical damage so that penetration of chemicals through physical defects can be minimized.

Thus, in selecting suitable PPE, it is necessary to include workers' behaviour in the selection procedure and ensure the correct application and maintenance of PPE. This requires appropriate training, an increased awareness of skin hazards at the workplace and motivation to take responsibility for one's own protection. Intervention studies have demonstrated that training and instruction on the proper use of PPE can lead to decreased dermal exposures (van der Jagt et al., 2004; Rawson et al., 2005). In addition, biological monitoring may be used as an effective tool to ensure the efficiency of PPE performance (Klingner & Boeniger, 2002). Finally, administrative controls (see section 8.3.3)

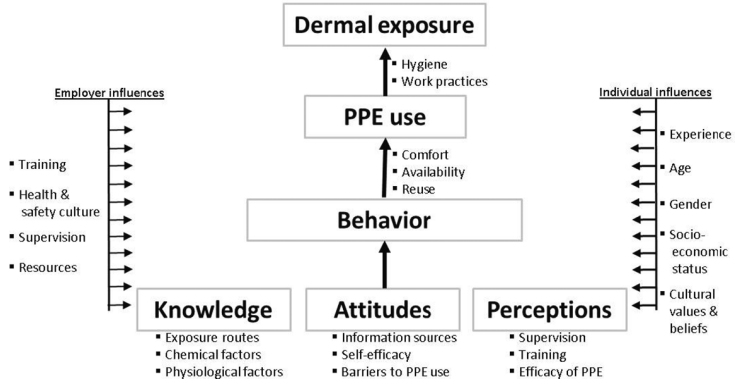

Fig. 26. Conceptual framework for evaluating the psychosocial determinants of worker dermal exposure (Geer et al., 2006; adapted from Lund & Aarø, 2004).

Reprinted from L.A. Geer, B.A. Curbow, D.H. Anna, P.S. Lees & T.J. Buckley, Development of a questionnaire to assess worker knowledge, attitudes and perceptions underlying dermal exposure, Scandinavian Journal of Work, Environment and Health, volume 32, issue 3, pages 209–218, reprinted by permission of the publisher (Taylor & Francis Ltd, http://www.tandf.co.uk/journals).

may help maintain the awareness of risks and positively influence the "human factor"—for example, by providing general cleanliness at the workplace, skin care plans or periodic monitoring.

In order to study the psychosocial factors (i.e. influence of knowledge, attitudes and risk perceptions) that underlie behaviour, Geer (2006) proposed a conceptual framework to evaluate the psychosocial determinants of dermal exposure of workers (see Fig. 26).

8.5.4 Protective gloves

Exposure of the hands has been identified as an important contributor to total skin exposure. Thus, gloves are one of the most widely used form of PPE intended to prevent skin exposure during operations with hazardous substances.

8.5.4.1 *General types, material and chemical resistance of protective gloves*

For practical purposes, gloves can be classified into several types according to their intended use and material thickness (Table 46).

Table 46. Classification of gloves[a]

Type	Thickness (mm)	Comments
Type I: Disposable gloves	0.007–0.25	Extremely thin, made of polymeric film, both sterile and non-sterile; gloves for special purposes with increased thickness of fingertips (cytogenetic agents)
Type II: Household gloves	0.20–0.40	Usually of thicker quality and velourized inside; made from natural rubber, polyvinyl chloride or plastic impregnated textile
Type III: Industrial gloves	0.36–0.85	Heavier quality, both supported and unsupported; usually made from rubber, leather or their combination
Type IV: Special gloves	—	Designed for special purpose (e.g. firefighters, butchers, drivers, electricians) with specific design (e.g. with cuffs, long sleeves, special materials)

[a] From Mellström & Boman (2005).

Gloves can be further classified in terms of their weight: ultra/very light weight (<0.20 mm), light weight (0.20–0.31 mm), medium weight (0.31–0.46 mm) and very high weight (>0.46 mm). It is evident that there are no sharp borderlines between the different types of gloves (Mellström & Boman, 2005). Protective gloves can be made out of rubber, plastics, leather, textiles and combinations of these materials, and they can offer protection against many different chemicals, bacteria, soap and detergents (see Table 47).

Exposure to multiple chemicals requires special consideration, as these can be significantly more aggressive towards protective materials than single chemicals alone, and mixtures/multicomponent products are often in use in real-life situations. Importantly, the material protecting effectively against two different solvents separately may be a bad barrier against their mixture. For instance, Tran et al. (2012) found, for a paint formulation containing several solvents, that nitrile rubber gloves offered 6–10 times greater chemical resistance compared with natural rubber latex gloves, regardless of the chemical properties

Table 47. General characteristics of glove materials[a]

Material	Good protection against:	Poor protection against / avoid contact with:	Comments
Natural and synthetic rubber materials			
Natural rubber latex (*cis*-isoprene)	Biologics, water-based materials, inorganic chemicals	Oils, solvents, grease, hydrocarbon derivatives, ozone, oxygen and UV light, chemicals in general	Good performance durability Good biohazard and infection protection Tear and puncture resistant, but hard to detect puncture holes Comfortable fit, good tensile strength and good elasticity Can cause or trigger latex allergies
Polyisoprene rubber (isoprene/natural rubber)	As above	As above	As for latex, but without inducing latex allergy
Nitrile ((acrylo)nitrile-butadiene rubber)	Solvents, oils, grease, fuels, hydrocarbons, selected acids and bases, glutaraldehyde, range of chemicals, some solvents	Ketones, aromatics, chlorinated hydrocarbons, esters, oxidizing, sulfuric and organic acids, organic compounds containing nitrogen, methylene chloride, trichloroethylene, ozone, oxygen and UV light	As for latex, but without inducing latex allergy Clear indication of tears and breaks Best choice for splash protection against chemicals Resistant to punctures and abrasion
Chloroprene rubber (neoprene, polychloroprene)	Acids, bases, alcohols, oils, fuels, range of chemicals, peroxides, hydrocarbons, phenols	Halogenated and aromatic hydrocarbons, ozone, oxygen and UV light	Grip in wet conditions, good tear strength and elasticity Many types available, also in combination with latex or textiles
Fluorocarbon rubber (vinylidene fluoride/ Viton®)	Chlorinated and aromatic solvents, aliphatics, alcohols	Ketones, esters, some amines	Expensive Only available as reusable Good resistance to cuts/abrasions/heat/oil Repels most liquids Poor touch sensitivity

Table 47 (continued)

Material	Good protection against:	Poor protection against / avoid contact with:	Comments
Butyl rubber (isobutene/ isoprene)	Corrosive chemicals, vegetable oils, phosphate esters, aldehydes, esters, gases, water vapours, some ketones	Gasoline/fuels, aliphatic, aromatic and halogenated hydrocarbons	Expensive Only available as reusable Poor touch sensitivity Used by the military (chemical warfare agents)
Plastic polymer materials			
Polyvinyl chloride	Acids, bases, oils, water, detergents, grease, peroxides, amines, ozone	Aromatic/organic/petroleum solvents, alcohols, aldehydes, ketones	Plasticizers in glove may contaminate solvents Best choice for protection against low hazards / food hygiene use Limited durability, tensile strength and elasticity
Polyvinyl alcohol	Aromatic/organic and chlorinated solvents, ketones, esters, methacrylate	Water-based materials	Expensive Only available as reusable Poor touch sensitivity
Polyurethane (polyisocyanate)	Oil	Alcohols	For use in clean room/electronics (low particulate shed) Resistant to abrasion and good tensile strength Hardens, embrittles at low temperatures, can be slippery

[a] Adapted from Ohm (1990); Johnson (1997); Korniewicz & Rabussay (1997); Adams (1999); Hinsch (2000); Kimberly-Clark (2001, 2013); Imperial College London (2005); Mellström & Boman (2005); Kwon et al. (2006).

of the individual solvent components. Nevertheless, they finally concluded that neither of the glove materials for the thicknesses used in their study provided adequate protection for this specific application (spray painting). Similar results were found by other authors (Mickelsen et al., 1986; Gunderson et al., 1989; Klingner & Boeniger, 2002; Chao et al., 2008). Lee & Lin (2009) analysed the permeation of hair dye ingredients (aminophenols) in single and mixed solutions through protective gloves typically worn by hairdressers. In addition to the conclusion that mixtures of solutions negatively affected the permeation behaviour, they found that disposable natural rubber and polyvinyl chloride gloves should not be used repeatedly in this occupation, in contrast to neoprene gloves. They particularly stressed that hairdressers need be informed about the short MBT (below 60 minutes) for natural rubber latex gloves, indicating the necessity for a frequent change of gloves—that is, after each dying process. This frequent changing of gloves should certainly be integrated in the operational procedures of hairdressers. Unfortunately, PPE manufacturing companies offer compatibility charts just for pure components and moreover do not relate their testing to the specific real-life working environments. In conclusion, for both mixtures and unknowns, selection should consider those materials with best chemical resistance against the widest range of chemicals (OSHA, 2008).

8.5.4.2 *(Testing) standards, categories and labelling of protective gloves*

In the following, standards and labelling of glove performance under standardized conditions in the EU and the USA are presented as examples, as they may support the potential user in the selection of a protective glove. In addition, a review of common in vitro and in vivo test methods for evaluation of the performance of protective gloves is provided in section A4.4 of Appendix 4.

(a) European Union

In 1989, the European Community adopted two directives in the field of protection devices outlining the certification procedures (Directive 89/686/EEC; EEC, 1989e) and the minimum safety requirements for the use of protective devices at the workplace

(Directive 89/656/EEC; EEC, 1989d). The original PPE Directive 89/686/EEC has subsequently been amended by both Directive 93/95/EEC (EEC, 1993b) and the "CE[1] marking" Directives 93/68/EEC (EEC, 1993c) and 95/58/EC (EC, 1995).

A third Council Directive, Directive 93/42/EEC (EEC, 1993d), covers gloves excluded from Directive 89/686/EEC (i.e. gloves for medical use). However, as it is focused on the safety of patients in medical facilities rather than the safety of the glove wearer, it is not further presented. The same applies for very specific occupational uses (e.g. EN 469:2005 and EN 1082:2000 relating to protective gloves of firefighters).

All chemical protective gloves marketed in the EU must be labelled with a CE marking (i.e. the initials "CE" in the form as stated in Annex IV of Directive 89/686/EEC; EEC, 1989e; EC, 2010b). This implies that the gloves comply with the basic requirements according to EN 420:2003, and the manufacturers must provide information about the designation of the glove, instructions for its care/use/storage, comfort (size and dexterity), water vapour transmission/absorption, pH, amount of detectable hexavalent chromium, list of allergenic incorporated substances, and name and address of the notified body that certified the product. In addition, other standards relate to specific types of hazards and provide a system for evaluating the performance of protective gloves according to stated levels. Most relevant for testing of protective gloves is standard EN 374:2003.

According to EN 374-1:2003, protective gloves are divided into three categories for which different certification procedures are applied and which enable safety professionals to select the appropriate PPE matching the hazards and risks identified during health and safety audits (Table 48).

Gloves of intermediate and complex design are further specified according to the other parts of EN 374:2003, providing information about the glove performance using the following technical parameters

[1] Originally stood for Communauté Européenne.

Table 48. Protective glove categories according to EN 374-1:2003 and Directive 89/686/EEC

Category	Description
I	Simple design for minimal risks – To be used in situations where the end user can identify the hazards and level of protection required and where consequences are reversible. – Examples: protection against cleaning materials of weak action, against heat (not above 50 °C) and other minor impacts and vibrations. – A declaration by the manufacturer about compliance with the requirements of the Directive is sufficient for CE marking of the product.
II	Intermediate design for intermediate risks – Examples of intermediate risks: general handling gloves requiring good cut, puncture and abrasion performance. – Must be subjected to independent testing and certification by an approved notified body, which may issue a CE mark.
III	Complex design for irreversible or mortal risk – Examples: protection against chemical attack or ionizing radiation, against heat (temperatures above 100 °C) and cold (temperatures below –50 °C) and against electrical risks (high voltage). – An additional quality control system or a regular control of the production is necessary for CE certification, and the body carrying out this evaluation will be identified by a number, which must appear alongside the CE mark.

and levels (also called protection index classes: the higher the level, the better the protection):

- According to EN 374-2:2003 (penetration) and ISO 2859-1:1999(2011), the acceptable quality level (AQL) is a measure of the number of defective gloves (not having passed the water and air leak tests) that are allowed to be in the sample before rejection of the entire batch (the smaller the AQL, the better). In addition, an inspection level (sample size based on the manufacturing batch size) is provided. The performance levels are defined as follows:
  - Level 3: AQL < 0.65, Inspection level G1
  - Level 2: AQL < 1.5, Inspection level G1
  - Level 1: AQL < 4.0, Inspection level S4

- According to EN 374-3:2003 (permeation), the technical parameter is the MBT (see section 8.3.4), relating to six different levels:
  - Level 1: MBT > 10 minutes
  - Level 2: MBT > 30 minutes
  - Level 3: MBT > 60 minutes
  - Level 4: MBT > 120 minutes
  - Level 5: MBT > 240 minutes
  - Level 6: MBT > 480 minutes

In addition to EN 374:2003, further labels, pictograms, level categories and codes are printed on the gloves' enclosure, showing their performance level against specific risks tested in specific standard tests (Table 49).

(b) United States of America

Although the use of PPE in the USA has been outlined by OSHA, which specifically addresses the need for hand protection (OSHA, 2013b,d), the reporting of glove performance related to chemical resistance or physical hazards is strictly voluntary and has not yet resulted in legislation (Groce, 2003). Standards have often been developed after voluntary consensus of standard-setting organizations, such as ASTM and the American National Standards Institute (ANSI). According to various types and intended uses of protective gloves (Table 50), different testing standards exist for the evaluation of performance under various exposure conditions (Table 51).

For choosing a protective glove, predominantly the standards ASTM F739-12 (permeation/resistance to specific chemicals), ASTM D3767-03 (thickness of a single-layer glove) and ASTM D412-06a-2013 (ultimate elongation/ability to stretch and resistance to movement or stress) are essential. Key parameters evaluated are the MDL, MBT/BDT and permeation rate (see section 8.3.4), which result in the following categorization levels:

- ND: Non-detectable (no breakthrough detected after 8 hours)
- NR: Not recommended
- NA: Not applicable
- NT: Not tested

Table 49. Common pictograms used for marking of protective gloves[a]

Test standard	Pictogram	Description	Code beneath pictogram / test performance against specific hazards (the higher the level/range/rank, the better)
EN 420:2003 General requirements / consult instructions for use		The user has to consult the instructions for use, while the standard EN 420:2003 lays out the general requirements (see text)	Sizing of glove (sizes 6–11) Glove dexterity (levels 1–5) (the higher the better, according to the smallest diameter of a pin that can be picked up with gloved hand 3 times for 30 seconds)
EN 388:2003 Physical/mechanical hazard		The performance of a fabric or layers of fabric to resist mechanical hazards such as rubbing or cutting	Four-letter code: A. abrasion (heavy rubbing) (levels 0–4) B. blade cut resistance (levels 0–5) C. tear resistance (levels 0–4) D. puncture resistance (levels 0–4)
EN 511:2006 Thermal resistance (cold)		Protection against convective and contact cold down to –50 °C	Three-letter code: A. convective cold (levels 0–4) B. contact cold (levels 0–4) C. permeability to water (levels 0–1)
EN 407:2004 Thermal resistance (heat/fire)		Protection against heat and fire	Six-letter code: A. flammability (burning behaviour) (levels 0–4) B. contact heat (levels 0–4) C. convective heat (levels 0–3) D. radiant heat (levels 0–4) E. small splashes of molten metal (levels 0–4) F. large splashes of molten metal (levels 0–4)
EN 374-3:2003 Chemical hazard (permeation)		Tested against chemical breakthrough (permeation), penetration of liquids and microorganisms	Three-letter code and level code: Letters referring to 3 chemicals from a list of 12 standard defined chemicals[b] for which an MBT level of 2 (>30 min) has been achieved (see definition of MBT and levels in text)

Table 49 (continued)

Test standard	Pictogram	Description	Code beneath pictogram / test performance against specific hazards (the higher the level/range/rank, the better)
EN 374-2:2003 Chemical splash protection (penetration)		Failed permeation minimum for at least three chemicals of standard list (see above), but still complies with the penetration test	Level code: Referring to AQL (levels 1–3) (see definition of AQL and levels in text above)
EN 374-2:2003 Biological hazard (microorganisms) (penetration)		Passed penetration test to at least level 2	See above
EN 421:2010 Radioactive hazard		Passed penetration test and is liquid proof	For gloves used in containment enclosures, in addition a specific air pressure leak test and test of resistance to ozone cracking are optional but recommended
EN 421:2010 Ionizing radiation		Has to contain minimum amount of lead or equivalent metal	Lead equivalence thickness (lead content in glove) in millimetres (optional: resistance to ozone cracking, see above)

[a] Adapted from CBI (2008).

[b] A: methanol, B: acetone, C: acetonitrile, D: dichloromethane, E: carbon disulfide, F: toluene, G: diethylamine, H: tetrahydrofuran, I: ethyl acetate, J: *n*-heptane, K: sodium hydroxide (40%), L: sulfuric acid (96%).

Table 50. Examples of standard specifications for different intentions of use of PPE in the USA

Document	Title
ANSI/NFPA 1971-2000	Protective clothing for structural fire fighters
ANSI/ADA 76-2005 (R2010)	Guide for the measurement and evaluation of gloves which are used to reduce exposure to vibration (non-sterile latex gloves for dentistry)
ASTM D120-09	Standard specification for rubber insulating gloves
ASTM D3577-09e1	Standard specification for rubber surgical gloves
ASTM D3578	Standard specification for rubber examination gloves
ASTM D4679-02(2007)	Standard specification for rubber household or beauticians' gloves
ASTM D5250-06(2011)	Standard specification for polyvinyl chloride gloves for medical application
ASTM F696-06(2011)	Standard specification for leather protectors for rubber insulating gloves and mittens

ADA, American Dental Association; ANSI, American National Standards Institute; ASTM, American Society for Testing and Materials; NFPA, National Fire Protection Association

A rating for resistance to degradation is provided, relating to the (gravimetric) per cent weight change of the material mass when exposed to a specific chemical at four time intervals:

- E: Excellent performance (<10% weight change)
- G: Good performance (10–20% weight change)
- F: Fair performance (>20–30% weight change)
- P: Poor performance (>30–50% weight change)
- NR: Not recommended (>50% weight change)
- DD: Degrades and delaminates (Viton/butyl gloves)

This simple grading was extended in 2005, as ANSI, together with the Industrial Safety Equipment Association (ISEA), published the ANSI/ISEA 105 standard. It includes reference information on special issues such as biological protection, extreme temperature and clean room applications, hazardous materials response, or protection against electrical and radiation hazards. In addition, the "human factor" was included by addressing selection criteria for vibration reduction and dexterity, such as fit, function and comfort (ANSI/ISEA 105-2005;

Table 51. Guides and standard test methods for protective gloves in the USA[a]

Standard	Title
Guides for selection of test methods and general advice	
ASTM F1001-12	Standard guide for selection of chemicals to evaluate protective clothing materials[b]
ANSI/ISEA 105-2011	Standard for hand protection selection criteria
Test methods most relevant for protective gloves	
ASTM F739-12	Test method for resistance of protective clothing materials to permeation by liquids or gases under conditions of continuous contact (resistance to specific chemicals)[b]
ASTM F903-10	Test method for resistance of protective clothing materials to penetration by liquids (less sensitive analysis than ASTM F739-12)
ASTM F1383-12	Test method for resistance of protective clothing materials to permeation by liquids or gases under conditions of intermittent contact (resistance to specific chemicals)
ASTM D3767-03	Thickness of a single layer of glove
ASTM D412-06a-2013	Ultimate elongation (ability to stretch), molulus, resistance to movement or stress
See Table 52	Test methods to assess physical hazards according to ANSI/ISEA 105-2011
Examples of additional available test methods for specific uses	
ASTM F1407-12	Test method for resistance of chemical protective clothing materials to liquid permeation—Permeation—Cup method
ASTM F1670-08	Test method for resistance of protective clothing materials to synthetic blood
ASTM F1671/F1671M-13	Standard test method for resistance of materials used in protective clothing to penetration by blood-borne pathogens using phi-X174 bacteriophage penetration as a test system
ASTM F1819-07(2013)	Test method for resistance of protective clothing materials to synthetic blood using mechanical pressure technique

ANSI, American National Standards Institute; ASTM, American Society for Testing and Materials; ISEA, Industrial Safety Equipment Association

[a] See ASTM (2013b).

[b] Standard testing chemicals according to ASTM F1001-12: *liquids*: acetone, acetonitrile, carbon disulfide, dichloromethane, diethylamine, dimethylformamide, ethyl acetate, hexane, methanol, nitrobenzene, sodium hydroxide (50%), sulfuric acid (95%), tetrahydrofuran, tetrachloroethylene, toluene; *gases*: ammonia, 1,3-butadiene, chlorine, ethylene oxide, hydrogen chloride, methyl chloride.

Henry, 2005). Most importantly, it provides a numerical scale method for manufacturers to rate their products against certain contaminants and exposures based on performance in a standard test method (ASTM, ISO or EN). By this classification, it is expected that users are better able to decide which glove is suitable for which task. The rating of performance properties is defined in terms of four to six levels. Gloves that have not achieved the lowest level are reported as level 0; thus, the higher the level, the better the protection performance. In addition, the rating is supported by a colour code provided for each glove in relation to a specific chemical (ANSI/ISEA 105-2005; Henry, 2005):

- *Green*: glove well suited
- *Yellow*: application should be carefully controlled
- *Red*: avoid the use of the glove with this chemical.

According to the latest revision of 2011 (ANSI/ISEA 105-2011), the importance of workplace injuries due to cuts and lacerations to the hands and fingers is increasing. Thus, in this version, different ASTM methods for evaluating cut resistance performance were included. Finally, ANSI/ISEA 105-2011 stresses the importance of educating users on how to use the data in the selection process. Table 52 lists the standard test methods to estimate the parameters included in ANSI/ISEA 105-2011 and the resulting level range of the classification rating.

As listed in Table 52, ANSI/ISEA 105-2011 also includes the European testing methods for chemical permeation (i.e. EN 374:2003). Although the rating levels and corresponding MBT values appear very similar, EN 374:2003 normalizes its rating to $1.0\,\mu g \cdot cm^{-1} \cdot min^{-1}$, in contrast to $0.1\,\mu g \cdot cm^{-1} \cdot min^{-1}$ as performed according to ASTM F739-12. Thus, the EU standard is 10 times less sensitive than the ASTM standard (Groce, 2003). In addition, in the EN rating, neither a Level 0 (glove must at least pass Level 1) nor a colour code exists.

In order to include realistic workplace conditions, ASTM F1383-12 provides an exposure testing designed to mimic intermittent contact (see Table 51). In addition, ANSI/ISEA 105-2011 provides ASTM F1790-05 for covering mechanical risks. Although similar to

Table 52. Tested physical hazards, the relevant standard methods and rating levels provided for protective gloves according to ANSI/ISEA 105-2011

Standard test method	Description	Range of code levels[a]
ASTM D3389-10	(Taber) abrasion resistance	Levels: 0–6
ASTM F1790-05 / EN 388:2003	Cut resistance	Levels: 0–5
ASTM F739-12	Permeation resistance	Levels: 0–6
ASTM D471-12a (rubber) ASTM D543-06 (plastic)	Degradation resistance	Levels: 0–4
ANSI/0 ISEA 105-2011 (gloves)	Hand protection selection criteria	
ASTM WK35278	Glove dexterity	Levels: 1–5
ASTM D5151-06(2011) (medical gloves)	Detection of holes (liquid-tight integrity)	(Pass or fail) (Minimum AQL of 2.5)
ASTM D7246-06(2011)e1 (polyethylene food service gloves)		
ASTM F1358-08	Flame resistance	Levels: 0–4
ISO 17493:2000-12	Heat degradation resistance	Levels: 0–5
ASTM F1060-08	Conductive heat resistance	Levels: 0–5
ISO 5085-1:1989-11	Conductive cold resistance	Levels: 0–4
ANSI S2.73-2002 (2007) / ISO 10819:1996-08	Antivibration or vibration reduction	(Pass or fail)

ANSI, American National Standards Institute; AQL, acceptable quality level; ASTM, American Society for Testing and Materials; EN, European norm; ISEA, International Safety Equipment Association; ISO, International Organization for Standardization

[a] The higher the level, the better the protection performance.

EN 388:2003, this rating system is not equivalent. It does not include tear resistance and differs slightly in the rating for puncture and cut resistance. For instance, ASTM F1790-05 uses a test weight to measure the required force to cut through a test specimen, whereas in the cut resistance test of EN 388:2003, the test parameter is the number of cycles (Groce, 2003). As a result, although both tests might reach similar conclusions, they are based on different methods, resulting in different test ratings.

8.5.4.3 Selecting and ensuring proper use of protective gloves

Gloves are an important element of controlling exposure and reducing health risks at home and at the workplace. The basis for glove selection is the identification of the nature of the chemical hazard encountered and the assessment of the pathway and magnitude of exposure. The selection procedure for suitable protective gloves should then consider the following (adapted from TRGS 401: BAuA, 2011a):

- Request information from the glove manufacturer and/or the chemical supplier; refer to the safety data sheet on the chemical to which exposure is expected.
- Take into account the glove material, material thickness, maximum wearing time, MBT and permeation rate, and check if standard testing information, pictograms and the "CE" marking are provided.
- Always make a choice in relation to the workplace, work process, intention and conditions of use (e.g. consider other substances, preparations, products or articles used, duration and intensity of the contact with chemicals per shift, mechanical and thermal loading of the glove, influence of temperature due to heating or cooling).
- Take into consideration ergonomic requirements (size and fit) and tactile sense.
- Include wearers in the selection process, and provide them with information, education and training.

Many manufacturers provide personal advice or charts and computer software to help in selecting the appropriate gloves. Generally, necessary information can also be obtained from safety data sheets, product information or the supplier of the hazardous substances.

Although the glove material is a key factor, there are vast differences between gloves of the same polymer type, but from different manufacturers. The labelling and rating based on performed standard tests can support the choice (see section 8.5.4.1, Tables 50 and 53).

Overall, the glove that has the longest MBT (at least 30 minutes) and allows the necessary dexterity for the job should be selected.

However, as MBT and permeation rate are temperature dependent and as higher temperatures may arise in the gloves when they are being worn, the MBT and permeation rate values provided may decrease under practical conditions. As MBT is often determined according to the standard EN 374-3:2003 at 23 °C, the maximum wearing time under practical conditions must be shortened to one third of the MBT (TRGS 401: BAuA, 2011a). No glove performs at the highest level in all categories (Henry, 2005; ANSI/ISEA 105-2011). In addition, the selection should consider the shortcomings of labelling and stated protection levels that are based on standardized testing procedures, for the reasons already presented in section 8.5.1. Actually, some gloves are required to be labelled with the open beaker symbol (indicating low-level protection; see Table 49) just because the chemicals against which they are designed to protect are not on the prescribed list of EN 374:2003 (e.g. gloves resistant against chemotherapy) (Watts, 2010), because they have not been tested according to EN 374:2003.

As described in section 8.5.3, ergonomic requirements, feasibility of proper application, maintenance and training have to be taken into account in the selection. It is generally recommended that the wearers be involved in the selection procedure so that they understand the issues that influence selection and the necessity of PPE use, to maximize PPE acceptance and to ensure proper use and maintenance of the gloves (Sithamparanadarajah, 2008).

In order to collect all relevant information for the information exchange with a supplier or for support during the selection procedure, several aids in the form of questionnaires or flow charts are available; these include the “glove selector” (Fig. A4.2) and the “memory aid” (Fig. A4.3), as presented in section A4.2 of Appendix 4 (Sithamparanadarajah, 2008; HSE, 2013a).

8.5.5 Skin protective products (creams)

Sometimes the use of protective clothing might be impractical because of the loss of dexterity, inhibited skin barrier function because of prolonged occlusion and insufficient protection against some low molecular mass chemicals. For such cases, other types of products

are designed to prevent or reduce the penetration of hazardous materials into the skin by external application to the skin (a comprehensive review is provided by Zhai & Maibach, 2007). For such SPP, several terms are used interchangeably in the technical and scientific literature:

- barrier creams, lotions, ointments or agents;
- (skin) protective/protection creams, lotions, ointments or agents;
- pre-work creams or lotions;
- invisible gloves.

It has frequently been emphasized that SPP by no means substitute for gloves, and the use of the term "invisible gloves" has been viewed as largely incorrect, because it provides a false sense of safety to the user (Kresken & Klotz, 2003). Thus, some authors consider "skin protective creams or products" a more appropriate terminology, whereas others prefer the term "barrier creams" (Zhai & Maibach, 2007). While sharing some characteristics and functionality, SPP should not be confused with skin-conditioning products, which are normally used after work to restore the natural barrier function of the skin. Overall, the distinction between skin protection and skin care is not always obvious.

A very general classification considers three types of nonspecific SPP: water repellent, oil repellent and silicone-based formulations (Schalock & Zug, 2007). Water-repellent SPP (also called water-in-oil emulsion) contain hydrophobic substances and are used by wet work professionals as a protection against water-soluble irritants (Kresken & Klotz, 2003). Oil-repellent products (called oil-in-water) are intended to protect against lipophilic agents and oils or oil-soluble hazards (Zhai & Maibach, 2007), whereas silicone-based products are used as a general protection against both classes of contaminants (also called water-in-oil-in-water). Other authors categorize SPP into nonspecific (passive) and chemically neutralizing (reactive) products (Chilcott et al., 2002), with or without silicone (de Fine Olivarius et al., 1996).

The detailed protective mechanism of SPP as well as their influence on the dermal absorption of chemicals are still poorly investigated. In addition to building a physical barrier, specific ingredients are added to the formulations that interact with the skin and/or irritant (Kresken

& Klotz, 2003). For instance, organic or physical UV-absorbing agents are included for protection against natural and artificial UV radiation; complexing agents are intended to, for example, bind nickel or chromate ions and prevent sensitization (Gawkrodger et al., 1995); or quaternium-18 bentonite is added to decrease skin irritation in sensitized people exposed to urushiol (Marks et al., 1995). Astringents are substances that cause contraction and hardening of the skin surface, thus increasing its resistance to mechanical or hydrophilic hazards, and are especially suited for occlusive use with other PPE. A sample of some commercially available products and their protective properties is summarized in Table A4.1 in section A4.3 of Appendix 4.

The effectiveness of SPP is often the subject of controversy, as some studies failed to show a significant difference between an SPP and its vehicle (Berndt et al., 2000). In addition, some studies have found that the dorsal aspects of the hands are likely to be incompletely protected (Wigger-Alberti & Elsner, 1997; Wigger-Alberti et al., 1997). Similarly, pretreatment with SPP did not reduce the percutaneous penetration of benzene and formaldehyde through excised human skin (Lodén, 1986). A few studies have even reported enhancement of penetration after application of SPP (e.g. for surfactants and PAHs) (Walters et al., 1993; van der Bijl et al., 2002). More recently, studies by Korinth et al. (2007, 2008) demonstrated that SPP can significantly enhance the percutaneous uptake of two aromatic amines, aniline and *o*-toluidine. This finding should not be surprising, as many SPP use components, such as glycerine and urea, that are known penetration enhancers. Factors that contribute to the ineffectiveness of SPP are non-compliance, excessively prolonged skin contact and simultaneous use with other skin products.

Thus, skilled occupational safety and health specialists, in particular company doctors, should be involved in the selection and use of SPP. For selecting suitable products, the following information is necessary: clear and easily identifiable labelling as SPP, concrete details of the products' areas of application and details of the verified effectiveness, with a description of the methodology or the verification procedure for the use advertised. However, because of the broad range of workplace materials and varieties of potential areas of application, there are currently no completely standardized methods for evaluation of SPP (zur Mühlen et al., 2007). Available methods that are in use (in

vitro and in vivo) for testing the effectiveness of SPP are reviewed in Zhai & Maibach (2007). Therefore, users should inform themselves about the tests performed by the manufacturer—that is, if they are in accordance with scientific and medical recommendations as well as relevant for the situation at the workplace—as the application method may significantly affect the effectiveness. Preference should be given to skin protection agents whose effectiveness has been verified (e.g. by the repetitive occlusive irritation test or at least the bovine udder skin test or a three-dimensional skin culture model) (see Fartasch et al., 2008).

In conclusion, if SPP are used as a personal protective measure at the workplace, the following points or requirements should be considered, as defined, for example, by TRGS 401 (BAuA, 2011a; see also Table A4.2 in section A4.3 of Appendix 4):

- SPP must not be used as primary protection against the action of burning, corrosive agents; high-risk, sensitizing, skin-resorptive substances; or mutagenic, carcinogenic and reproductive-toxic substances.
- SPP should be used only if there is repeated and extended contact with mild irritants (R21/H312, R38/H315, R66) and in the case of wet work.
- SPP should be used only if they have undergone an effectiveness test by the manufacturer according to scientific and medical recommendations.
- The application must be matched with the working procedures and other chemicals or products in use (as SPP may increase uptake of substances through the skin).
- SPP must not adversely affect other PPE, especially gloves (e.g. fatty products).
- SPP must be applied to clean and dry skin (also before reapplication) in order to avoid increased uptake of irritants remaining on the skin surface.
- SPP must be applied before every activity that places a burden on the skin (e.g. commencement of work, after breaks, after every cleaning of the skin during the activity or at the latest after the specified efficiency period defined by the manufacturer), which must be considered in the work organization.

- SPP should not contain any irritant or allergenic substances (preference must be given to products free of fragrances and preservatives).

8.5.6 Personal protective equipment acting as source of exposure

PPE can essentially decrease dermal exposure. However, it is important to bear in mind that the use of PPE itself can also create significant hazards—due to the PPE material, due to the circumstances of using PPE or when PPE is used that is inappropriate for the relevant task.

The material of PPE is essential for the protection performance; however, substances may be included that are associated with allergic reactions after skin contact. For instance, instead of using natural rubber gloves made from latex, polyisoprene rubber (see Table 47), for example, combines the protective properties of natural rubber gloves without inducing latex allergy. Phthalates are under discussion as a health concern, and BgVV (2001) estimated that prolonged dermal exposure due to intensive occupational use of gloves might even exceed the tolerable daily intake of bis(2-ethylhexyl)phthalate (see also EFSA, 2005). In addition, emollients contained in disposable vinyl gloves (up to 50%) may be transferred not only to the skin of the wearer, but also, for example, to food in the food industry sector, which again may lead to indirect dermal exposure when touching the food or oral exposure by consumption (Tsumura et al., 2001a,b; BfR, 2003). In addition to PPE ingredients, substances used in the manufacture of PPE have to be considered. For instance, isothiazolinones are used as slimicides in the manufacture of PPE, and Aalto-Korte et al. (2007) stated that 1,2-benzisothiazolin-3-one in powder-free disposable polyvinyl chloride gloves had caused a small epidemic of contact dermatitis in Finland, affecting dental personnel and other health-care workers (see also Aalto-Korte et al., 2006). Further examples of substances that may act as a source of dermal exposure are provided in chapter 4.

It is essential to determine if and which PPE should be used under particular circumstances; just adding up different PPE does not increase protection. Van Rooij et al. (1993c) demonstrated that extra

protective clothing did not reduce dermal PAH (pyrene) contamination effectively; in contrast, 3 out of 10 workers showed even higher results, and measurable contamination was actually found on skin regions that were definitely covered by coveralls. The authors assumed that air was sucked between the skin and the coveralls, resulting in deposition, and thus the main source of contamination was contact with the internally contaminated work clothes (Van Rooij et al., 1993c). Further, the effect of continuous occlusion of the skin should be considered for prolonged use of PPE; there is controversial evidence in current literature concerning the effects of glove occlusion, relating these effects to the definitions of wet work (Wetzky et al., 2009; Visser et al., 2011).

8.6 Default setting for effectiveness of personal protective equipment in regulation

As discussed previously, the real-life performance of PPE can vary considerably, and protection efficiency at the workplace can deviate significantly from values obtained in laboratory tests. Thus, several regulatory authorities use a set of default values (protection factors) for assessing the exposure mitigation efficiency (i.e. effectiveness of exposure reduction). At present, default exposure reduction values vary widely, and the scientific basis behind their use is often not clear. In many cases, default values are linked to generic descriptions, ignoring important parameters such as use scenario and field performance.

In an effort to harmonize the international use of protection factors for regulatory purposes, Gerritsen-Ebben et al. (2007) collected opinions and underlying evidence on PPE effectiveness within regulatory authorities, industry organizations and academic groups. The report gave an overview of PPE defaults (expressed as per cent exposure reduction) used in predictive agricultural pesticide exposure models or tools (Table 53) and used by authorities in Europe, the USA and Canada (Table 54). An important finding from this study is the fact that permeation through the material depends on the chemical loading (or challenge). Therefore, several regulatory bodies propose the use of different factors for different ranges of loading instead of one single factor for the whole (exposure) range (Gerritsen-Ebben et al., 2007).

Table 53. Overview of PPE defaults used in agricultural pesticide models[a]

Predictive operator exposure model/tool (agricultural pesticides)	Default (% dermal exposure reduction)	Body	Hands	Comment
EUROPOEM	50	x	—	Normal working clothes
	90	x	x	Chemical protective clothing and gloves
United Kingdom POEM	90	—	x	Gloves, handling EC and organic solvents[b]
	95	—	x	Gloves, mixing and loading, handling SC and aqueous-based solutions[b]
	99	—	x	Gloves, handling solids
	80–98 (trunk)	x	—	Different scenarios (e.g. hand-held or vehicle-mounted with or without cap)
	80–95 (legs)			
German model	99	—	x	Universal protective gloves
	95	x (body and feet)	—	Protective garment and sturdy footwear
	100	x	—	Chemical protective clothing (light-tight)
	50	x (face/head)	—	Cap (broad-brimmed headgear)
	95	x (face/head)	—	Hood and visor
	20	x (face)	—	Particle filtering half-mask
	20	x (face)	—	Half-mask with combination filter
PHED	50	x	—	Long-sleeved shirt / long pants or full coveralls
	90	—	x	Gloves

EUROPOEM, European Predictive Operator Exposure Model; PHED, Pesticide Handlers Exposure Database; POEM, Predictive Operator Exposure Model; PPE, personal protective equipment

[a] From Gerritsen-Ebben et al. (2007).

[b] Abbreviations EC/SC not further specified in Gerritsen-Ebben et al. (2007).

Table 54. Overview of PPE defaults used by authorities in Europe, the USA and Canada[a]

Authority and country	EUROPOEM[b]	United Kingdom POEM[b]	German model[b]	PHED[b]	Other PPE defaults (% dermal exposure reduction)
APVMA, Australia	—	+	—	+	—
BfR, Germany	—	—	+	—	—
BAuA, Germany (non-agricultural pesticides)	—	—	—	—	50%: for summer work clothing used for biocides (non-agricultural pesticides) 90%: for heavy work clothing used for biocides (non-agricultural pesticides) (both from RISKOFDERM Toolkit)
CTB, the Netherlands	+	+	+	—	—
DPR, California	—	—	—	+	58–96.4%: dermal (no hand) exposure using a single layer of permeable clothing
ICPS, Italy	—	+	+	—	95%: dermal body exposure by using impermeable coverall while making hand-held applications (derived from HSE data)
INRA, France	—	—	—	—	—
PMRA, Canada	—	—	—	+	75%: second layer of clothing (no hands) 90%: chemical-resistant non-tear coveralls (no hands) 90%: chemical-resistant gloves

Table 54 (continued)

Authority and country	EUROPOEM[b]	United Kingdom POEM[b]	German model[b]	PHED[b]	Other PPE defaults (% dermal exposure reduction)
PSD, United Kingdom	—	+	—	—	95%: as for ICPS above
USEPA, USA	—	—	—	+	58–96.4%: as for DPR above (agricultural pesticides) 50%: one-layer chemical protective clothing (non-agricultural pesticides) 90%: chemical-resistant gloves (non-agricultural pesticides)

APVMA, Australian Pesticides and Veterinary Medicines Authority; BAuA, German Federal Institute for Occupational Safety and Health; BfR, German Federal Institute for Risk Assessment; CTB, Dutch Board for the Authorisation of Plant Protection Products and Biocides; DPR, California Department of Pesticide Regulation; EUROPOEM, European Predictive Operator Exposure Model; HSE, United Kingdom Health and Safety Executive; ICPS, International Centre for Pesticides and Health Risk Prevention; INRA, French National Institute for Agricultural Research; PHED, Pesticide Handlers Exposure Database; PMRA, Health Canada's Pest Management Regulatory Agency; POEM, Predictive Operator Exposure Model; PPE, personal protective equipment; PSD, Pesticides Safety Directorate; USEPA, United States Environmental Protection Agency

[a] From Gerritsen-Ebben et al. (2007).

[b] For per cent dermal exposure reduction used by the agricultural pesticide models, see Table 53.

EFSA (2008) identified an additional 20 papers published in the 2 years after the literature included in the TNO review by Gerritsen-Ebben et al. (2007) and suggested that these papers be reviewed and included as an addendum to the TNO report. The only paper that was considered to contribute new information was the publication of Driver et al. (2007) on an analysis of mainly patch data from the PHED database, but the insights found were already integrated in the original TNO report.

In contrast to the default data used in models (Table 53; Tiramani et al., 2007), Protano et al. (2009) showed that protection was above 97% when using a complete set of PPE (full face mask, Tyvek coverall, rubber boots and gloves) in pesticide applications with

tractors equipped with boom sprayers. The authors assumed that since the development of the models, progress in the design and manufacture of protective coveralls had increased their performance. In accordance with Aprea et al. (2004), the authors suggested that incomplete protection can be explained by improper utilization (e.g. due to incomplete closure of the coveralls, rolling up of the sleeves) or penetration through seams and zippers. Similar data were obtained in other studies (Machera et al., 2003; Aprea et al., 2004). Protano et al. (2009) concluded that PPE is necessary to minimize dermal exposure to pesticide applications, but can provide protection only when used appropriately.

Protano et al. (2009) also investigated the protection of normal work garments (i.e. long- or short-sleeved cotton shirt, long or short trousers, and rubber boots or gym shoes). The protection ranged between 84.1% and 92.5%, thus providing far lower protection than PPE. Moreover, the upper part of the body showed the lowest protection.

9. CONCLUSIONS AND RECOMMENDATIONS

9.1 Importance

Workers are exposed dermally when handling chemicals (e.g. pesticides, paints) in the chemical industry. Consumers are exposed from household products or use of personal care products. There is special concern for toddlers, who are exposed dermally to chemicals in the dust when crawling on the ground and who in addition may be exposed via hand-to-mouth contact.

While dermal exposure has received less attention than inhalation and oral exposure, the scientific and regulatory community recently became aware that certain substances may be absorbed very efficiently via the dermal route and have the potential to cause or contribute to systemic effects. In addition, an important health concern is local effects—that is, irritant contact dermatitis at workplaces and allergic contact dermatitis for consumers.

Therefore, understanding and awareness of the importance of dermal exposure should be increased among scientists, regulators, health practitioners and the general public.

9.2 Terminology and reporting of data

Dermal exposure is defined as the process of contact between a particular agent and the skin over a period of time. The level of exposure is influenced by preceding loading processes as well as subsequent absorption or desorption processes.

Currently, differing terminology is used within different countries or regulatory contexts to describe dermal exposure:

- exposure mass: the amount present on the entire skin (mg);
- exposure loading: exposure mass per unit surface area (mg·cm^{-2}); this information should always be given together with the corresponding body site and surface area;

- estimates including units of time (dermal exposure rates) are usually related to sampling duration ($mg \cdot h^{-1}$ or $mg \cdot cm^{-2} \cdot h^{-1}$). This is important, as the influence of exposure duration on dermal exposure is unknown. Extrapolations or interpolations of such "rates" for risk assessment purposes, for example, without knowing the measurement conditions, should be avoided.

9.3 Analytical approaches to estimate dermal exposure

Different analytical approaches to estimate dermal exposure are available. Each method bears special advantages and disadvantages related to its general applicability (subprocesses covered), ease of application, accuracy or reliability. Most experience has involved the use of interception and removal techniques for the measurement of dermal exposure to pesticides, and only a few field studies are available for other chemicals. Additionally, only a few studies compare the different methods directly, but the results indicate that the measurement results of the different methods are not very comparable. Therefore, many more studies are needed to improve the understanding of the nature of and differences between the analytical approaches so that appropriate multiplier or conversion factors between the different methods can be derived. Several additional aspects of the different sampling methods and approaches also need to be considered, as described below.

With respect to interception techniques, the available material for patches and coveralls or gloves should be systematically checked in terms of their applicability for different substance groups. Additionally, new material should be tested to enlarge the possible substance spectrum. Some studies are available using differently designed patches for specific substances, and this list should be extended and confirmed. A guide should be developed for selection of the proper material depending on the substance and to enable internationally harmonized procedures. In contrast, a material is needed that simulates the skin, and parameters should be derived to characterize the similarities or the differences of the material used compared with natural skin.

The location of the sampling material on the body is also important in order to distinguish sites that are heavily contaminated from sites

that are not affected. General guidance should be developed for selecting the appropriate location depending on the exposure scenario and the physicochemical properties of a substance.

Video imaging is applied mainly for qualitative or semiquantitative measurements. Owing to the technical equipment needed, it is considered to be complicated and expensive and is therefore not widely used. However, using better sensor technology and more sophisticated computer software, a time-resolved continuous and/or three-dimensional monitoring of the whole body simultaneously might be possible.

In general, the use of fluorescent tracers should be considered for screening dermal exposure. It allows simple qualitative or semiquantitative exposure assessment by observation and thus identification of typically contaminated body parts and the level of contamination. It is therefore useful for training courses and workplace surveillance in developing countries. However, there is a need for other simple and inexpensive educational techniques to identify important aspects of dermal exposure in developing countries.

If expected dermal exposure is out of the range of analytical methodology due to detection limits, migration can be used to estimate possible exposure to substances in articles (e.g. textiles, toys).

The concept of transfer parameters is used mainly for pesticides and is adaptable to all kinds of products used to treat plants, surfaces or materials (e.g. soil types, household surfaces, dust). Product and substance properties determine the retention on the material, and the dislodgeability is also influenced by the material properties and the activity. To ensure proper extrapolation from experience with pesticides to other circumstances, a catalogue for different substance groups, material properties and activities should be developed. Current approaches of probabilistic analysis and collection of all suitable data for dermal transfer efficiencies could be combined and analysed in regard to substance or product properties or activities.

Efforts should be made to increase the research supporting the understanding of basic parameters and processes involved in the assessment of dermal exposure (transfer coefficients, migration, etc.).

This is necessary for the evaluation of models, the advancement of analytical methodologies or techniques and the understanding of the effectiveness of risk-reducing measures.

Biomonitoring is suitable to confirm systemic exposure and for risk assessment. Only if the extent of dermal exposure and absorption or the contribution of other routes of exposure is known can it be used for monitoring. However, it does not allow the characterization of dermal exposure in terms of duration or frequency.

Currently, it is difficult to choose a suitable method based on physicochemical properties of the substance, the special exposure situation, practicability and accuracy requirements. In some situations, semiquantitative methods may be sufficient. However, a "best" method for all purposes or exposure situations is not available. Therefore, each sampling method should be assessed with respect to:

- recovery of substances with different physicochemical properties;
- effect of exposure duration and delay time until sampling;
- concentration dependence (saturation);
- effect of repeated exposures;
- effect of exposure pathway in combination with substance or product properties;
- conversion factors for exposure estimates derived by different sampling methods depending on physicochemical properties of a substance and exposure scenarios.

In conclusion, based on a better understanding of the process of dermal exposure as well as the advantages and disadvantages of the different sampling or assessment methods, guidance is needed that will aid the choice of a suitable approach. The guidance should provide a strategy on the selection of a suitable method for dermal exposure assessment and standard procedures for the different approaches, including standard sampling methods. Ideally, the guidance should be internationally harmonized to ensure consistency with respect to comparable exposure scenarios, suitable exposure measures and, finally, the analytical value. Recommended work should build upon similar initiatives being undertaken by other international working groups, such as the ISO.

9.4 Models and tools to estimate dermal exposure

Several models and tools are available to predict dermal exposure. They cover different application domains, and each has its own advantages and disadvantages. Therefore, it is important to choose the most suitable model based on physicochemical properties of the substance, the special exposure situation, practicability and accuracy requirements. Further efforts should be undertaken to develop recommendations that describe the practicability of the different available models for different exposure situations.

Models are usually developed for typical conditions in industrialized countries. Therefore, transfer to other working conditions may require modification of parameters in the models or introduction of safety factors for special working conditions (e.g. hot climate or humid environment).

For appropriate use of models and tools, documentation in a transparent, traceable and comprehensible manner is of paramount importance. The algorithms and concepts used, their derivation and the data basis used, along with details about the analytical methods of included measurement values, determinants (defaults) provided and their applicability ranges, should be described. Integrated warning systems are desirable that automatically warn the user when utilizing the model or tool outside of its applicability domain (e.g. when choosing a duration out of the analytical scope covered). Although harmonized approaches are aimed for, the user should be able to handle determinants flexibly (e.g. in order to adapt defaults when more relevant data are available). In addition, free and easy access to the model or tool itself as well as to specific data that might be needed for input has to be ensured.

Almost all models and tools are not validated, which is essential for the reliability of the modelled outputs. Validation includes an assessment of the quality and extent of the underlying data, the reliability of the estimation algorithm, and the quality and extent of input data and information provided about the characteristics of the investigated substance and exposure descriptions on which the model is based. Validation studies, such as the BROWSE project for pesticide exposure models and the eteam project considering Tier 1

exposure models under REACH, should be extended to all relevant models used at present.

Some models and tools have specific equipment or operational conditions implemented and should therefore be updated periodically. Furthermore, in order to improve the models, research should be increased on understanding the basic parameters and processes influencing exposure (migration, transfer or desorption processes from skin). Also, the effect of exposure-reducing methods (e.g. the influence of skin washing) should be better investigated and implemented in the models.

Several dermal exposure models are based on measured dermal exposure data. It is therefore advisable to generate a relational database or extend already existing databases with dermal exposure measurements. These databases should include a large number of chemicals with differing physicochemical properties, as well as details on methods for measuring exposure and the corresponding exposure scenarios. Such a database readily allows regular updating of models with new data and simplifies the development of new models for new applications.

9.5 Methods for exposure prevention and reduction

Generally, five approaches are distinguished: the elimination of the substance, the substitution of the substance by a less hazardous substance, reducing the exposure by changing operational conditions via technical measures, reducing the exposure by changing operational conditions via organizational measures and, finally, use of PPE.

At workplaces, methods that change the operational conditions, such as production of hazardous substances in closed systems, installing ventilation or ensuring proper and careful handling (e.g. training, organization of work flows), are frequently applied. However, the ability to implement such methods differs between large and small companies and rich and poor countries. Therefore, there is a need for less cost-intensive or easier procedures for exposure prevention.

The "human factor" (i.e. proper handling of chemicals) is another important component of exposure, and awareness should be increased, as the exposure caused by the human factor can be significantly reduced by information and training.

Protective equipment (PPE, e.g. gloves, coveralls) should be recommended only as a last resort. Cost analysis may also reveal that engineering controls are more cost-effective than PPE over time. The PPE should provide an adequate level of protection while ensuring practicality under given work conditions. Also, suitable information and training (standards, selection guides, criteria) may increase workers' safety. In addition, the ability of regulatory bodies to enforce or monitor such requirements is limited and could be improved.

In addition, evaluation, comparison and harmonization of different PPE types for various possible exposure conditions are needed to enable reproducible and comparable results. Eventually, further research and standards will be necessary that also consider specific needs and applications (e.g. effectiveness of PPE, including circumstances of developing countries or the use of substance mixtures).

For the general public, the critical consumer may avoid a substance if the substance is labelled on a consumer product (elimination or substitution). On the other side, industry may reduce exposure by decreasing the concentration of a harmful substance in a product or changing the product's form (e.g. pellets or granules instead of powder). Generally, more information and some more restrictions are necessary to protect the consumer more efficiently (information, labelling, ban). Some specific recommendations with respect to exposure of consumers are presented below:

- Despite regulations in many countries to reduce exposure to nickel, this metal is still by far the most important allergen. Therefore, there should be better controls on the use of nickel in jewellery and better labelling to help the consumer.
- Exposure of the consumer, especially in personal care products, cosmetics and household products, to allergenic compounds such as fragrances and preservatives is widespread in modern society, and the variety of available substances or products is increasingly diverse. Although some progress has been made

in their avoidance through regulation and labelling requirements in some countries, more information for the general public about possible effects due to exposure of hazardous substances (e.g. allergens) in consumer products should be made available.

- Cosmetic products containing hazardous metals (e.g. lead and mercury), such as kohl and skin lighteners, should be identified and eliminated. Consumers should be informed about their possible effects.
- The presence of *p*-phenylenediamine in henna tattoos should not be allowed, and information should be given on the consequences of early exposure to this allergen, particularly for children.
- The presence of fragrances in toys and children's articles should be avoided.
- Pesticides, biocides, paints or other hazardous products should not be stored at home within the reach of children, and it must be ensured that containers are appropriately labelled.

9.6 Risk assessment

An exposure assessment is a prerequisite for risk assessment. Quantitatively, the risk is a unitless figure and results from the ratio of the reference value to the exposure estimate. In the context of dermal exposure, three generally different toxicological effects have to be distinguished: systemic effects, local effects and sensitization. As a consequence, knowledge of the hazardous characteristics of the compound under consideration should trigger the exposure assessment.

For systemic effects, the reference value is given in milligrams per kilogram body weight. For comparison with such a reference value, knowledge of the amount available on the skin for systemic absorption as well as the kinetics of absorption should be known. Alternatively, biomonitoring could provide systemic levels of the substance or metabolite. In the latter case, metabolism in humans has to be known, as well as the percentage of metabolite in the overall systemic dose. Many questions concerning the process of dermal absorption have already been addressed in the EHC on dermal absorption (IPCS, 2006).

In addition, the factors influencing the amount of a substance on the skin that is available for absorption are insufficiently understood. We do not know the dose or concentration dependence (is it always the same fraction of substance remaining on the skin with different substance doses/concentrations?), influence of repeated exposures (are the amounts additive, or is there saturation?) and the influence of exposure duration (is steady state reached?). Furthermore, the skin may act as a reservoir. Therefore, the efficiency of skin washing should be investigated more quantitatively. In addition, the influence of solvents in solutions or other substances in mixtures (formulations) on the amount deposited or remaining on the skin is not known. Therefore, there is considerable research needed for an understanding of the complex interactions with respect to the different activities and pathways as well as the physicochemical properties of substances or products (e.g. aggregate state, vapour pressure, water solubility).

The situation is less complicated for local effects, such as irritation, which usually depend on the concentration of the irritating substance and on the exposure duration. Sensitizing effects usually depend on the concentration of a substance, exposure duration, uptake (to some degree) and frequency of contact. Thus, in terms of risk assessment, these parameters should also be taken into consideration. The concentration of a substance is, however, relevant only for solutions. The suitable dose measure for dermal contact with solids is not clear.

Generally, the measure of dermal exposure that is most meaningful for toxicological assessments (e.g. $mg \cdot (kg\ bw)^{-1} \cdot d^{-1}$, $mg \cdot cm^{-2}$, $mg \cdot cm^{-2} \cdot h^{-1}$) should be determined for each of these end-points.

Risk assessment for dermal exposure is addressed by some regulatory frameworks, but should be further extended, and additionally internationally harmonized (for an example of such guidance, see the WHO/IPCS guidance for immunotoxicity; IPCS, 2012). In particular, the introduction of DOELs should be considered, taking into account local effects, sensitization and systemic effects. However, the introduction of DOELs would require standard procedures to measure dermal exposure in a suitable unit with respect to the toxicological concern.

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Standards, test methods, guidelines and technical specifications[1]

ANSI/ADA 76-2005 (R2010)	Non-sterile natural rubber latex gloves for dentistry
ANSI/ISEA 1052011	American national standard for hand protection selection criteria
ANSI/NFPA 1971-2000	Standard on protective ensemble for structural fire fighting, 2000 Edition
ANSI S2.73-2002 (R 2007)	Mechanical vibration and shock-hand-arm vibration—method for the measurement and evaluation of the vibration transmissibility of gloves at the palm of the hand
ASTM D120-09	Standard specification for rubber insulating gloves
ASTM D412-06a-2013	Standard test methods for vulcanized rubber and thermoplastic elastomers—tension
ASTM D471-12a	Standard test method for rubber property—effect of liquids
ASTM D543-06	Standard practices for evaluating the resistance of plastics to chemical reagents
ASTM D3389-10	Standard test method for coated fabrics abrasion resistance (rotary platform abrader)
ASTM D3577-09e1	Standard specification for rubber surgical gloves
ASTM D3578-05(2010)	Standard specification for rubber examination gloves
ASTM D3767-03	Standard practice for rubber—measurement of dimensions
ASTM D4679-02(2007)	Standard specification for rubber household or beauticians' gloves
ASTM D5151-06(2011)	Standard test methods for detection of holes in medical gloves
ASTM D5250-06(2011)	Standard specification for polyvinyl chloride gloves for medical application
ASTM D7246-06(2011)e1	Standard test method for detection of holes in polyethylene food service gloves

[1] Abbreviations used are defined at the end of this list.

(continued)

ASTM F696-06(2010)	Standard specification for leather protectors for rubber insulating gloves and mittens
ASTM F739-12	Standard test method for permeation of liquids and gases through protective clothing materials under conditions of continuous contact
ASTM F903-10	Standard test method for resistance of materials used in protective clothing to penetration by liquids
ASTM F1001-12	Guide for selection of chemicals to evaluate clothing material
ASTM F1060-08	Standard test method for thermal protective performance of materials for protective clothing for hot surface contact
ASTM F1154-11	Standard practices for qualitatively evaluating the comfort, fit, function and durability of protective ensembles and ensemble components
ASTM F1358-08	Standard test method for effects of flame impingement on materials used in protective clothing not designated primarily for flame resistance
ASTM F1383-12	Standard test method for permeation of liquids and gases through protective clothing materials under conditions of intermittent contact
ASTM F1407-12	Standard test method for resistance of chemical protective clothing materials to liquid permeation—Permeation cup method
ASTM F1670-08	Standard test method for resistance of materials used in protective clothing to penetration by synthetic blood
ASTM F1671/F1671M-13	Standard test method for resistance of materials used in protective clothing to penetration by blood-borne pathogens using phi-X174 bacteriophage penetration as a test system
ASTM F1790-05	Standard test method for measuring cut resistance of materials used in protective clothing
ASTM F1819 -07(2013)	Standard test method for resistance of protective clothing materials used in protective clothing to penetration by synthetic blood using mechanical pressure technique

(continued)

ASTM WK35278	New test method for evaluating whole glove dexterity—tool test
EN 71-3:2013	Safety of toys—Part 3: Migration of certain elements
EN 71-10:2005	Safety of toys—Part 10: Organic chemical compounds—Sample preparation and extraction
EN 388:2003	Protective gloves against mechanical risks
EN 407:2004	Protective gloves against thermal risks (heat and/or fire)
EN 420:2003 + A1:2009	Protective gloves—General requirements and test methods
EN 421:2010	Protective gloves against ionizing radiation and radioactive contamination
EN 455-1:2000	Medical gloves for single use. Part 1: Requirements and testing for freedom from holes
EN 469:2005 + A1:2006 + AC:2006	Protective clothing for firefighters—Performance requirements for protective clothing for firefighting
EN 511:2006	Protective gloves against cold
EN 1082: 2000	Protective clothing—Gloves and arm guards protecting against cuts and stabs by hand knives
EN 1499:2013	Chemical disinfectants and antiseptics—Hygienic handwash—Test method and requirements (phase 2/ step 2)
ISO 2859-1:1999(2011)	Sampling procedures for inspection by attributes—Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection
ISO 5085-1:1989-11	Textiles–determination of thermal resistance–Part 1: low thermal resistance
ISO 6529:2013-02	Protective clothing—Protection against chemicals—Determination of resistance of protective clothing materials to permeation by liquids and gases
ISO 10819:1996-08	Mechanical vibration and shock-hand-arm vibration—Method for the measurement and evaluation of the vibration transmissibility of gloves at the palm of the hand

(continued)

ISO 11641:2012	Leather—Tests for colour fastness—Colour fastness to perspiration
ISO 17493:2000-12	Clothing and equipment for protection against heat. Test method for convective heat resistance using a hot air circulating oven
ISO/TR 14294:2011	Workplace atmospheres—Measurement of dermal exposure—Principles and methods

Abbreviations and relevant links for documents: ADA, American Dental Association; ANSI, American National Standards Institute (http://webstore.ansi.org/default.aspx); ASTM, American Society for Testing and Materials (http://www.astm.org, last two figures reflect year of publication, additional four figures in parentheses indicate year of update); EN, European norm (http://ec.europa.eu/enterprise/policies/european-standards/harmonised-standards/personal-protective-equipment/); ISEA, International Safety Equipment Association; ISO, International Organization for Standardization (http://www.iso.org/iso/home.html); ISO/TR, International Organization for Standardization Technical Report; NFPA, National Fire Protection Association

APPENDIX 1: TERMINOLOGY

General terms and concepts relating to exposure can be reviewed in the EHC monographs *Human exposure assessment* (IPCS, 2000) and *Principles for the assessment of risks to human health from exposure to chemicals* (IPCS, 1999). Proposed terminology to be used in exposure assessment is presented, for example, in IPCS (2001a, 2004) and Meek et al. (2011).

It is recognized that terms are often used inconsistently in the scientific literature. Likewise, the same term may be interpreted differently in, for example, safety regulations or different jurisdictions or may be defined in ways that result in different regulatory consequences (see, for example, the definition of the terms "aggregate, combined, cumulative and concurrent exposure").

This document follows the terminology defined in Part 2 (a glossary of key exposure assessment terminology) of *IPCS risk assessment terminology* (IPCS, 2004). In addition to the definitions provided in chapter 3, terms relevant to this document are discussed in more detail in the glossary below (in alphabetical order).

Absorbed dose
: *see* "Dermal dose"

Absorption
: *see* "Dermal (percutaneous, skin) absorption"

Actual (dermal) exposure (mass)
: *see* "Dermal exposure mass"

Actual dose
: *see* "Dermal dose"

Administered dose
: *see* "Dermal dose"

Agent
: Any chemical or biological entity on its own or admixed as it occurs in the natural state or as produced, used or released, including release as waste, by any work activity, whether or not produced intentionally and whether or not placed on the market that contacts a target (ISO/TR 14294:2011).

Aggregate, combined, cumulative and concurrent exposure

The terms aggregate, combined, cumulative and concurrent exposure are widely used. However, the definition of these terms is often interpreted inconsistently, resulting in different meanings, depending on the regulatory area or scientific context (e.g. human health/toxicology or ecotoxicology):

Aggregate exposure

The demographic, spatial and temporal characteristics of exposure to a single chemical through all relevant/multiple pathways, sources (e.g. food, water, residential uses, occupational) and routes (e.g. oral, dermal, inhalation); thus, aggregate risk is the risk associated with multiple pathways/routes of exposure to a single chemical (USEPA, 1999a; EFSA, 2008; IPCS, 2009a; Meek et al., 2011; Silins et al., 2011).

Although this term is widely used in some jurisdictions, Meek et al. (2011) and IPCS (2009a) propose to use the term "single chemical, all routes" instead for a more precise terminology.

Combined exposure

The exposure to multiple chemicals by a single route or multiple routes. Substances grouped together for evaluation of combined exposure are referenced as an "assessment group". Combined exposure to multiple chemicals is also defined in the context of whether or not the components act by similar or different modes of action in induction of critical effects (i.e. "single mode of action" or "multiple modes of action"; Meek et al., 2011).

In contrast, in the field of ecotoxicology, the term combined exposure is often used in the context of exposure of humans to a substance via two or more routes (EC, 2003a, Part I) or under different circumstances (e.g. exposure at the workplace and exposure from consumer products / indirect exposure via the environment) (EC, 2003a, Part III). This also applies in the REACH guidance, in which the term combined exposure is set equivalent to cumulative exposure, and the definition for both is provided that elsewhere is used for the term aggregate exposure—i.e. for exposure to one substance by different routes and pathways (see the above definition of aggregate exposure; ECHA, 2012e).

Cumulative exposure
This term is used very differently in the literature:

- The demographic, spatial and temporal characteristics of exposure to multiple chemicals through all relevant pathways (e.g. food, water, residential uses, occupational) and routes (e.g. oral, dermal, inhalation). Cumulative risk is the combined risk from aggregate exposure to multiple chemicals (and may be restricted to chemicals that have a common mechanism of toxicity) (IPCS, 2009a; Meek et al., 2011).
- The risk deriving from exposure to compounds sharing the same mode of action or similar effects (EFSA, 2008).
- The sum of exposures of an organism to a pollutant over a period of time (USEPA, 2013c).
- The exposure to one substance, taking into account all routes and pathways or from different products, including indirect exposure via the environment (ECHA, 2012e).
- The total accumulated exposure resulting from repeated (radiation) exposures (of the whole body or of a particular region) (Zwemer, 1998).

Concurrent exposure
Sometimes used to express the exposure by all relevant pathways, durations and routes that allows one chemical to add to the exposure of another chemical such that the total risk is an estimate of the sum of the exposures to the individual chemicals (USEPA, 1997d; EFSA, 2008).

In contrast, in the REACH guidance, the definition "the exposure to one substance taking into account all routes and pathways or from different products, including indirect exposure via the environment" is provided for the terms combined or cumulative exposure (ECHA, 2012e).

It is recommended that the above four terms not be used. Instead, as proposed in the report of a WHO/IPCS workshop on aggregate/cumulative risk assessment (IPCS, 2009a) and Meek et al. (2011), the following definitions have been adopted for this document in order to differentiate properly between them:

- "single chemical, all routes" (exposure to the same substance by multiple pathways and routes);
- "multiple chemicals by a single route";
- "multiple chemicals by multiple routes".

Applicant

see "Worker"

Applied dose

see "Dermal dose"

Bayesian statistics

A branch of statistics that is concerned with improving an initial estimate of some parameter after obtaining new evidence. A Bayesian approach to a problem begins with the formulation of a probabilistic model that is used to develop a prior distribution for the unknown parameter—e.g. the distribution of likely mean exposures in a specific situation. After obtaining a number of exposure measurements, the Bayes' Rule is applied to obtain a posterior distribution for the likely values of the exposure parameter. This takes account of the prior distribution, which can be updated with empirical data to create a posterior distribution. In most cases, the posterior distribution will be less variable than the prior distribution because the additional information in the measurements helps to increase the understanding of the likely exposure.

Bayes' Rule is formally written as:

$$P(A/B) = \frac{P(B/A)P(A)}{P(B)}$$

where:

- P(A/B) is the posterior probability of A given B, i.e. the probability of A given a specific value of B;
- P(A) is the prior probability of A. It is considered prior because it does not take into account any information about B;
- P(B/A) is the conditional probability of B given A;
- P(B) is the prior or marginal probability of B. Its function is to normalize the posterior probability to ensure it sums to unity.

Bias

An effect that deprives a statistical result of representativeness by systematically distorting it, as distinct from a random error, which may distort on any one occasion but balances out on the average. Bias is most commonly assumed with a systematic error and can arise for a number of reasons, including failure to respect either representativity or comparability (OECD, 2007).

Inherent bias: Due to the nature of the situation, it expresses the inability to measure accurately and directly what one would wish to measure, leading to indirect measurements. The bias cannot be removed by, for example, increasing the sample size (OECD, 2007).

Bioavailable dose

see "Dermal dose"

Biocide

see "Pesticide, biocide, plant protection product"

Biological markers

see "Biomarker (biological marker)"

Biomarker (biological marker)

A measure of internal dose in order to evaluate human exposure—i.e. any substance, structure or process that can be measured in the body or its products and influence or predict the incidence of outcome or disease. Biomarkers can be classified into markers of exposure, effect and susceptibility. Numerous biological media are available for use in exposure assessment (collected in a non-invasive or invasive manner): blood, urine, exhaled breath, saliva, keratinized tissues (hair and nails), ossified tissue (teeth and bone), adipose tissue, breast milk, faeces, nasal lavage, tears, sputum, semen, cord blood and buccal cells. Further information on biomarkers of exposure is available in IPCS (1993, 2000, 2001a, 2010).

Boundaries

In relation to models/tools, *see* "Model boundaries"

Breakthrough detection time (BDT)

see "Measured breakthrough (detection) time (MBT/BDT)"

Bystander

A person potentially exposed to agents but not necessarily engaged in the application procedure of, for example, pesticides (OECD, 1997).

Combined exposure

see "Aggregate, combined, cumulative and concurrent exposure"

Concurrent exposure

see "Aggregate, combined, cumulative and concurrent exposure"

Contaminant layer

see "Skin contaminant layer compartment"

Cosmetic

see section 4.2.1.1 and Appendix 2

Cumulative exposure

see "Aggregate, combined, cumulative and concurrent exposure"

Degradation

In relation to PPE material: Indicator of the deterioration (getting harder, getting softer or swelling) of the material on contact with a specific chemical.

Delivered dose

see "Dermal dose"

Dermal (percutaneous, skin) absorption

A global term that describes the transport (diffusion) of chemicals from the outer surface of the skin into both the skin and the systemic circulation (OECD, 1997, 2004; IPCS, 2006). This process can be divided into (IPCS, 2006):

- **penetration**, which is the entry of a substance into a particular layer or structure, such as the entrance of a compound into the stratum corneum;
- **permeation**, which is the penetration through one layer into a second layer that is both functionally and structurally different from the first layer;
- **resorption**, which is the uptake of a substance into the skin lymph and local vascular system and in most cases will lead to entry into the systemic circulation (systemic absorption).

Dermal contact volume

The volume containing the agent that contacts the dermal exposure surface. The unit used is litres. It is a theoretical term, equivalent to the volume of the skin contaminant layer (*see*

"skin contaminant layer compartment"); however, for practical reasons, it is defined by the mass of all substances contained in the skin contaminant layer in kilograms (IPCS, 2004; ISO/TR 14294:2011).

Dermal dose

The amount of agent that enters a target by crossing the skin. The following terms refer to an agent crossing an absorption barrier and thus are consistent with the definition of an absorbed dose (Sexton et al., 1995; IPCS, 2000, 2001a, 2004; USEPA, 2009):

- **Dermal (internal/absorbed/actual) dose** is the amount of the chemical agent that enters the body via skin; thus, this term refers to the amount of agent that has entered the body via uptake (was absorbed) and therefore is available to undergo metabolism, transport, storage or elimination.
- **Systemic (bioavailable) dose** is the dose of the agent within the body (i.e. not localized at the point of contact). Thus, skin irritation caused by contact with an agent is not a systemic effect, but liver damage due to absorption of the agent through the skin is a systemic effect.
- **Delivered dose** is the portion of the internal (absorbed) dose that reaches a tissue of interest.

In contrast, terms such as **administered (applied) dose** and **potential dose** refer to the amount of agent in contact with an exposure surface (see section 3.6.1) and thus are describing the **exposure mass** or **loading**, depending on whether an exposure surface is specified.

While it is recognized that these terms are often used in a way that does not refer to the crossing of an exposure surface, dermal dose is used exclusively in this context in this document in order to eliminate confusion between exposure mass and dose, as has been done in *IPCS risk assessment terminology* (IPCS, 2004). In addition, Zartarian et al. (1997, 2006) have provided a thorough review and basic definitions of exposure and related concepts.

Dermal exposure

The process of contact between a particular agent that reaches the skin (ISO/TR 14294:2011). The exposure to a biological,

chemical or physical agent is an external process and provides no information about the success of the absorption. Consequently, dermal exposure describes the contact of an agent with the skin without any information on whether penetration or permeation occurs (*see* "dermal exposure mass" for information about its unit). In addition, Zartarian et al. (1997, 2006) have provided a thorough review and basic definitions of exposure and related concepts.

Dermal exposure concentration

A theoretical term for the amount of a substance that is present in unit quantity in a medium such as air, water, food or soil, expressed per volume or mass (IPCS, 2000). It is also usually given as density, as the exposure mass divided by the dermal contact volume, expressed in grams per litre, or divided by the corresponding mass, expressed in grams per kilogram (IPCS, 2004; ISO/TR 14294:2011).

Dermal exposure loading

The dermal exposure mass divided by the dermal exposure surface area (USEPA, 2009). For practical reasons, dermal exposure loading can be expressed as time-averaged mass of agent in an exposed part of the skin contaminant layer (*see* "skin contaminant layer compartment") divided by area-averaged skin layer surface area of that part, expressed in grams per square centimetre (ISO/TR 14294:2011). For example, a dermal exposure measurement based on a skin wipe sample, expressed as a mass per skin surface area, is an exposure loading (IPCS, 2004; USEPA, 2009).

Dermal exposure mass

The mass of agent present in the dermal contact volume. For practical reasons, dermal exposure mass is defined by the amount of agent in grams present in the skin contaminant layer (*see* "skin contaminant layer compartment"). However, the outcome of the process of dermal exposure (i.e. the contact) can be expressed by different parameters of exposure and units (ISO/TR 14294:2011). For example, the total mass collected with a skin wipe sample over the entire exposure surface is an exposure mass (IPCS, 2004). For assessment of occupational exposure, a distinction is made between potential and actual dermal exposure (mass):

- **Actual dermal exposure (mass)** describes the mass in direct contact with the (bare) skin that is available for absorption (OECD, 1997).
- **Potential dermal exposure (mass)** expresses the actual dermal exposure that could occur without any exposure-reducing method.

Dermal exposure period
: The time the agent is present in the skin contaminant layer (i.e. the contact time) (ISO/TR 14294:2011).

Dermal exposure surface
: The skin surface area where an agent is present. For practical reasons, it is represented by a two-dimensional representation of the contaminant layer (*see* "skin contaminant layer compartment), expressed in square centimetres (ISO/TR 14294:2011).

Dermal penetration
: *see* "Dermal (percutaneous, skin) absorption"

Dermal permeation
: *see* "Dermal (percutaneous, skin) absorption"

Dermal resorption
: *see* "Dermal (percutaneous, skin) absorption"

Dermal uptake
: The transport of an agent from the skin contaminant layer into the skin—i.e. crossing the interface between skin contaminant layer and the stratum corneum as an absorption barrier. The time–exposure concentration profile for an identified area of the skin contaminant layer over a defined period of time is relevant for uptake (ISO/TR 14294:2011). However, crossing the interface does not necessarily mean that the agent will be systemically available—e.g. by entering the blood circulation system (*see* "Dermal dose" and "Dermal (percutaneous, skin) absorption"). This differs from the concept of intake, which is the process of an agent crossing an outer exposure surface of a target without passing an absorption barrier—e.g. through ingestion (IPCS, 2004).

Deterministic mode
: *see* "Model type"

Dose
: *see* "Dermal dose"

Empirical mode

see "Model type"

Estimate

An empirical value derived from or by modelling (IPCS, 2009b).

Exposure

The (process of) contact between a particular agent and a target (outer boundary of an organism) or the amount of a particular agent contacting the target in a specific frequency for a defined duration (USEPA, 1992; IPCS, 2004, 2009b; ISO/TR 14294:2011). Thus, contact takes place at a defined exposed surface and period. However, exposure to an agent is an external process that provides no information about the success of uptake/intake (e.g. dermal absorption, considering dermal exposure).

Exposure assessment

The process of estimating or measuring the extent of contact with chemical substances experienced or anticipated under different conditions. This includes the magnitude, frequency and duration of exposure to an agent, along with the number and characteristics of the population exposed. Ideally, it describes the sources, pathways, routes and uncertainties in the assessment (IPCS, 1999, 2004).

Exposure concentration

The concentration of a chemical in its transport or carrier medium at the point of contact (USEPA, 1992, 2009). Thus, it describes the thermodynamic activity of the agent in a specified exposure matrix (medium), whether the matrix is infinite or finite during the process of contact. In the context of exposure, the dimension is usually given as density, as exposure mass divided by the contact volume or divided by the mass of contact volume, depending on the medium (e.g. mg/l in fluids, mg/kg in solids or mg/m^3 in gaseous media) (IPCS, 2008). For the dermal route, it is important to keep in mind that in cases where the agent is present in diluted form as part of a carrier medium, not all of the exposure mass will actually be touching the skin (Sexton et al., 1995; IPCS, 2000, 2001a).

Exposure duration/period

The time of continuous contact between an agent and a target—i.e. the length of time over which continuous or intermittent contact occurs (USEPA, 2009).

Exposure event
: The occurrence of continuous contact between an agent and a target (IPCS, 2004).

Exposure frequency
: The number of exposure events for an exposure duration (IPCS, 2004).

Exposure loading
: *see* "Dermal exposure loading"

Exposure pathway
: The physical course taken by an agent as it moves from a source to a point of contact with a person (target) (IPCS, 2000, 2004).

Exposure period
: *see* "Exposure duration/period"

Exposure route
: The way in which a chemical enters an organism after contact (e.g. ingestion, inhalation or dermal absorption) (IPCS, 2000, 2001a).

Exposure scenario
: A combination of facts, assumptions and inferences that define a discrete situation where potential exposures may occur. These may include the source, the exposed population, exposure pathways, amount or concentration of agents involved, exposed organism, system or (sub)population (as well as, for example, habits), time frame of exposure, microenvironment(s) and activities. Scenarios are often created to aid exposure assessors in estimating exposure (OECD, 2003; IPCS, 2004).

Extrapolation
: Occurs when quantitative estimates are determined by values outside the range of measured values (OECD, 1997).

Handler
: *see* "Worker"

Inherent bias
: *see* "Bias"

Inner clothing contaminant layer compartment
: *see* "Skin contaminant layer compartment"

Intake
: *see* "Dermal uptake"

Internal dose
: *see* "Dermal dose"

Loading

see "Dermal exposure loading"

Measured breakthrough (detection) time (MBT/BDT)

The time it takes the chemical to permeate through the protective material until it can be seen on the unexposed side of the material and reaches a specific flow rate.

Measured breakthrough time (MBT)

see "Measured breakthrough (detection) time (MBT/BDT)"

Mechanistic mode

see "Model type"

Method efficiency

- **Overall method efficiency**: Product of sampling efficiency and recovery efficiency (for interception and removal methods), or mass of agent detected divided by mass of agent in analysed dermal contact volume (for in situ methods). Note: Regarding in situ methods, efficiency is the mass of agent detected either directly or indirectly by use of a tracer.
- **Sampling efficiency**: Ratio between the mass of agent determined on the collection medium and the mass of agent loaded onto the sampled area.
- **Recovery efficiency**: Ratio between the mass of agent recovered from the collection substrate and the mass of agent present (loaded) on the collection medium.

Migration

Possible mass of substance on a surface that is available for transfer to skin—e.g. due to contamination of surface or due to leaching out of product (see section 5.2).

Minimum detectable limit (MDL)

The smallest amount of chemical detectable by an analytical system being used to measure permeation. The MDL qualifies the MBT as being the safest, most reliable information achievable.

Model

A mathematical abstraction of physical (complex) reality derived from assumptions and approximations. The purpose of a model is to represent as accurately and precisely as necessary with respect to particular decision objectives a particular system of interest (IPCS, 2008).

Thus, an **exposure model** is a conceptual or mathematical representation or a computational framework designed to reflect real-world exposure scenarios and processes defining the physical, chemical and behavioural information and exposure algorithms. By this, models may obviate the need for extensive measuring/monitoring programmes by providing estimates of population exposures (and doses) that are based on a smaller number of representative measurements (analytical methodologies) (USNRC, 1991; IPCS, 2000, 2004, 2005).

Model boundaries

Designated areas of competence of the model, including time, space, pathogens, pathways, exposed populations and acceptable ranges of values for each input and jointly among all inputs, for which the model meets data quality objectives. Risks can be understated or overstated if the model boundary is misspecified. A common challenge in exposure modelling is to achieve the proper representation of averaging times for exposures when considering all model inputs and to account for the proper geographic scope of sources of agents, microenvironments and human activity (IPCS, 2008).

Model structure

A set of assumptions and inference options upon which a model is based, including underlying theory as well as specific functional relationships (IPCS, 2008).

Model type

- **Mechanistic**: A mathematical construct of physical/chemical processes simulating the behaviour of an agent in the environment or target organism as it is transported and undergoes transformations relevant for the exposure of interest. Fixed outputs for a fixed set of inputs (e.g. physicochemical characteristics and mass relationships based on balance principles) are used (IPCS, 2005).
- **Empirical**: A numerical representation of the relationship between input and output variables based on historic measurements predicting concentrations and exposures (e.g. regression models that relate air concentrations and blood levels of a chemical or ambient pollutant concentrations with personal exposures). The terms of the

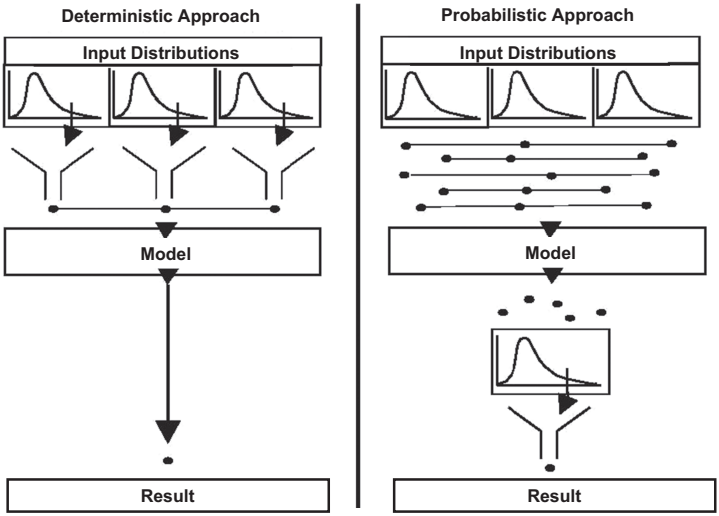

Fig. A1.1. Comparison of deterministic and probabilistic modelling (Mosbach-Schulz, 1999).

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empirical model are related to the data set from which they have been derived, and there are no grounds other than expert opinion or experimental confirmation with which to assess if they can be used to calculate exposures in some other system (location or population), or even in the same system at another time. Empirical models do not require or imply any causal relationships between the model variables (IPCS, 2005).

- **Deterministic**: An estimate that is based on a single value for each model input and a corresponding individual value for a model output, without quantification of the cumulative probability or, in some cases, plausibility of the estimate with respect to the real-world system being modelled. This term is also used to refer to a model for which the output is uniquely specified based on selected single values for each of its inputs (point estimate) (IPCS, 2008) (see Fig. A1.1).

- **Probabilistic**: An estimate where the variability and/or uncertainty in the model input and output parameters are expressed as statistical distributions (probability distributions rather than single values). Probabilistic models may be based on an underlying deterministic model or some other model structure (see Fig. A1.1).

Model uncertainty
: *see* "Uncertainty"

Model validation
: *see* "Validation"

Model variability
: *see* "Variability"

Monte Carlo technique/simulation
: The repeated random sampling from a distribution of values for each of the parameters in a generic equation to derive an estimate of the distribution of the population (USEPA, 1992, 1997c; REAP, 1995; Jayjock et al., 2000; IRIS, 2011). This technique can provide a probability function of estimated exposure using probability distributions of the input variables and uses methods of statistical inference (e.g. percentiles, mean, variance and confidence intervals). The Monte Carlo simulation can also be used to test the effect that an input parameter has on the output distribution (IPCS, 2001a).

Normalization
: Standardized expression (e.g.) of exposure as a function of another variable (e.g. micrograms per amount handled) (OECD, 1997).

Operator
: *see* "Worker"

Outer clothing contaminant layer compartment
: *see* "Skin contaminant layer compartment"

Overall method efficiency
: *see* "Method efficiency"

Parameter uncertainty
: *see* "Uncertainty"

Penetration
: in relation to skin: *see* "Dermal (percutaneous, skin) absorption"
in relation to PPE material: substance/chemical leaking through imperfections in the material (e.g. seams, zippers, pinholes and other) (CCOHS, 2009).

Percutaneous absorption

see "Dermal (percutaneous, skin) absorption"

Permeation

in relation to skin: *see* "Dermal (percutaneous, skin) absorption"
in relation to PPE material: The diffusion/movement through the intact protective materials (PPE) and following transfer of substances between the equipment surface and the skin—i.e. the passage of a chemical through a barrier layer at a molecular level involving the absorption of molecules into the contacted (outside) surface of a material, diffusion of the absorbed molecules in the material and desorption from the opposite (inside) surface of the material (EN 374:2003; Watts, 2010).

Permeation rate

in relation to PPE material: Rate at which a chemical moves through a specific area of the material and reaches equilibrium with the material during a specified test period duration.

Personal care product

see section 4.2.1.1 and Appendix 2

Pesticide, biocide, plant protection product

As these three terms are used in different sections of this document, a clear distinction is provided below, acknowledging that all three terms might be referring to the same substance, yet are defined in another context by a different term.

Pesticide means any substance intended for preventing, destroying, attracting, repelling or controlling any pest, including unwanted species of plants or animals, during the production, storage, transport, distribution and processing of food, agricultural commodities or animal feeds or which may be administered to animals for the control of ectoparasites (FAO/WHO, 2011).

However, pesticides and products that fall under the scope of the above definition might be regulated differently, sometimes varying considerably from country to country. While the majority of these products are regulated in pesticide legislation, in some countries, for some products, other legislation might apply, such as the regulation for medicines/drugs, chemicals or toxic substances (OECD, 1999).

This broad definition of pesticides leads to overlaps with other regulations (e.g. plant protection products or biocide regulations in Europe). In contrast, the term biocide is not defined in

any statutes or regulations in the USA and is not generally used, but is sometimes used in common parlance (OECD, 1999).

In Europe, the term pesticide relates to two regulatory frameworks, one for biocides and plant protection products.

A **biocide** or non-agricultural pesticide is a poisonous substance represented by a broad class of chemical agents, including, among others, disinfectants/sanitizers, preservatives/microbiocides, antifouling products, wood preservatives, insecticides, rodenticides, piscicides and products used for vertebrate and invertebrate pest control (OECD, 1999).

A **biocidal product** is additionally defined by Directive 98/8/EC (EC, 1998a):

> Active substances and preparations containing one or more active substances, put up in the form in which they are supplied to the user, intended to destroy, deter, render harmless, prevent the action of, or otherwise exert a controlling effect on any harmful organism by chemical or biological means.

Plant protection products are agricultural pesticides that are distinguished from biocides in the European regulation and defined in the European Council Directive 91/414/EEC (EEC, 1991) as:

> Active substances and preparations containing one or more active substances, put up in the form in which they are supplied to the user, intended to protect plants or plant products against all harmful organisms or prevent the action of such organisms, in so far as such substances or preparations are not otherwise defined below; influence the life processes of plants, other than as a nutrient (e.g. growth regulators); preserve plant products, in so far as such substances or products are not subject to special Council of Commission provisions on preservatives; destroy undesired plants; or destroy parts of plants, check or prevent undesired growth of plants.

Plant protection product
: *see* "Pesticide, biocide, plant protection product"

Potential (dermal) exposure (mass)
: *see* "Dermal exposure mass"

Potential dose
: *see* "Dermal dose"

Probabilistic model
: *see* "Model type"

Professional user
: *see* "Worker"

Recovery efficiency
: *see* "Method efficiency"

Resident
: A person who lives or works adjacent to an area that has been treated.

Resorption
: *see* "Dermal (percutaneous, skin) absorption"

Sampling efficiency
: *see* "Method efficiency"

Scenario uncertainty
: *see* "Uncertainty"

Screening tool
: *see* "Tier"

Secondary exposure
: Exposure due to an indirect pathway—e.g. due to contact with contaminated surfaces (see section 3.1.2).

Skin absorption
: *see* "Dermal (percutaneous, skin) absorption"

Skin contaminant layer compartment
: The compartment on top of the stratum corneum of the human skin. It is formed by sebum lipids, sweat and additional water from transepidermal water loss, including products from cornification and unshed corneocytes (ISO/TR 14294:2011).

Steady-state permeation rate
: in relation to PPE material: *see* "Permeation rate"

Systemic dose
: *see* "Dermal dose"

Tier
: A "screening-level" or "Tier 1" assessment typically refers to conservative scenario descriptions and a summation of deterministic estimates addressing a range of somewhat similar uses, with limited numbers of parameters being based on measured or modelled data, or both, to suffice as a basis for comparison with a measure of hazard to determine whether further assessment is necessary (Meek et al., 2011) (see also section 6.4).

Tool
: A computer-based software or other product (e.g. a spreadsheet) in the context of exposure estimation, which implements one or more modelling approaches (mathematical model or database). A tool allows scientists to leverage computational power

to simulate, visualize, manipulate and gain intuition about the entity, phenomenon or process being represented. Similarly, different tools may implement the same model. A tool simplifies the calculation/estimation procedure from the input parameters to the outcome and enables an automated performance of a definite task. In the case of exposure assessment, the user needs only the input parameters for the respective model.

Transfer

The "carryover" of a substance from a surface to the skin (see section 5.2).

Uncertainty

Can be defined as lack of precise knowledge/information or partial ignorance as to what the truth is, whether qualitative or quantitative (USNRC, 1994a; Frey & Burmaster, 1999). In exposure assessment, uncertainty is the lack of knowledge or imperfect knowledge about the correct value for a specific exposure measure or estimate that arises as a result of the limitations in the representations of complex processes (USEPA, 1992; IPCS, 2008). As the true value is not known or cannot be measured, estimates are made using modelling procedures based upon available data. However, in exposure assessment, uncertain information of different quality from different sources must be combined. Uncertainty can be conceptualized as dependent on the current state of knowledge. Over time, the quality of data (more representative, precise or improved knowledge) or models (less systematic error and greater precision) might improve, resulting in a decrease in the amount of uncertainty inherent in a prediction (Frey & Burmaster, 1999).

Three different types of uncertainty are generally considered (USEPA, 1992; IPCS, 2000, 2008):

- **Scenario uncertainty**: Arising from a lack of knowledge or missing/incomplete information required to fully specify the problem and define the exposure and dose (USEPA, 1992; IPCS, 2000). Examples are descriptive errors (errors or misinterpretation in information/exposure pathways/scenario exposure estimates) and aggregation errors (assumptions of homogeneous populations, spatial and temporal approximations, e.g. steady-state conditions).

- **Model uncertainty**: Arising from a lack of knowledge required to formulate the appropriate conceptual or computational models (USEPA, 1992; IPCS, 2000). Limitations of the model might be due to gaps in the scientific theory, relationship/correlation errors or modelling errors (representing reality in an oversimplified manner, excluding relevant variables, using surrogate variables, excluding correlations) (USEPA, 1992; USNRC, 1994a; IPCS, 2008).
- **Parameter uncertainty**: Arising from a lack of knowledge about the true value or distribution of a model parameter, reflecting, in part, the level of confidence in model predictions (USEPA, 1992; IPCS, 2000; Barton et al., 2007). Often best estimates that are not actually very accurate are used (USEPA, 1992). Examples are the variety of sources, measurement/sampling errors, generic/surrogate data used, variability and misclassifications (ambiguous information, non-representativeness of parameters, limited availability of empirical information, as well as limitations in the measurements/techniques) (USNRC, 1994a; IPCS, 2008).

Uptake

see "Dermal uptake"

Validation

The process by which the reliability (reproducibility of the outcome) and relevance (establishing the meaningfulness and usefulness) of a particular approach, method, process or assessment are established for a defined purpose (OECD, 2003; IPCS, 2004). An especially useful form of validation is where the results of an assessment can be compared with independent data or information (e.g. comparing predicted exposure with biomarker measurements or epidemiological studies) (IPCS, 2004). Although measurements are preferable as the "gold standard" in validation of models, comparison of results from different assessment methods or modelling approaches can also be used to evaluate validity, or at least agreement (IPCS, 2000). Model validation is a necessary precondition for the generalization of model results to a different or larger population (IPCS, 2000).

Variability

A reflection of the degree to which predictions may differ across a population (Barton et al., 2007); thus, it represents diversity or heterogeneity in a well-characterized population due to interindividual differences (across space, time, individuals) (USNRC, 1994b; Frey & Burmaster, 1999). As many parameters are more realistically described as probability distributions, variability is an inherent property of the system being modelled and a source of uncertainty in risk assessment (Price & Michaud, 1993; Frey & Burmaster, 1999; Jayjock et al., 2000; IPCS, 2008). Variability may arise when there are day-to-day changes in the amount of emissions at the workplace, for example, because of variation in the quantity of hazardous substance used or because of differences in the work methods used by operators.

Worker

It must be noted that the term "worker" in the REACH context is used differently compared with its usage in other regulatory environments (e.g. agricultural pesticide regulation in the EU).

REACH Worker relates to any kind of occupational personnel and is further specified as an "industrial user" or outside an industrial setting as a "professional user" to reflect the typical conditions of use. For example, a worker undertaking spray painting in an automotive plant is termed an "industrial user", but a construction worker spray painting a bridge is termed a "professional user" (ECHA, 2012c).

(Agricultural) Pesticides/plant protection products
Workers: Persons who, as part of their employment, enter an area or handle a crop that has been treated (re-entry; example tasks are harvesting and/or pruning/thinning of orchard fruit, grapes, vegetables or ornamentals). Note the different definition of "worker" in contrast to the use in models/tools presented elsewhere in this document.

Operators(/handlers/applicants): Persons involved in activities relating to application (mixing/loading, application, repair and maintenance).

APPENDIX 2: ADDITIONAL INFORMATION ON CHAPTER 4: SOURCES OF DERMAL EXPOSURE—DEFINITION AND DIFFERENCES IN THE REGULATION OF "COSMETICS"

In this document, dermal exposure to "cosmetics" or "personal care products" does not relate to a specific regulatory framework. The definition of a cosmetic, as well as the resulting regulations and requirements, varies between countries. Although all international regulatory circumstances aim for consumer safety, there are major differences in their approaches and classifications; these result in different regulatory requirements, such as for efficacy or safety testing. In the following, the definitions and regulatory frameworks for the EU, the USA, Canada and Japan are briefly presented.

In the EU (Directive 93/35/EEC [EEC, 1993e], modifying the Cosmetics Directive 76/768/EEC [EEC, 1976]):

> a "cosmetic product" shall mean any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition.

Antiperspirants, sunscreens, fragrances, hair preparations/dyes and oral hygiene products are some examples of these products. The Directive requires cosmetics to cause no damage to human health when applied under normal conditions, and the safety of the products is the responsibility of the manufacturer. A list of concentration-limited substances exists, as well as a list of ingredients that may be banned for safety reasons or because they were not supported by industry (Antignac et al., 2011). In general, no authorization procedure for cosmetic products is required, meaning that no pre-marketing clearance to prove the safety of the product is required (Nohynek et al., 2010). However, certain ingredients, such as UV filters, preservatives, colourants and, most recently, hair dyes, require approval of their safety prior to marketing (Nohynek et al., 2010).

In the USA, the legal difference between a cosmetic and a drug is determined by a product's intended use. Specifically, the Federal Food, Drug, and Cosmetic Act (USFDA, 2004) defines cosmetics as

> articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body [. . .] for cleansing, beautifying, promoting attractiveness, or altering the appearance.

Products included in this definition are skin moisturizers, perfumes, lipsticks, fingernail polishes, eye and facial makeup preparations, shampoos, permanent waves, hair colours, toothpastes and deodorants, as well as any material intended for use as a component of a cosmetic product. When products meet the definitions of both cosmetics and drugs, these products must comply with the requirements for both. In contrast to Europe, the USA handles another type of product category—over-the-counter drugs, including products containing UV filters (sunscreens as well as makeup products or modern skin creams), anticavity toothpastes, antiperspirants, antidandruff preparations, skin protectants and hair restorers (USFDA, 2004). Unlike the situation with cosmetics, for these products, additional clinical testing is required in order to demonstrate efficacy and safety, as well as approval by the respective medical agencies. As in Europe, the USA does not have a pre-market approval system for cosmetic products or ingredients, with the important exception of colour additives, and the manufacturer is responsible for the safety of cosmetic products.

In Canada, a cosmetic is "any substance, or mixture of substances, that is manufactured, sold or represented for use in cleansing, improving, or altering the complexion, skin, hair or teeth". Examples are makeup, perfume, skin moisturizers, nail polish and grooming aids, such as soap, shampoo, shaving cream or deodorant. Sunless tanning products are considered cosmetics, as they help moisturize the skin. The manufacturer must notify a cosmetic to Health Canada and declare its composition to the government within 10 days of first selling the cosmetic. Health Canada may also request evidence of the safety of a cosmetic product (Health Canada, 2011). In contrast, sunscreens or sunburn protectants are considered over-the-counter drugs, because the products claim to prevent sunburn by shielding the skin from the sun's UV radiation. Such products have additional regulatory requirements and must undergo pre-market review.

The Japanese have the most stringent regulatory demands for cosmetic products (Nohynek et al., 2010). The definition of a cosmetic is similar to the definition in the USA. However, in Japan, another product category exists, the "quasi-drugs", including hair dyes, skin bleaching agents, and hair growing and anti–hair loss agents (Nohynek et al., 2010). This type of product has to pass a registration process, including proven efficacy and safety, that is similar to the regulatory requirements that are applied for drugs. In general, only ingredients that are on an official list are allowed to be used. During recent years, other Asian countries, such as China and the Republic of Korea, have introduced cosmetic regulations similar to the Japanese model (Nohynek et al., 2010).

APPENDIX 3: ADDITIONAL INFORMATION ON CHAPTER 6: MODELS AND TOOLS TO ESTIMATE DERMAL EXPOSURE

A3.1 Links for downloading the presented modelling tools

Links for downloading the modelling tools presented in this report are provided in Table A3.1.

Table A3.1. Links for downloading the presented tools for modelling exposure

Tool	Link (as of May 2013)
AISE REACT Consumer Tool	http://www.aise.eu/reach/documents/AISE_Guidance_Use_reporting030609_FINAL.doc (Excel file in Word file)
ARTF	Database is not publicly available Further information: http://www.epa.gov/pesticides/science/post-app-exposure-data.html http://www.exposuretf.com/Home/ARTF/tabid/57/Default.aspx
BEAT	http://xnet.hsl.gov.uk/download/ (installation password will be provided after registration: beat@hsl.gov.uk) Further information: http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/doc/TNsG/TNsG_ON_HUMAN_EXPOSURE/WORKSHOP_HUMAN_EXPOSURE_BIOCIDES_2009/Session_BEAT.zip/view
BREAM	http://randd.defra.gov.uk/Default.aspx?Menu=Menu&Module=More&Location=None&ProjectID=14534&FromSearch=Y&Status=2&Publisher=1&SearchText=ps2005&SortString=ProjectCode&SortOrder=Asc&Paging=10
Calendex™	USEPA free testing version: http://www.epa.gov/oppfead1/cb/csb_page/updates/2012/calendex.html http://www.epa.gov/pesticides/science/calendex/CalendexWWEIAFCID.zip
CARES®	http://www.ilsi.org/ResearchFoundation/Pages/CARES.aspx
ConsExpo	http://www.rivm.nl/en/healthanddisease/productsafety/ConsExpo.jsp

Table A3.1 (continued)

Tool	Link (as of May 2013)	
Control banding	http://www.eurofins.com/product-testing-services/services/research-development/projects-on-skin-exposure-and-protection/riskofderm-skin-exposure-and-risk-assessment/download-of-riskofderm-toolkit.aspx https://stoffenmanager.nl/Default.aspx?lang=en	
DERM	Not publicly available	
DREAM	COSHH Essentials: Stoffenmanager: RISKOFDERM Toolkit: EMKG tool:	http://www.hse.gov.uk/coshh/essentials/index.htm See below http://www.eurofins.com/product-testing-services/services/research-development/projects-on-skin-exposure-and-protection/riskofderm-skin-exposure-and-risk-assessment.aspx Valid only for inhalation: http://www.reach-clp-helpdesk.de/en/Downloads/EMKG-EXPO-TOOL.xls?__blob=publicationFile&v=2
Dutch model	Not available	
EASE	No longer available or recommended	
ECETOC TRA	http://www.ecetoc.org/tra	
EUROPOEM	Not publicly available (home page, last revised 2003: http://www.enduser.co.uk/europoem/)	
German (operator) model	http://www.pesticides.gov.uk/guidance/industries/pesticides/topics/pesticide-approvals/pesticides-registration/data-requirements-handbook/toxicity-working-documents (Excel files: http://www.pesticides.gov.uk/Resources/CRD/Migrated-Resources/Documents/G/German_Model_PSD1.xls or http://www.kemi.se/Documents/Bekampningsmedel/Vaxtskyddsmedel/Vagledning/German_Model_PSD2.xls)	
LifeLine™	http://www.thelifelinegroup.org/lifeline/index.php (after registration, free CD copy will be sent)	
MEASE	http://www.ebrc.de/industrial-chemicals-reach/projects-and-references/mease.php	

Table A3.1 (continued)

Tool	Link (as of May 2013)
PHED	http://www.epa.gov/pesticides/science/handler-exposure-data.html#phed (The actual PHED computer program was developed in a database language no longer technically supported; thus, just the surrogate exposure tables and the "PHED Surrogate Exposure Guide" are available: http://www.epa.gov/pesticides/science/handler-exposure-table.pdf)
RISKOFDERM	http://www.tno.nl/downloads/RISKOFDERM%20potential%20dermal%20exposure%20model%20vs%202.1t.xls
SHEDS	http://cfpub.epa.gov/crem/knowledge_base/crem_report.cfm?deid=75824 http://www.epa.gov/heasd/products/sheds_multimedia/sheds_mm.html
SprayExpo	http://www.baua.de/en/Topics-from-A-to-Z/Hazardous-Substances/SprayExpo.html
Stoffenmanager	https://www.stoffenmanager.nl/ (login after registration)
SWIMODEL	http://www.epa.gov/oppad001/swimodel.htm
United Kingdom POEM	http://www.pesticides.gov.uk/guidance/industries/pesticides/topics/pesticide-approvals/pesticides-registration/data-requirements-handbook/toxicity-working-documents and/or http://www.pesticides.gov.uk/guidance/industries/pesticides/topics/pesticide-approvals/pesticides-registration/applicant-guide/updates/updates-to-the-uk-poem-operator-exposure-model (Excel file: http://www.pesticides.gov.uk/Resources/CRD/Migrated-Resources/Documents/U/UK_POEM_07.xls)

A3.2 Relevant determinants for modelling dermal exposure

An adequate allocation of determinants is important if exposure scenarios are to be compared, particularly to support the selection of a model (see sections 3.3 and 6.4).

Determinants are sometimes grouped in loosely defined categories that include various factors that are the true determinants affecting exposure. In other circumstances, the determinants are further distinguished and their definitions refined (see section A3.2.1). To date,

few data have been published about the correlation between determinants (see section A3.2.2). The determinants used in the models described in this report and their underlying algorithms are presented in section A3.2.3.

Various terms, abbreviations and metrics for each determinant are in use, although they often refer to the same characteristic. As well, the same term may be used even though it implies a contradictory meaning between the models and tools. Thus, in addition to the original terminology provided in section A3.2.3, an adapted (harmonized) form for the abbreviations is presented. This allows a very general but comparative analysis of what determinants each model or tool actually includes for its estimation of dermal exposure (see also sections 6.3 and A3.2.4) and what outputs were chosen to represent dermal exposure.

A3.2.1 Relevant exposure determinants according to RISKOFDERM

In relation to RISKOFDERM, Marquart et al. (2003) proposed a categorization approach, providing six major categories of relevant determinants:

1) substance and product characteristics;
2) tasks done by the worker;
3) process, technique/equipment;
4) exposure control measure;
5) worker characteristics;
6) area and situation.

Each of these is a rather loosely defined major category of determinants whose actual influence is due to several parameters that are the actual determinants (Marquart et al., 2003; see Table A3.2). As the relevant determinants of a major category may change depending on the pathway, a distinction is again made between the three main transport categories (i.e. direct contact, surface contact and deposition from air).

In addition, these determinants can be further divided into subdeterminants. Potential determinants and subdeterminants for each major category and in relation to the type of transport process are

Table A3.2. Parameters (determinants) concluded to be relevant for exposure modelling[a]

Major category	Potential determinant (parameter)	Potential subdeterminants	Relevant transport process/pathway		
			Direct contact	Surface contact	Deposition from air
Substance and product characteristics	General product features	Composition, percentage of substance in product, density, visibility, corrosiveness, toxicological characteristics	x	x	x
	Physical state: liquid, solid, gas/vapour	Melting point, boiling point; in addition: *Liquids*: viscosity, volatility, stickiness, surface tension *Particles*: particle size distribution, moistness, dustiness, shape, friability, cohesion/coagulation	x	x	x
Tasks done by the worker	Identified tasks		x		x
	Amount of substance handled	Volume of product, concentration of substance, application rate (amount handled per unit of time)	x		x
	Intensity of contact	Frequency, duration and force of contact	x	x	
	Treated area or objects	Level of contamination, area dimension, type/form of treated material, number of objects treated		x	
Process, technique/equipment	Identified type of process/equipment		x		x
	Process/equipment	Pressure, orientation of application, manual vs automatic			x

Table A3.2 (continued)

Major category	Potential determinant (parameter)	Potential subdeterminants	Relevant transport process/pathway		
			Direct contact	Surface contact	Deposition from air
Exposure control measure	Gloves	Use, material	x	x	
	Clothing	Use, surface area covered, material	x	x	x
	Organization of work	Interval between event and contact		x	
	Segregation				x
	Ventilation				x
Worker characteristics	Accuracy of working	Training/experience	x	x	x
	Personal manner of work	Place (proximity) relative to source			x
	Skin characteristics	Moistness	x	x	
	Skin characteristics	Roughness, electrical chargeability			x
	Personal care	(Frequency of) handwashing	x	x	x
Area and situation	Weather conditions	Temperature, wind speed, crop height, indoors vs outdoors, humidity/rainfall			x
	Type of surface: roughness			x	

[a] From Marquart et al. (2003).

provided in Table A3.2. Each of these categories is dependent on various underlying factors that are the actual determinants. Hence, the category "task done by the worker" is a rather loosely defined major category of determinants whose actual influence is due to several parameters (Marquart et al., 2003). One example of a potential determinant that is determined by this major category is the "amount of substance handled". Further, this potential determinant may be influenced by other underlying parameters, such as the "concentration of substance" (so-called subdeterminant). In conclusion, considering the overall influence of this subdeterminant, it does not exert an influence solely on its own major category ("substance/product characteristics"), but may also determine other major categories that might not obviously be associated at first glance (in this example: "task done by the worker").

A3.2.2 Correlation between determinants

As dermal exposure is a complex process, information about correlations between parameters is rare. Investigations on the influence of physicochemical properties on dermal exposure led to the conclusion that (potential) correlations between viscosity and dustiness and dermal exposure depend on the pathway (Gorman Ng et al., 2012a, 2013):

- Correlation between dermal exposure and viscosity depends on the pathway:
  - Immersion: significant correlation ($P < 0.001$)
  - Deposition: correlation trend, but not significant ($P = 0.19$)
  - Surface contact: no correlation
  - Brushing fluids: inverse correlation (Roff, 1997)
- Correlation between dermal exposure and dustiness depends on the pathway:
  - Surface contact: significant correlation ($P = 0.016$)
  - Immersion: no correlation ($P = 0.403$)
  - Deposition: statistical analysis was not feasible.

A3.2.3 Underlying algorithms and determinants of models/tools

In the following, the underlying algorithms of the models and tools presented in chapter 6 are provided. For some cases, only general simplifications could be provided that do not present all possible

models implemented in a tool or all options of an exposure scenario. Sometimes, instead of the algorithm, only the exposure determinants (indicative values, modifier, influencing factors or parameters) could be interpreted from the tool itself and are provided in a very general manner. The dermal exposure output is given as either "mass" or "loading"; thus, steps or outputs, including dermal absorption, are not presented (see following tables).

The abbreviations are different for the same parameter in different tools. In order to compare the tools, the abbreviations have been harmonized. The following two tables provide a general summary of the harmonized abbreviations. The harmonized abbreviations are also used in Table 33, where the tools are compared. The list of harmonized abbreviations (Table A3.3) can be used to easily check which exposure determinants are used by which model.

Abbreviation	Unit	Definition
c	$mg \cdot ml^{-1}$	Mass concentration, i.e. mass of a constituent (substance of interest) divided by the volume of the mixture (product/formulation)
D	See next table	Output for dermal exposure
M	kg	Mass
L	$mg \cdot cm^{-2}$	Loading, i.e. mass per unit area that can relate to, e.g. • the dermal exposure mass (M) divided by the dermal exposure surface area (A_{skin}) • surface loading, i.e. mass of substance on surface available for transfer to skin
R	d^{-1}	Rates (per unit of time) (in addition, often representing mass (M) or volume (V) per unit of time, e.g. $mg \cdot d^{-1}$)
F	—	General and predominantly unitless factors (modifiers)
TC	$cm^2 \cdot h^{-1}$	Transfer coefficients, i.e. a measure of the intensity of contact for a specific task (area of contact per unit of time)

The different presentations for the outputs of dermal exposure can be identified by the following scheme:

Abbreviation	Unit	Definition
D-score	—	Unitless numerical estimate/score
DM	mg	Dermal exposure mass
$DM_{per\ mass\ handled}$	$mg \cdot kg^{-1}$	Dermal exposure mass related to handling 1 kg
DMR	$mg \cdot d^{-1}$	Dermal exposure mass rate
$DMR_{per\ mass\ handled}$	$mg \cdot kg^{-1} \cdot d^{-1}$	Dermal exposure mass rate per kilogram used/ handled
DL	$mg \cdot cm^{-2}$	Dermal exposure loading
DLR	$mg \cdot cm^{-2} \cdot d^{-1}$	Dermal exposure loading rate
DV	ml	Dermal exposure (contact) volume
DVR	$ml \cdot h^{-1}$	Dermal exposure (contact) volume rate

These harmonized presentations of output for dermal exposure focus on the units provided and thus cannot always adequately present all included assumptions. For example, some outputs include a specific exposed skin area in the calculation or refer, for example, just to the hands, but do not indicate this information along with the output or present it adequately in the terminology or units. In addition, although a term for the frequency of dermal exposure is often included (e.g. use rates, contact levels or the quantity of applications), this information is seldom presented transparently in the output.

A3.2.3.1 DREAM

Dermal exposure is provided as a numerical estimate (DREAM score) by weighting the actual exposure estimates for a specific exposure area (body part) for all three transport mechanisms relating to the task, application frequency, probability of transfer and time-related factors. A general form to present the influencing parameters is represented by:

$$Skin_w\text{-}A_{job} = f\left(\left[\sum_{TASK=1-N}(E_{BP},\ D_{BP},\ T_{BP},\ BS_{BP},\ O_{BP})\right],\ RTD,\ WH,\ EH,\ CE\right)$$

with, for each transport mechanism (E_{BP}, D_{BP}, T_{BP}) and body part ("$_{BP}$"):

$$E_{BP}/D_{BP}/T_{BP} = f(P_{E.BP}, P_{D.BP}, P_{T.BP}, I_{E.BP}, I_{D.BP}, I_{T.BP}, ER, E_I, C)$$

where:

Original abbreviation	Definition	Harmonized abbreviation
$Skin_w$-A_{job}	"Total weighted actual dermal exposure estimated at job level" (final score given in a DREAM unit, providing ranking of exposure in following DREAM categories: 0 = no exposure; 0–10 = very low exposure; 10–30 = low exposure; 30–100 = moderate exposure; 100–300 = high exposure; 300–1000 = very high exposure; > 1000 = extremely high exposure)	D-score
BP (index)	Nine different body parts "i" are considered: head, upper or lower arms, hands, torso front or back, lower body part, lower legs, feet	i (index)
E_{BP} D_{BP} T_{BP}	Transport mechanism (exposure route) to the skin per body part "i" with relevant index "x" corresponding to: $_{x=E}$: "emission": mass transport by direct release from a source $_{x=D}$: "deposition": mass transport from air that subsequently deposits $_{x=T}$: "transfer": mass transport from contaminated surfaces	$T_{x\ i}$
BS_{BP}	Body surface factor: exposed surface area of an individual body part "i" divided by the mean surface area of the nine body parts	$A_{skin\ mean\ i}$
O_{BP}	Clothing protection factor per body part "i" depending on the kind of material, replacement frequency of clothing (hands and the use of gloves are treated differently)	$F_{cloth\ pen\ i}$
RTD	"Relative task duration estimate": ratio of "task frequency" multipled by "task duration" to the total working time	F_t

(continued)

Original abbreviation	Definition	Harmonized abbreviation
WH EH CE	Adjustment factors for reduction of dermal exposure, in tool depending on the three estimates: – "workers' hygiene": handwash frequency/ efficiency (WH) – "hygiene": cleaning frequency/efficiency of floor, worktables, machines and working tools (EH) – "continued exposure": circumstances of working clothes (CE)	$F_{s\ red}$
$P_{E.BP}$, $P_{D.BP}$, $P_{T.BP}$	"Probability" (frequency) of transfer for body part "i" and exposure route "x": – for exposure route "emission" ($P_{E.BP}$) and "deposition" ($P_{D.BP}$): frequency of occurrence of the concerned exposure route – for exposure route "transfer" ($P_{T.BP}$): contact frequency with surfaces such as floor, worktables, machines and working tools (provided categories: unlikely, e.g. with $<$ 1% of task duration; occasionally; repeatedly; and almost constantly)	n_{appl}
$I_{E.BP}$, $I_{D.BP}$, $I_{T.BP}$	Dermal exposure score: "Intensity": amount (mass) of substance of interest in relation to transport mechanism (exposure route) "x" for body part "i": – for exposure route "emission" and "deposition": mass (amount) of substance of interest on clothing and uncovered skin – for exposure route "transfer": contamination level of the contact	DM-score$_{s\ DREAM\ x\ i}$
ER	"Exposure route factor": weighting the different transport mechanisms (exposure routes) to the skin "x" (more weight assigned to exposure route "emission" than the others due to direct release from a source)	F_R
E_I	"Intrinsic emission": physical and chemical characteristics of the substance, concentration of active substance, etc. (e.g. for liquids, including the physical state, boiling point and viscosity)	$F_{s\ char}$
C	Mass fraction provided as concentration of substance of interest in product/formulation (provided categories: $<$1%, 1–90%, $>$90% substance of interest; in tool, this parameter is included in $F_{s\ char}$)	m_f

A3.2.3.2 DERM

Dermal exposure is provided as a numerical estimate (DERM score) by multiplying the score for the clothing protection factor (C) by the sum of the score of transport process (T_i) multiplied by body surface area (A) (Blanco et al., 2008), along with an example, and presented as:

$$DERM = C \cdot \sum(T_i \cdot A)$$

where:

Original abbreviation	Definition	Unit	Harmonized abbreviation
DERM	Numerical estimate (DERM score) for the dermal exposure level	—	D-score
C	Clothing penetration/protection factor: for exposure reduction due to protective effect of clothing (yes/no option with default exposure reduction per determinant as listed above)	—	$F_{cloth\ pen}$
T_i	Numerical score for each determinant (option) for transport (mechanism) to the skin (score of 1–5 for each of the following options: transfer from previously contaminated surfaces, deposition, emission)	—	T_i
A	Numerical score for each determinant (option) in relation to the exposed surface area (area of body surface) (score of 1–5 for each of the following options: 0–20%, 21–40%, 41–60%, 61–80%, 81–100%)	—	A_i

A3.2.3.3 EASE

Dermal exposure is provided as dermal exposure (loading rate) to the substance of interest on the hands and forearms per day, including the frequency of application (contact level). In addition to the evaluation scheme of EASE (see section A3.3), a general algorithm is presented in order to demonstrate the influencing factors for the dermal exposure assessment:

$$DLR_s = f(F_{s\ char}, F_{use\ pat}, F_{cont\ pat}, n_{appl})$$

where:

Original abbreviation	Definition	Unit	Harmonized abbreviation
Dermal exposure	Dermal exposure (loading rate) to substance of interest per day (relating to hands and forearms) (provided in ranges: "very low", 0–0.1, 0.1–1, 1–5 and 5–15 $mg \cdot cm^{-2} \cdot d^{-1}$)	$mg \cdot cm^{-2} \cdot d^{-1}$	DLR_s
Physical state	Choice of physical state of substance of interest (provided options: solid, liquid, gas/vapour)	—	$F_{s\ char}$
Pattern of use	Choice of the pattern of use (provided options: closed system, incorporation onto matrix or non-dispersion, wide dispersion)	—	$F_{use\ pat}$
Pattern of control	Choice of the exposure control pattern (provided options: direct or non-direct handling)	—	$F_{cont\ pat}$
Contact level	Choice of the contact level (provided options: none, incidental, intermittent, extensive)	—	n_{appl}

A3.2.3.4 MEASE

Dermal exposure is provided as dermal exposure (mass rate) to a substance for a specific exposure area per day. The initial exposure estimate (DLR) and the PROC-dependent exposed skin area result in dermal exposure mass per day. The dermal exposure can be further modified by factors for operational conditions, pattern of use, contact level, control measures, duration modifiers and concentration modifiers.

As the algorithms of the tool are not publicly available, a general form, in order to present the influencing factors for calculating dermal exposure in MEASE, can be given as:

$$\text{total dermal loading} = \text{dermal exposure estimate} \cdot A_{skin}$$

$$\text{dermal exposure estimate} = f(F_{s\ char},\ F_{use\ pat},\ F_{cont\ pat},\ n_{appl},\ m_f,\ t_{exp},\ F_{cloth\ pen})$$

where:

Original abbreviation	Definition	Unit	Harmonized abbreviation
Total dermal loading	Dermal exposure (mass rate) to substance of interest per day for a specific surface area	$mg \cdot d^{-1}$	DMR_s
Dermal exposure estimate	Dermal exposure (loading rate) to substance of interest per application (n_{appl}) (default estimate provided by tool, e.g. based on EASE) and further adjusted/ determined by choice of substance characteristics, operational conditions and risk management measures	$mg \cdot cm^{-2} \cdot d^{-1}$	$DLR_{s\ default}$
Exposed skin area	Exposed skin area (defaults provided by tool dependent on chosen PROC)	cm^2	A_{skin}
Physical form	Adjustment factor to account for the physicochemical specific, i.e. physical, form (options: massive, solid with different ranges for dustiness, aqueous solution, liquid, gaseous)	—	$F_{s\ char}$
Pattern of use	Adjustment factor to account for the pattern of use (options: “wide dispersive use”, “non-dispersive use”, “inclusion in matrix”, “closed system without breaches”)	—	$F_{use\ pat}$
Pattern of exposure control	Adjustment factor to account for the exposure control pattern (options: “direct handling” or “non-direct handling”)	—	$F_{cont\ pat}$
Contact level	Frequency of applications (tasks/events) per day (options: “none”; “incidental”, i.e. one event per day including splashes/ spills; “intermittent”, i.e. 2–10 events per day; “extensive”, i.e. >10 events per day due to work where hands are part of process, e.g. transfer of wet objects)	—	n_{appl}

(continued)

Original abbreviation	Definition	Unit	Harmonized abbreviation
Content in preparation	Mass fraction of the substance of interest in the product (formulation) (tool provides ranges to choose from: >1%, 1–5%, 5–25%, >25%)	—	m_f
Duration of exposure	Exposure duration/contact with material (options: <15 min, 15–60 min, 60–240 min, >240 min)	min	t_{exp}
Risk management measures	Clothing penetration/protection factor: adjustment factor to account for use of gloves (default estimate provided by tool, fraction of exposure dependent on options: – no gloves: 100% – properly selected gloves: 10%)	— (see column to left)	$F_{cloth\ pen}$

A3.2.3.5 ECETOC TRA: Occupational (workers)

Dermal exposure is provided as actual dermal exposure (mass rate) to the substance of interest per day for a specified exposed area of skin. The initial exposure estimate depends on the application (the PROC number), the physical state and the type of setting. This initial estimate can be further modified by factors for substance concentration, duration and use of gloves. The duration modifiers are applied only to high- and moderate-volatility liquids and non-dusty solid substances. The algorithm for dermal exposure (excluding dermal absorption) is presented in a general form:

$$DMR_s = f(DLR_{s\ default}, A_{skin}, m_f, t_{exp}, F_{LEV}, F_{cloth\ pen})$$

where:

Original abbreviation	Definition	Unit/default	Harmonized abbreviation
Dermal exposure	Dermal exposure (mass rate) to substance of interest per day	$mg \cdot d^{-1}$	DMR_s
EASE value (initial dermal exposure estimate)	Initial dermal exposure (loading rate) (depends on chosen PROC)	$mg \cdot cm^{-2} \cdot d^{-1}$	$DLR_{s\ default}$
Exposed skin surface	Surface area of exposed skin (depends on chosen PROC)	cm^2	A_{skin}
PROC	Descriptor of use: process, application	—	$F_{use\ pat}$
Concentration modifiers	Mass fraction of the substance in the product: >1%, 1–5%, 5–25%, >25%	—	m_f
Duration modifiers	Exposure duration: <15 min, 15–60 min, 60–240 min, >240 min (depends on $F_{s\ char}$)	—	t_{exp}
Substance	Physical state (solid/liquid) implanted in initial exposure estimate	—	$F_{s\ char}$
Dermal PPE/gloves	Gloves: efficacy depends on worker's training conditions	%	$F_{cloth\ pen}$
LEV	Depends on operational conditions and PROC	%	F_{LEV}
Operational condition	Industrial/professional	—	$F_{op\ cond}$

A3.2.3.6 ECETOC TRA: Consumer

Dermal exposure is provided as dermal exposure (mass rate) to the substance of interest for a specific exposure area per day, including the frequency of applications (potential is equivalent to actual exposure, as risk management measures are not considered for consumers). The algorithm is presented without inclusion of the dermal absorption:

$$\text{Dermal exposure} = PI \cdot CA \cdot FQ \cdot TL \cdot D$$

where:

Original abbreviation	Definition	Unit default	Harmonized abbreviation
Dermal exposure	Dermal exposure (mass rate) to substance of interest for a specific exposure area per day	$g \cdot d^{-1}$	DMR_s
PI: Product ingredient fraction	Mass fraction of substance of interest in the product (formulation) or article ($mg \cdot mg^{-1}$)	— ($mg \cdot mg^{-1}$) (defaults provided)	m_f
CA: Contact area	Surface (contact) area of exposed skin (depends on chosen PC)	cm^2	A_{skin}
FQ	Frequency of applications (tasks/events) per day (depends on chosen PC)	d^{-1}	n_{appl}
TL	Thickness of layer of liquid (product) in contact with skin	cm (default: 0.01[1])	TH
D	Density of the product liquid	$g \cdot cm^{-3}$ (default: 1)	ρ_{prod}

A3.2.3.7 RISKOFDERM

Dermal exposure is provided as a numerical estimate based on measured data that were used to derive linear mixed effect models for six different tasks: the DEO units (Marquart et al., 2006; Warren et al., 2006). As an example, a general form derived from the Excel sheet for DEO 1 (mixing, filling, loading) is presented here to illustrate the influencing factors (for other DEOs, see Table A3.7 in section A3.5):

$$DMR = f(F_{s\ char}, F_{op\ cond}, F_{emission}, F_{LEV}, F_{cont\ pat}, MR_{s\ appl}, n_{contact}, F_{fraction}, t_{exp})$$

where:

[1] For REACH, the defaults are as follows (ECHA, 2012a):

the assumed thickness of layer in contact with skin is reduced from 0.01 cm (widely accepted default for preparations and used already in EU existing chemicals risk assessment procedures) to 0.001 cm for most products in order to take account of the reduced mobility of substances in an article matrix. Unless products have prolonged contact with the skin, then a layer of 0.001 cm is considered. The figure 0.001 cm was chosen based on expert judgement, as no scientific data was available.

Original abbreviation	Definition	Unit	Harmonized abbreviation
DE	Exposure loading per shift (related to hands and/or body)	µl or mg (e.g. mg·(8 h·hands)$^{-1}$)	DMR (DLR)
Type of product	Physical state: Liquid / Low or moderately dusty solid / Highly dusty solid	—	$F_{s\ char}$
Automation	Automation: Manual process / Automated or semiautomated processes	—	$F_{op\ cond}$
Aerosol	Significant amounts of aerosols or splashes: yes/no	—	$F_{emission}$
Ventilation	Quality of ventilation: Poor ventilation / Normal or good ventilation	—	F_{LEV}
Kind of (skin) contact	Intensity of skin contact: Rare contact / More than rare contact	—	$F_{cont\ pat}$
Use rate	Use rate	kg·min^{-1}	$MR_{s\ appl}$
Frequency of (skin) contact	Frequency of skin contact: Light contact / More than light contact	—	$n_{contact}$
Percentile for exposure rate distribution	Exposure rate distribution	—	$F_{fraction}$
Cumulative duration of the scenario in the shift	Exposure duration	min	t_{exp}

A3.2.3.8 BEAT

Dermal exposure is provided as actual dermal exposure (mass rate) of the hands and potential exposure of the body (in mg·min^{-1}) for both a specific defined area of the skin and a specific application rate presented in the database.

Although the algorithms for searching the database for analogous exposure data were noted as being transparently described in the

helpfiles of the tool, they are not displayed in the current version. For the influencing parameters considered in BEAT, see Table A3.7 in section A3.5.

Background information about the implemented hierarchical Bayesian model to integrate the various analogous data sets into a single exposure distribution as well as the subsequent selection of the most appropriate distribution in relation to the indicative distribution approach of Phillips & Garrod (2001) (see section A3.6) is not published.

A3.2.3.9 ConsExpo

Dermal exposure is provided as the actual dermal mass (amount) of the substance of interest for a specific exposed area (i.e. loading) per application (assuming one application per day) for five different exposure scenarios. The application frequency is not further included in the calculation, and potential exposure is equivalent to actual exposure, as risk management measures are not considered (Delmaar et al., 2005)[1]. Algorithms for the five exposure scenarios are as follows:

(1) Instant application:

$$L_{derm} = \frac{A_{prod} \cdot wf}{S_{exp}}$$

(2) Constant rate:

$$L_{derm} = \frac{R \cdot T \cdot wf}{S_{exp}}$$

(3) Rubbing off:

$$L_{derm} = \frac{S_{area} \cdot F_{dislodge} \cdot wf}{S_{exp}}$$

(4) Migration[2]:

$$L_{derm} = \frac{A_{prod} \cdot F_{leach} \cdot S_{contact}}{S_{exp}}$$

(5) Diffusion:

$$\frac{\partial C(x,t)}{\partial t} = L_{derm} \frac{\partial^2}{\partial x^2} C(x,t)$$

where:

[1] For the diffusion scenario (5), see further information—e.g. about the boundary options for integration—in Delmaar et al. (2005).

[2] In ConsExpo, the definition of "migration" differs from that used in this document, which differentiates between "transfer" (= transfer to skin) and "migration" (= possible amount on surface that is available for transfer, for example, due to leaching out of product); see section 5.2.1.

Original abbreviation	Definition	Unit	Harmonized abbreviation
L_{derm} (dermal load)	Dermal exposure loading of substance of interest for specified exposed area of skin per application (event) (n_{appl}, although frequency not included in calculation, thus one application assumed per day)	$mg \cdot cm^{-2}$	DL_s
A_{prod}	Amount (mass) of product (formulation) directly applied to or in contact with skin	mg	$M_{prod\ skin}$
wf	Mass fraction of the substance of interest in the product (formulation) (e.g. 10% w/w = 0.10)	—	m_f
S_{exp}	Surface area of exposed skin	cm^2	A_{skin}
R	Use rate (application rate) of product applied directly to the skin	$mg \cdot s^{-1}$	$MR_{prod\ appl\ skin}$
T	Exposure duration: loading time or release / application duration	s	t_{exp}
S_{area}	Total area rubbed during exposure, determined by the area rubbed per unit of time and limited by the total treated surface area	m^2	$A_{skin\ rub}$
$F_{dislodge}$	Transferable/dislodgeable residue: amount (mass) of product that can be rubbed off per unit of surface area	$mg \cdot cm^{-2}$	$L_{s\ trans}$
F_{leach}	Transfer factor to account for the fraction of substance of interest that is leachable from the product (formulation) to be transferred (“migrate” according to ConsExpo) to the skin per unit amount of product (in decimal form as fraction: 10% w/w = 0.10)	—	$F_{trans\ fraction\ s}$
$S_{contact}$	Skin contact factor to account for the fact that the product is only partially in contact with the skin (in decimal form as fraction of product that is in direct contact with bare skin: 10% w/w = 0.10)	—	$F_{trans\ fraction\ p}$
C(x,t)	Mass concentration of substance of interest in the product (formulation) at depth “x” and time “t”	$mg \cdot cm^{-3}$	$c_s(x,t)$

A3.2.3.10 SprayExpo

Dermal exposure is provided as total mass of sprayed aerosol deposited on the body (for a specified exposed area of skin) per application (spraying event) at the time point "t" by (Koch, 2004; potential exposure is equivalent to actual exposure, as risk management measures are not considered):

$$D_{derm} = \int_0^{t_R} dt\, R(t)$$

with:

$$R(t) = C(\upsilon_{set} \cdot A_{hori} + \upsilon_{dep} \cdot A_{vert})$$

where:

Original abbreviation	Definition	Unit/default	Harmonized abbreviation
D_{derm} (dermal dose)	Dermal exposure (mass), i.e. total deposition after exposure duration	mg	DM_s
	Average deposition rate during application	$mg \cdot s^{-1}$	DMR_s
R(t)	Deposition rate at time point "t"	$mg \cdot s^{-1}$	$MR_{s\ dep}$
t_R	Release time (exposure duration)	s	t_{exp}
C	Total concentration "c" of aerosols at time point "t" calculated in SprayExpo (for details, see program: Koch, 2004)	$mg \cdot cm^{-3}$	c_{air}
υ_{set}	Settling velocity: velocity of sedimentation of sprayed aerosols (for details, see program: Koch, 2004; see also Hinds, 1999)	$cm \cdot s^{-1}$	υ_{set}
A_{hori}	Horizontal body area that is available for deposition (assumed 10% of total body surface area of 1.96 m^2 according to the USEPA [1997c] exposure factors handbook)	m^2	$A_{skin\ hori}$

(continued)

Original abbreviation	Definition	Unit/default	Harmonized abbreviation
υ_{dep}	Deposition velocity: velocity of the deposition on the other parts of the body surface by turbulent diffusion	0.01 $cm \cdot s^{-1}$	υ_{dep}
A_{vert}	Vertical body area that is available for deposition (assumed 90% of total body surface area of 1.96 m^2 according to the USEPA [1997c] exposure factors handbook)	m^2	$A_{skin\ vert}$

A3.2.3.11 The German BBA model

Dermal exposure is provided as dermal exposure (mass rate) to substance of interest per mass of handled substance per person per day, including application frequency. The basic algorithm is presented as (EFSA, 2008):

$$D = D^* \cdot R \cdot A$$

where:

Original abbreviation	Definition	Unit	Harmonized abbreviation
D	Dermal exposure (mass rate) to substance of interest per kilogram of substance of interest used or handled per person and per application for a specific duration	$mg \cdot kg^{-1} \cdot d^{-1}$	$DMR_{s\ per\ mass\ handled}$
D*	Dermal exposure (mass) related to handling 1 kg of substance of interest, experimentally determined	$mg \cdot kg^{-1}$	$DM_{s\ per\ mass\ handled\ EXP}$
R	The use rate (application rate) of active substance	$kg \cdot ha^{-1}$	$L_{s\ appl}$
A	Area treated per day	ha	A_{appl}

A3.2.3.12 The Dutch model

No algorithm has been published, nor are the influencing parameters for dermal exposure assessment using the Dutch model described (EFSA, 2008).

A3.2.3.13 PHED

Dermal exposure is provided as dermal exposure mass per mass handled (in $\mu g \cdot (\text{pound active substance})^{-1}$ and called "unit exposure"). The actual PHED computer program was developed in a database language that is no longer technically supported, and no published algorithm is available. Today, the principles of PHED are included in the USEPA reference document known as the "PHED Surrogate Exposure Guide" (USEPA, 2013b).

A3.2.3.14 United Kingdom POEM

Dermal exposure is provided as dermal exposure (mass rate) to substance of interest per day for the hands in the mixing and loading step, including application frequency, and for the specific exposure area of hands, legs and the trunk for the application step, assuming one spraying application. The algorithms of the tool are not publicly available, but a general form can be derived from the spreadsheet in order to present the influencing determinants when calculating dermal exposure (HSE, 2007).

In relation to defaults used in United Kingdom POEM, please see Tables 54, 55 and A3.11 (in section A3.8).

Here, as examples, liquids in the "mixing and loading" and "spraying (application)" steps are presented:

Mixing and loading

$$DMR_{s\ M\&L\ hands} = f\left(c_{s\ in\ product}, f\left(n_{appl}, DV_{prod\ M\&L}, DVR_{prod\ M\&L\ hands}, F_{cloth\ pen}\right)\right)$$

where:

Original abbreviation	Definition	Unit	Harmonized abbreviation
Dermal exposure to a.s.	Dermal exposure (mass rate) to substance of interest in product (spray formulation) on the hands per day during mixing and loading	$mg \cdot d^{-1}$	$DMR_{s\ M\&L\ hands}$
a.s. concentration	Concentration of substance of interest in product (concentrate)	$mg \cdot ml^{-1}$	$c_{s\ in\ product}$
Number of operations	Number of applications (operations) per day (default provided by tool, determined by chosen application method, volume and neck aperture width of container, application volume and dose, i.e. the final diluted formulation that is to be prepared in litres per hectare)	d^{-1}	n_{appl}
Hand contamination per operation	Dermal contact volume of product (formulation) per application (operation) during mixing and loading (default provided by tool, determined by chosen application method, volume and neck aperture width of container)	ml	$DV_{prod\ M\&L}$
Dermal exposure to formulation	Dermal exposure (volume rate) to product on hands (hand contamination) per day during mixing and loading (default provided by tool, determined by chosen application method, volume and neck aperture width of container and whether gloves are used)	$ml \cdot d^{-1}$	$DVR_{prod\ M\&L\ hands}$
Transmission to skin	Clothing penetration/protection factor to account for transmission to skin during mixing and loading if gloves are used (default provided by tool, dependent on whether gloves are chosen for protection)	— (gloves: 5%, otherwise 100%; see also section 8.6)	$F_{cloth\ pen}$

a.s., active substance

Spraying (application)

$$DMR_{s\ appl} = f(c_{s\ in\ dilution}, f(t_{exp}, f(F_{trans\ fraction\ p}, F_{cloth\ pen\ i}, f(F_{op\ equip}))))$$

or expressed as:

dermal exposure to a.s. =
f (total dermal exposure to spray, a.s. concentration)

with:

total dermal exposure to spray =
f (dermal exposure of trunk/hands/legs, duration of exposure)

dermal exposure of trunk/hands/legs =
f (volume of surface contamination, distribution on body part, penetration through clothing)

volume of surface contamination = f (application method)

where:

Original abbreviation	Definition	Unit/default	Harmonized abbreviation
Dermal exposure to a.s.	Dermal exposure (mass rate) to substance of interest during spray application per day (one application per day; relating to sum of exposure of hands, trunk and legs)	$mg \cdot d^{-1}$	$DMR_{s\ appl}$
a.s. concentration	Concentration of substance of interest in diluted spray formulation during application	$mg \cdot ml^{-1}$	$c_{s\ in\ dilution}$
Duration of exposure (spraying)	Duration of exposure (spraying) (one application for whole exposure per day assumed)	h	t_{exp}

(continued)

Original abbreviation	Definition	Unit/default	Harmonized abbreviation
Distribution (on body part)	Transfer/contact factor (distribution) for the product (spray formulation) for spray application per body part ("i": hands, trunk or legs) (default provided by tool as percentage/fraction, determined by chosen application/spraying method)	—	$F_{trans\ fraction\ p}$
Penetration through clothing	Clothing penetration/protection factor during spray application, dependent on protective equipment chosen, penetration per body part ("i"): hands: gloves 10%, otherwise 100% trunk: 2% legs: 25%	— (defaults, see column to left)	$F_{cloth\ pen\ i}$
Application method	Application (operation) method/ equipment used for spray application (defaults provided: different hand-held or tractor-mounted sprayers)	—	$F_{op\ equip}$
Total dermal exposure to spray	Sum of dermal exposure (volume rates) of body parts ("i": hands, trunk and legs) to product (spray formulation) during spray application (one application per day)	$ml \cdot h^{-1}$	$DVR_{prod\ appl\ tot}$
Dermal exposure of trunk/hands/ legs	Dermal exposure (volume rates) to product (spray formulation) per body part ("i": hands, trunk and legs) (one application per day)	$ml \cdot h^{-1}$	$DVR_{prod\ appl\ i}$
Volume of surface contamination	Volume of dermal exposure (surface contamination) to the product (spray formulation) during spray application per hour (one application per day; default provided by tool, determined by chosen application/spraying method)	$ml \cdot h^{-1}$ (default: 2–400)	$DVR_{prod\ appl}$

a.s., active substance

A3.2.3.15 Pesticides: Post-application and bystanders (EUROPOEM II)

In EUROPOEM II, the application rate was directly related to DFR, resulting in a change of the unit. Moreover, the term "transfer factor" (TF) was replaced by the parameter "transfer coefficient" (TC), expressed as the area of contact per unit of time for a specific task ($cm^2 \cdot h^{-1}$), in order to exclude the causality that TF erroneously implied. This resulted in (EFSA, 2008; BROWSE, 2011b):

$$PDE = DFR \cdot TC \cdot t \,(\cdot P)$$

where:

Original abbreviation	Definition	Unit/defaults	Harmonized abbreviation
PDE	Potential dermal exposure (mass rate) to substance of interest per day (if "P" is included: Actual dermal exposure (mass rate))	$\mu g \cdot d^{-1}$	DMR_s
DFR	Dislodgeable foliar residue	$\mu g \cdot cm^{-2}$ (worst-case default: 1 or 3 $\mu g \cdot cm^{-2} \cdot (kg\ a.i.)^{-1} \cdot ha^{-1}$ multiplied by the application rate in $(kg\ a.i.) \cdot ha^{-1}$)	$L_{s\ trans}$
TC	Transfer coefficient	$cm^2 \cdot h^{-1}$ (vegetables: 2500 $cm^2 \cdot ha^{-1}$; berries: 3000 $cm^2 \cdot ha^{-1}$; tree fruit: 4500 $cm^2 \cdot ha^{-1}$; ornamentals: 5000 $cm^2 \cdot ha^{-1}$) (according to EUROPOEM II; worst-case default: 30 000 $cm^2 \cdot ha^{-1}$)	TC_s

(continued)

Original abbreviation	Definition	Unit/defaults	Harmonized abbreviation
t	Duration of work (application/task)	$h \cdot d^{-1}$ (harvesting: $8\ h \cdot d^{-1}$, inspection tasks: $2\ h \cdot d^{-1}$)	$t_{exp\ day}$
P	Clothing penetration/ protection factor to account for penetration through protective clothing and gloves	—	$F_{cloth\ pen\ i}$

a.i., active ingredient

A3.2.3.16 Calendex™

The computer codes are intended for use only by the USEPA Scientific Advisory Panel in reviewing the Calendex model, and no algorithm has been published (Petersen et al., 2000).

A3.2.3.17 CARES

Dermal exposure is provided as dermal exposure (mass rate) to substance of interest for a specific exposure area considering one application per day. Some algorithms are presented in a condensed form (i.e. no differentiation between adults and children / between hand and whole-body exposure / between transferable residue in calculation for "area treated" or "amount of formulation used" mode), and no details about the correction factors are presented. In addition, the division by body weight is excluded, as it would provide the dermal dose (ILSI, 2008):

Unit Exposure, Area Treated or Amount/Mass of Product/ Formulation:

$$\text{Exposure} = \frac{\text{Unit Exposure}_{\text{Dermal}} \cdot \text{Application}_{\text{Area treated}} \cdot \text{Area Treated}}{\text{Reference Duration}}$$

or

$$\text{Exposure} = \frac{\text{Unit Exposure}_{\text{Dermal}} \cdot \text{Application}_{\text{Amt Form Used}} \cdot \text{Amount of Form Used}}{\text{Reference Duration}}$$

Transfer Coefficient:

$$\text{Exposure} = \text{Trans Residue} \cdot \text{Transfer Coefficient} \cdot \text{Exposure Duration}$$

Transfer Factor:

$$\text{Exposure} = \frac{\sum\{\text{Trans Factor} \cdot \text{Surf Area} \cdot \text{Cloth Pen Factor}\} \cdot \text{Trans Residue}}{\text{Reference Duration}}$$

Fraction Transferred:

$$\text{Exposure} = \frac{\text{Trans Residue} \cdot \text{Fraction Transferred}_{\text{Whole body/hands}}}{\text{Reference Duration}}$$

Flux Rate:

$$\text{Exposure} = \frac{\text{Flux Rate Al} \cdot \text{Surface Area}_{\text{contact}} \cdot \text{Exposure Duration} \cdot \text{CF}}{\text{Reference Duration}}$$

Water Concentration:

$$\text{Exposure} = \frac{\text{Conc Al Water} \cdot \text{Surface Area} \cdot \text{Exposure Duration} \cdot \text{CF}}{\text{Reference Duration}}$$

Film Thickness:

$$\text{Exposure} = \frac{\text{Density Formulation} \cdot \text{Fraction Al Formulation} \cdot \text{Film Thick} \cdot \text{Surf Area}_{\text{exposed}}}{\text{Reference Duration}}$$

where:

Original abbreviation	Definition	Unit	Abbreviation
Exposure	Dermal exposure (mass) to substance of interest considering one application per day	$mg \cdot d^{-1}$	DMR_s
Unit $Exposure_{dermal}$	Dermal exposure (mass) to substance of interest in relation to amount of handled substance during application (default taken from PHED)	$mg \cdot kg^{-1}$	$DM_{s\ per\ mass\ handled}$
$Application_{Area\ treated}$	Amount (mass) of substance of interest used per unit of area treated	$mg \cdot m^{-2}$	$L_{s\ appl}$
Area Treated	Area treated	m^2	A_{appl}
Reference Duration	Reference duration of exposure (generally 1 day for agricultural pesticides)	d	$t_{exp\ ref}$
$Application_{Amt\ Form\ Used}$	Amount (mass) of substance of interest used per unit volume of product (formulation) used	$mg \cdot m^{-3}$	c_s
Amount of Form Used	Amount (volume) of product (formulation) used	m^3	$V_{prod\ appl}$
Trans Residue	Transferable/dislodgeable residue: amount (mass) of substance of interest (pesticide) available for transfer from a treated surface at a specified time after application	$mg \cdot cm^{-2}$	$L_{s\ trans}$
Transfer Coefficient	Residue transfer rate of substance of interest to human skin during the completion of specific activities, calculated using concurrently collected environmental residue data	$cm^2 \cdot h^{-1}$	TC_s
Exposure Duration	Exposure/application duration	$h \cdot d^{-1}$, h	t_{exp}, $t_{exp\ day}$
Trans Factor/ Fraction $Transferred_{whole\ body/hands}$	Transfer factors to account for fractions of substance of interest transferred to hands, upper/lower body and feet (each covered/ uncovered)	—	$F_{trans\ fraction\ s}$

(continued)

Original abbreviation	Definition	Unit	Abbreviation
Surf Area/Surface Area/ Surface $Area_{contact}$/ $Surf\ Area_{exposed}$	Surface area of exposed skin (for hands, upper/lower body and feet, each covered/uncovered)	cm^2	A_{skin}
Cloth Pen Factor	Clothing penetration/protection factor (options: uncovered/covered)	—	$F_{cloth\ pen}$
Flux Rate AI	Flux rate of substance of interest through impregnated material	$mg \cdot m^{-2} \cdot d^{-1}$	$LR_{s\ flux}$
CF	Correction factors for units (not further presented in this document)	—	F_{unit}
Conc AI Water	Mass concentration of substance of interest in pool water	$mg \cdot m^{-3}$	c_s
Density Formulation	Density of product (formulation)	$g \cdot cm^{-3}$	ρ_{prod}
Fraction AI Formulation	Mass fraction of the substance of interest in the product (formulation) (e.g. 10% w/w = 0.10)	—	m_f
Film Thick	Film thickness of product (formulation) on dermal area	cm	TH

A3.2.3.18 Lifeline™

Different equations are used to calculate dermal exposure during application for residues on surfaces and for residues in water using a historical approach to first determine dermal exposure (amount that reaches the skin) and to separately consider amount absorbed (dose). A very different approach has been used for dermal exposure to dilute aqueous phases, for which dose is addressed directly, taking dermal absorption into consideration in the structure of the equations used to assess exposure (DAF, i.e. the compound- or product-specific dermal absorption factor). The manual gives as a reason for this that "a model of a loading of contaminant on skin does not work well with the constant flush/refresh regimen of the shower, or the essentially infinite theoretical source term for dermal contact during

swimming" for which "exposure situations are really driven by partitioning between the skin and water, rather than a simple determination of the amount that reaches the skin". The potential dermal dose rate from dermal contact with a residue resulting from a specific activity in one microenvironment is calculated as follows (LifeLine, 2002):

$$\text{Dermal Dose}_{jk} = DR_{\text{surface k}} \cdot TCj' \cdot SA \cdot ET_{jk} \cdot CF_j \cdot DAF$$

Thus, although not provided as final output, dermal exposure is provided as dermal exposure (mass rate) to the substance of interest for a specific exposure area per day, including application frequency, by:

$$\text{Dermal Exposure} = DR_{\text{surface k}} \cdot TCj' \cdot SA \cdot ET_{jk} \cdot CF_j$$

where:

Original abbreviation	Definition	Unit	Harmonized abbreviation
Dermal Dose_{jk} (dose rate)	Dermal exposure dose of substance of interest per day	$mg \cdot d^{-1}$	—
Dermal Exposure (not provided as output)	Dermal exposure (mass rate) to substance of interest per day (usage/application frequency, n_{appl}, is included in the tool, although not presented in the equation)	$mg \cdot d^{-1}$	DMR_s
$DR_{\text{surface k}}$	Dislodgeable residue level of substance of interest on the surface of the microenvironment (varies as a function of the microenvironment)	$mg \cdot cm^{-2}$	$L_{s\ trans}$
TCj'	Age- and activity-specific transfer coefficient for transfer of substance of interest to skin, normalized to the individual's surface area (user-modifiable property of the relevant activity; for residues on pets, defined by both the area of the person that comes into contact with the pet and the size of the pet)	h^{-1}	TC_s

(continued)

Original abbreviation	Definition	Unit	Harmonized abbreviation
SA	Surface area of the exposed skin for the individual	cm^2	A_{skin}
ET_{jk}	Duration of the behaviour in the microenvironment (for residues on pets specified by user, for residues on surfaces)	$h \cdot d^{-1}$	$t_{exp\ day}$
CF_j	Clothing penetration/protection factor: age- and activity-specific clothing factor	—	$F_{cloth\ pen}$

A3.2.3.19 SHEDS-Residential

Dermal exposure is provided as dermal exposure (mass rate) to the substance of interest for a specified exposed area of skin (i.e. a specific body part) per day, either "new exposure" (additional amount of chemical transferred onto skin per day) or "running exposure" (amount of chemical already transferred onto the skin), including application frequency in the calculation.

In version 4.0, the following two equations for dermal exposure are provided. Version 4.0 reflects comments from the reviewed SHEDS-Multimedia version 3.0 (USEPA, 2007b; Glen et al., 2012)[1]:

[1] Main changes concerning the algorithms (Glen et al., 2012):

- one option for calculation, two options for entering variables ("transfer coefficient" or "transfer efficiency");
- exposure surfaces are at the external surface of the human body (i.e. outermost skin layer and oral/nasal boundary), resulting in the deletion of algorithmic details that applied to internal body chemistry;
- the chemical (potential for contact) in dust or soil is no longer distinguished from the chemical in other forms;
- non-professional applicators (handler exposure) have been included;
- rate of chemical transfer onto the skin was reduced (when pre-existing dermal loading is present);
- maximum dermal loading was changed into a fixed limit for each person.

"New dermal exposure" on diary event per body part:

$$E_{b,e} = C_{surf,e} \cdot TC_{eff,b,e} \cdot T_e \cdot F\_skin_{b,e} \cdot F\_load_{b,e}$$

where:

Original abbreviation	Definition	Unit	Harmonized abbreviation
$E_{b,e}$	"New dermal exposure" (mass rate) to substance of interest on body part "b" ("i") on diary event "e" relating to one event per day, i.e. additional mass (amount) of substance (chemical) transferred onto skin per day (usage/application frequency, n_{appl}, is included in the tool, although not presented in the equation)	µg	$DM_{s\ new\ i}$
$C_{surf,e}$	Transferable residue: available loading of substance of interest on the surface contacted on diary event "e"	$µg \cdot cm^{-2}$	$L_{s\ res}$
$TC_{eff,b,e}$	Transfer coefficient: residue transfer rate of substance of interest to skin on diary event "e" (may be calculated by SHEDS-Residential)	$cm^2 \cdot h^{-1}$	TC_s
T_e	Duration of diary event "e"	$h \cdot d^{-1}$	t_{exp}
$F\_skin_{b,e}$	Adjustment factor for clothing on body part "b" ("i") on diary event "e"	—	$F_{cloth\ pen\ i}$
$F\_load_{b,e}$	Adjustment factor for pre-existing dermal loading on body part "b" ("i") on diary event "e" (if maximum dermal loading is exceeded, the excess is immediately lost)	—	$F_{s\ load\ i}$

"Running dermal exposure" on diary event per body part:

$$RunExp_{b,e} = RunExp_{b,e-1} + E_{b,e} - MaxL_{b,e} - Abs_{b,e} - HTM_e - Brush_{b,e} - Bath_{b,e} - Wash_{b,e}$$

where:

Original abbreviation	Definition	Unit	Harmonized abbreviation
$RunExp_{b,e}$	"Running dermal exposure" (mass) to substance of interest on body part "b" ("i") on diary event "e", i.e. mass (amount) of substance (chemical) already transferred onto the skin	µg	$DM_{s\ run\ i}$
$RunExp_{b,e-1}$	"Running dermal exposure" (mass) to substance of interest on body part "b" ("i") on diary event "e" ("e–1"), i.e. mass (amount) of substance (chemical) already transferred onto the skin before diary event "e"	µg	$DM_{s\ run\ i-1}$
$E_{b,e}$	"New dermal exposure" (mass) to substance of interest on body part "b" ("i") on diary event "e", i.e. additional mass (amount) of substance (chemical) transferred onto skin per day	µg	$DM_{s\ new\ i}$
	Reduction of dermal exposure (mass) to substance of interest on diary event "e" for:	µg	$M_{s\ red}$
$MaxL_{b,e}$	– being over maximum loading limit		
$Abs_{b,e}$	– absorption (binding) in stratum corneum on diary event "e"		
HTM_e	– hand-to-mouth transfer of chemical on diary event "e"		
$Brush_{b,e}$	– brush-off of loading on body part "b" on diary event "e"		
$Bath_{b,e}$ $Wash_{b,e}$	– hand loading removal on diary event "e" by bath or shower / handwashing		

A3.2.3.20 WHO generic model for indoor residual spraying

Dermal exposure is provided as actual or potential dermal exposure (mass rate) to the substance of interest per day and for a specified exposed area of skin. The final output of the model provides a systemic dose by including dermal absorption and body weight (USEPA, 2008). In addition, several pathways are considered together, including hand-to-mouth behaviour of children and the fact that operators (handlers) are exposed as residents as well. The following algorithms for dermal exposure were extracted (WHO, 2011d):

Mixing and loading (liquids):

$$\text{Dermal exposure} = \frac{VF_{dermal} \cdot CF \cdot (PPE) \cdot EF}{AT}$$

Mixing and loading (solids):

$$\text{Dermal exposure} = \frac{UE_{dermal} \cdot ML \cdot (PPE) \cdot EF}{AT}$$

Application (spraying):

$$\text{Dermal exposure} = \frac{VS_{dermal} \cdot CS \cdot EF}{AT}$$

Residential:

$$\text{Dermal exposure} = \text{contact ratio} \cdot AV \cdot TC \cdot Transl \cdot ESA$$

where:

Original abbreviation	Definition	Unit/ default	Harmonized abbreviation
Dermal exposure	Potential or acute dermal exposure (mass rate) to substance of interest per operator for either mixing and loading or application; or residential person for a specific exposed skin area (see A_{skin}) per day	$mg \cdot d^{-1}$ / $\mu g \cdot d^{-1}$	DMR_s
VF_{dermal}	Volume of non-diluted pesticide formulation on unprotected hands for mixing and loading when preparing liquids per operation; in original tool, a multiplication of VF_{dermal} by n_{appl} (i.e. the number of tanks loaded daily/frequency of operation) is already included in VF_{dermal}	ml (0.01 for package sizes $\leq$2 litres, otherwise 0.01–0.5, depending on container size and diameter of opening)	$DV_{prod\ M\&L}$
No. daily operations	Number of daily operations (12 tanks per day) (in original tool, included in VF_{dermal})	d^{-1} (12)	n_{appl}

(continued)

Original abbreviation	Definition	Unit/ default	Harmonized abbreviation
CF	Concentration of substance of interest in product before dilution (pesticide concentrate)	$g \cdot ml^{-1}$	$c_{s\ in\ product}$
PPE	Protection provided by personal protective equipment	Guideline scenario = 0.1; i.e. 90% protection Lax standard scenario = 1; i.e. no protection)	$F_{cloth\ pen}$
EF	Exposure duration (called "frequency") (6 days per week, 6 weeks per treatment round, 2 rounds per year)	d (72)	t_{exp}
AT	Averaging time in days (1 year)	d (365)	t_{exp}
UE_{dermal}	Unit exposure (default value) for dermal exposure (mass) to substance of interest per product mass handled on unprotected hands during mixing and loading when preparing solids	$\mu g \cdot g^{-1}$	$DM_{s\ per\ mass\ handled}$
ML	Mass (amount) of substance of interest (active ingredient) mixed and loaded per day and per spray operator, i.e.: $MR_s = c_{s\ in\ dilution} \cdot V_{spray\ day}$ with the following assumptions:	$g \cdot d^{-1}$	MR_s

Abbreviation	Unit	Default	Definition
$c_{s\ in\ dilution}$	$g \cdot l^{-1}$	—	(Final) concentration of substance of interest (active ingredient) in (diluted) spraying formulation, i.e. $c_{s\ in\ dilution} = \frac{L_{s\ appl}}{V_{p\ wall}}$

(continued)

Original abbreviation	Definition			Unit/ default	Harmonized abbreviation
	$L_{s\ appl}$	$g \cdot m^{-2}$	—	Aimed target loading (concentration) of substance of interest on the wall (product specific)	
	$V_{p\ wall}$	$l \cdot m^{-2}$	0.04 (WHO, 2007b)	Volume of diluted spray formulation applied onto the walls	
	$V_{spray\ day}$	$l \cdot d^{-1}$	120	Volume of diluted spray formulation used per day, i.e. $V_{spray\ day} = V_{tank} \cdot n_{appl}$	
	V_{tank}	l	10	Volume of tank	
	n_{appl}	d^{-1}	12	Number of loads/tanks per day	
VS_{dermal}	Volume of (diluted) spraying formulation on hands per day for application and washing and maintenance of the equipment; i.e.: TH · A_{skin}			$l \cdot d^{-1}$ (0.0093)	$DV_{prod\ appl}$
	– TH: Film thickness of a non-viscous liquid likely to be in contact with unprotected, immersed skin after runoff			cm (0.01)	TH
	– A_{skin}: Total surface area of hands (for spraying application and washing and maintenance of equipment)			cm^2 (930; USEPA, 2008)	A_{skin}
CS	(Final) concentration of substance of interest (active ingredient) in (diluted) spraying formulation; see above parameter “ML” for definition			$g \cdot ml^{-1}$	$c_{s\ in\ dilution}$

(continued)

Original abbreviation	Definition	Unit/ default	Harmonized abbreviation
Default concentration of the insecticide (weighted)	Fraction (called concentration) of substance of interest to the wall target loading ($L_{s\ appl}$) for surfaces with which inhabitants are in contact (10% of this contact with the walls, 90% with the floors and furniture)	— (0.15)	m_{fw}
AV	Average proportion (fraction) of spray residue on wall during 6 months of first-order kinetics decay with a half-time of 60 days	— (0.42)	F_{decay}
TC	Aimed target loading (concentration) of substance of interest on the wall (product specific) (see above for "ML")	$g \cdot m^{-2}$	$L_{s\ appl}$ (see above)
Transl	Proportion/fraction present on the surfaces assumed to be translodged onto skin	—	$F_{trans\ fraction\ s}$
ESA	Exposed skin area:	m^2	A_{skin}
	– adults/older children: hands and forearms	0.201	
	– 6- to 11-year-old children: hands and arms	0.191	
	– toddlers: head, hands, arms, legs, feet, i.e. 61% of total skin area	0.37 (USEPA, 2008)	

A3.2.4 Harmonized abbreviations of algorithm parameters of models/tools

Table A3.3. List of harmonized and original abbreviations used for determinants of the algorithms for dermal exposure modelling

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
A_{appl}	Area Treated	Area treated	m^2	CARES
A_{appl}	A	Area treated per day	ha	German model
A_{skin}	Exposed skin surface	Surface area of exposed skin (implemented in chosen PROC)	cm^2	ECETOC TRA (worker)
A_{skin}	Surf Area/Surface Area/ Surface $Area_{contact}$/ Surf $Area_{exposed}$	Surface area of exposed skin (for hands, upper/lower body and feet, each covered/uncovered)	cm^2	CARES
A_{skin}	S_{exp}	Surface area of exposed skin	cm^2	ConsExpo
A_{skin}	CA: Contact area	Surface (contact) area of exposed skin	cm^2 (default: 30–840)	ECETOC TRA (consumer)
A_{skin}	SA	Surface area of the exposed skin for the individual	cm^2	LifeLine
A_{skin}	Exposed skin area	Exposed skin area (defaults provided by tool dependent on chosen PROC)	cm^2	MEASE
A_{skin}	In tool included in $DV_{prod\ appl}$	Total surface area of hands (for spraying application and washing and maintenance of equipment)	cm^2 (930; USEPA, 2008)	WHO operator / residential indoor
A_{skin}	ESA	Exposed skin area: – adults/older children: hands and forearms – 6- to 11-year-old children: hands and arms – toddlers: head, hands, arms, legs, feet, i.e. 61% of total skin area)	m^2; USEPA, 2008 0.201 0.191 0.37	WHO operator / residential indoor

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$A_{skin\ hori}$	A_{hori}	Horizontal body area that is available for deposition (assumed 10% of total body surface area of 1.96 m^2 according to the USEPA [1997c] exposure factors handbook)	m^2	SprayExpo
$A_{skin\ mean\ i}$	BS_{BP}	Body surface factor: exposed surface area of an individual body part "i" divided by the mean surface area of the nine body parts	—	DREAM
$A_{skin\ rub}$	S_{area}	Total area rubbed during exposure, determined by the area rubbed per unit of time and limited by the total treated surface area	m^2	ConsExpo
$A_{skin\ vert}$	A_{vert}	Vertical body area that is available for deposition (assumed 90% of total body surface area of 1.96 m^2 according to the USEPA [1997c] exposure factors handbook)	m^2	SprayExpo
c_{air}	C	Total concentration "c" of aerosols at time "t" calculated in SprayExpo (for details, see program: Koch, 2004)	$mg \cdot cm^{-3}$	SprayExpo
c_s	$Application_{Amt\ Form\ Used}$	Amount (mass) of substance of interest used per volume of product (formulation) used	$mg \cdot m^{-3}$	CARES
c_s	Conc AI Water	Mass concentration of substance of interest in pool water	$mg \cdot m^{-3}$	CARES
$c_{s\ in\ dilution}$	a.s. concentration	Concentration of substance of interest in diluted spray formulation during application	$mg \cdot ml^{-1}$	United Kingdom POEM
$c_{s\ in\ dilution}$	CS / CF	(Final) concentration of substance of interest (active ingredient) in (diluted) spraying formulation	$g \cdot ml^{-1}$	WHO operator / residential indoor

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$c_{s\ in\ dilution}$	In tool, included in MR_s	(Final) concentration of substance of interest (active ingredient) in (diluted) spraying formulation; i.e. $c_{s\ in\ dilution} = \frac{L_{s\ appl}}{V_{p\ wall}}$	$g \cdot l^{-1}$	WHO operator / residential indoor
$c_{s\ in\ product}$	a.s. concentration	Concentration of substance of interest in product (concentrate)	$mg \cdot ml^{-1}$	United Kingdom POEM
$c_{s\ in\ product}$	CF	Concentration of substance of interest in product before dilution (pesticide concentrate)	$g \cdot ml^{-1}$	WHO operator / residential indoor
$c_s(x,t)$	C(x,t)	Mass concentration of substance of interest in the product (formulation) at depth "x" and time "t"	$mg \cdot cm^{-3}$	ConsExpo
D-score	DERM	Numerical estimate (DERM score) for the dermal exposure level	—	DERM
D-score	$Skin_w\text{-}A_{job}$	"Total actual dermal exposure estimated at job level" (final score given in a DREAM unit, providing ranking of exposure in following DREAM categories: 0 = no exposure; 0–10 = very low exposure; 10–30 = low exposure; 30–100 = moderate exposure; 100–300 = high exposure; 300–1000 = very high exposure; >1000 = extremely high exposure)	—	DREAM
DL_s	L_{derm} (dermal load)	Dermal exposure loading of substance of interest for specified exposed area of skin per application (event) (n_{appl}, although frequency not included in calculation, thus one application assumed per day)	$mg \cdot cm^{-2}$	ConsExpo

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
DLR_s	Dermal exposure	Dermal exposure (loading rate) to substance of interest per day (relating to hands and forearms) (provided in ranges: "very low", 0–0.1, 0.1–1, 1–5 and 5–15 $mg \cdot cm^{-2} \cdot d^{-1}$)	$mg \cdot cm^{-2} \cdot d^{-1}$	EASE
$DLR_{s\ default}$	EASE value (initial dermal exposure estimate)	Initial dermal exposure (loading rate) to substance of interest for specified exposed area of skin (based on EASE)	$mg \cdot cm^{-2} \cdot d^{-1}$	ECETOC TRA (worker)
$DLR_{s\ default}$	Dermal exposure estimate	Dermal exposure (loading rate) to substance of interest per application (n_{appl}) (default estimate provided by tool, e.g. based on EASE) and further adjusted/determined by choice of substance characteristics, operational conditions and risk management measures	$mg \cdot cm^{-2} \cdot d^{-1}$	MEASE
DM_s	D_{derm} (dermal dose)	Dermal exposure (mass), i.e. total deposition after exposure duration	mg	SprayExpo
$DM_{s\ new\ i}$	$E_{b,e}$	"New dermal exposure" (mass) to substance of interest on body part "b" ("i") on diary event "e", i.e. additional mass (amount) of substance (chemical) transferred onto skin per day	µg	SHEDS
$DM_{s\ per\ mass\ handled}$	Unit $Exposure_{dermal}$	Dermal exposure (mass) to substance of interest in relation to handling 1 kg of substance of interest during application (default provided by tool taken from PHED)	$mg \cdot kg^{-1}$	CARES
$DM_{s\ per\ mass\ handled}$	UE_{dermal}	Unit exposure (default value) for dermal exposure (mass) to substance of interest per mass of substance of interest handled on unprotected hands during mixing and loading when preparing solids	$µg \cdot g^{-1}$	WHO operator / residential indoor

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$DM_{s\ per\ mass\ handled\ EXP}$	D*	Dermal exposure (mass) related to handling 1 kg of substance of interest, experimentally determined	$mg \cdot kg^{-1}$	German model
$DM_{s\ run\ i}$	$RunExp_{b,e}$	"Running dermal exposure" (mass) to substance of interest on body part "b" ("i") on diary application (event) "e", i.e. mass (amount) of substance (chemical) already transferred onto the skin	µg	SHEDS
$DM_{s\ run\ i-1}$	$RunExp_{b,e-1}$	"Running dermal exposure" (mass) to substance of interest on body part "b" ("i") on diary application (event) "e" ("e–1"), i.e. mass (amount) of substance (chemical) already transferred onto the skin before diary event	µg	SHEDS
$DM\text{-}score_{s\ DREAM\ x\ i}$	$I_{E.BP}$, $I_{D.BP}$, $I_{T.BP}$	Dermal exposure score: "intensity": amount (mass) of substance of interest in relation to transport mechanism (exposure route) "x" for body part "i": – for exposure route "emission" and "deposition": mass (amount) of substance of interest on clothing and uncovered skin – for exposure route "transfer": contamination level of the contact	—	DREAM
DMR (DLR)	DE	Exposure loading per shift (related to hands and/or body)	µl or mg (e.g. $mg \cdot (8\,h \cdot hands)^{-1}$)	RISKOFDERM
DMR_s	Dermal exposure	Dermal exposure (mass rate) to substance of interest per day	$mg \cdot d^{-1}$	ECETOC TRA (worker)

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
DMR_s	Exposure	Dermal exposure (mass) to substance of interest, considering one application per day	$mg \cdot d^{-1}$	CARES
DMR_s	Dermal exposure	Dermal exposure (mass rate) to substance of interest for a specific exposure area per day	$g \cdot d^{-1}$	ECETOC TRA (consumer)
DMR_s	PDE	Potential dermal exposure (mass rate) to substance of interest per day (if "P" is included: Actual dermal exposure (mass rate))	$\mu g \cdot d^{-1}$	EUROPOEM II
DMR_s	Dermal Exposure (not provided as output)	Dermal exposure (mass rate) to substance of interest per day (usage/application frequency, n_{appl}, is included in the tool, although not presented in the equation)	$mg \cdot d^{-1}$	LifeLine
DMR_s	Total dermal loading	Dermal exposure (mass rate) to substance of interest per day for a specific surface area	$mg \cdot d^{-1}$	MEASE
DMR_s	Average deposition rate during application	Average amount (mass) deposited per second during application	$mg \cdot s^{-1}$	SprayExpo
DMR_s	Dermal exposure	Potential or acute dermal exposure (mass rate) to substance of interest per operator for either mixing and loading or application; or residential person for a specific exposed skin area (see A_{skin}) per day	$mg \cdot d^{-1}$/$\mu g \cdot d^{-1}$	WHO operator / residential indoor
$DMR_{s\ appl}$	Dermal exposure to a.s.	Dermal exposure (mass rate) to substance of interest during spray application per day (one application per day; relating to sum of exposure of hands, trunk and legs)	$mg \cdot d^{-1}$	United Kingdom POEM
$DMR_{s\ M\&L\ hands}$	Dermal exposure to a.s.	Dermal exposure (mass rate) to substance of interest in product (spray formulation) on the hands per day during mixing and loading	$mg \cdot d^{-1}$	United Kingdom POEM

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$DMR_{s\ per\ mass\ handled}$	D	Dermal exposure (mass rate) to substance of interest per kilogram of substance of interest used or handled per person and per application for a specific duration	$mg \cdot kg^{-1} \cdot d^{-1}$	German model
$DV_{prod\ appl}$	VS_{dermal}	Volume of (diluted) spraying formulation on hands per day for application and washing and maintenance of the equipment; i.e.: $TH \cdot A_{skin}$	$l \cdot d^{-1}$	WHO operator / residential indoor
$DV_{prod\ M\&L}$	Hand contamination per operation	Dermal contact volume of product (formulation) per application (operation) during mixing and loading (default provided by tool, determined by chosen application method, volume and neck aperture width of container)	ml	United Kingdom POEM
$DV_{prod\ M\&L}$	VF_{dermal}	Volume of non-diluted pesticide formulation on unprotected hands for mixing and loading when preparing liquids per operation	ml (defaults: 0.01–0.5)	WHO operator / residential indoor
$DVR_{prod\ appl}$	Volume of surface contamination	Volume of dermal exposure (surface contamination) to the product (spray formulation) during spray application per hour (one application per day; default provided by tool, determined by chosen application/spraying method)	$ml \cdot h^{-1}$ (default: 2–400)	United Kingdom POEM
$DVR_{prod\ appl\ i}$	Dermal exposure of trunk/hands/legs	Dermal exposure (volume rates) to product (spray formulation) per body part (“i”: hands, trunk and legs) during spray application (one application per day)	$ml \cdot h^{-1}$	United Kingdom POEM
$DVR_{prod\ appl\ tot}$	Total dermal exposure to spray	Sum of dermal exposure (volume rates) of body parts (“i”: hands, trunk and legs) to product (spray formulation) during spray application (one application per day)	$ml \cdot h^{-1}$	United Kingdom POEM

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$DVR_{prod\ M\&L\ hands}$	Dermal exposure to formulation	Dermal exposure (volume rate) to product on hands (hand contamination) per day during mixing and loading (default provided by tool, determined by chosen application method, volume and neck aperture width of container and whether gloves are used)	$ml \cdot d^{-1}$	United Kingdom POEM
$F_{cloth\ pen}$	C	Clothing penetration/protection factor: the score for exposure reduction due to protective effect of clothing	—	DERM
$F_{cloth\ pen}$	CF_j	Clothing penetration/protection factor: age- and activity-specific clothing factor	—	LifeLine
$F_{cloth\ pen}$	Dermal PPE/gloves	Gloves: efficacy depends on worker's training conditions	%	ECETOC TRA (worker)
$F_{cloth\ pen}$	Cloth Pen Factor	Clothing penetration/protection factor (options: uncovered/ covered)	—	CARES
$F_{cloth\ pen}$	Risk management measures	Clothing penetration/protection factor: adjustment factor to account for use of gloves (default estimate provided by tool, fraction of exposure dependent on options: – no gloves: 100% – properly selected gloves: 10%)	— (see column to left)	MEASE
$F_{cloth\ pen}$	Transmission to skin	Clothing penetration/protection factor to account for transmission to skin during mixing and loading if gloves are used (default provided by tool, dependent on whether gloves are chosen for protection)	— (gloves: 5%, otherwise 100%)	United Kingdom POEM
$F_{cloth\ pen}$	PPE	Protection (penetration factor) for personal protective equipment	0.1–1	WHO operator / residential indoor

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$F_{cloth\ pen\ i}$	$F\_skin_{b,e}$	Adjustment factor for clothing on body part "b" ("i") on diary application (event) "e" (one event per day)	—	SHEDS
$F_{cloth\ pen\ i}$	O_{BP}	Clothing protection (penetration) factor per body part "i" depending on the kind of material, replacement frequency of clothing (hands and the use of gloves are treated differently)	—	DREAM
$F_{cloth\ pen\ i}$	P	Clothing penetration/protection factor to account for penetration through protective clothing and gloves	—	EUROPOEM II
$F_{cloth\ pen\ i}$	Penetration through clothing	Clothing penetration/protection factor during spray application, dependent on protective equipment chosen, penetration per body part ("i"): – hands: gloves 10%, otherwise 100% – trunk: 2% – legs: 25%	— (for defaults, see column to left)	United Kingdom POEM
$F_{cont\ pat}$	Kind of (skin) contact	Intensity of skin contact: Rare contact / More than rare contact	—	RISKOFDERM
$F_{cont\ pat}$	Pattern of control	Choice of the exposure control pattern (provided options: direct or non-direct handling)	—	EASE
$F_{cont\ pat}$	Pattern of exposure control	Adjustment factor to account for the exposure control pattern (options: "direct handling" or "non-direct handling")	—	MEASE
F_{decay}	AV	Average proportion (fraction) of spray residue on wall during 6 months of first-order kinetics decay with a half-time of 60 days	— (0.42)	WHO operator / residential indoor
$F_{emission}$	Aerosol	Significant amounts of aerosols or splashes: yes/no	—	RISKOFDERM

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$F_{fraction}$	Percentile for exposure rate distribution	Exposure rate distribution	—	RISKOFDERM
F_{LEV}	Ventilation	Quality of ventilation: Poor ventilation / Normal or good ventilation	—	RISKOFDERM
F_{LEV}	LEV	Depends on operational conditions (industrial/professional) and PROC	%	ECETOC TRA (worker)
$F_{op\ cond}$	Operational condition	Industrial/professional	—	ECETOC TRA (worker)
$F_{op\ cond}$	Automation	Automation: Manual process / Automated or semiautomated processes	—	RISKOFDERM
$F_{op\ cond}$	PROC	Process category	—	MEASE
$F_{op\ equip}$	Application method	Application (operation) method/equipment used for spray application (defaults provided: different hand-held or tractor-mounted sprayers)	—	United Kingdom POEM
$F_{op\ scale}$	Scale of operation	Adjustment factor to account for industrial or professional use	—	MEASE
F_R	ER	"Exposure route factor": weighting the different transport mechanisms (exposure routes) to the skin "x" (more weight assigned to exposure route "emission" than the others due to direct release from a source)	—	DREAM
$F_{s\ char}$	Substance	Physical state (solid/liquid) implanted in initial exposure estimate	—	ECETOC TRA (worker)
$F_{s\ char}$	Type of product	Physical state: Liquid / Low or moderately dusty solid / Highly dusty solid	—	RISKOFDERM

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$F_{s\ char}$	E_I	"Intrinsic emission": physical and chemical characteristics of the substance, concentration of active substance, etc. (e.g. for liquids, including the physical state, boiling point and viscosity)	—	DREAM
$F_{s\ char}$	Physical state	Choice of physical state of substance of interest (provided options: solid, liquid, gas/vapour)	—	EASE
$F_{s\ char}$	Physical form	Adjustment factor to account for the physicochemical specific, i.e. physical, form (options: massive, solid with different ranges for dustiness, aqueous solution, liquid, gaseous)	—	MEASE
$F_{s\ load\ i}$	$F\_load_{b,e}$	Adjustment factor for pre-existing dermal loading on body part "b" ("i") on diary application (event) "e" (if maximum dermal loading is exceeded, the excess is immediately lost)	—	SHEDS
$F_{s\ red}$	WH EH CE	Adjustment factors for reduction of dermal exposure, in tool depending on the three estimates: – "workers' hygiene": handwash frequency/efficiency (WH) – "hygiene": cleaning frequency/efficiency of floor, worktables, machines and working tools (EH) – "continued exposure": circumstances of working clothes (CE)	—	DREAM
F_t	RTD	"Relative task duration estimate": ratio of "task frequency" multiplied by "task duration" to the total working time	—	DREAM
$F_{trans\ fraction\ p}$	$S_{contact}$	Skin contact factor to account for the fact that the product is only partially in contact with the skin (in decimal form as fraction of product that is in direct contact with bare skin: 10% w/w = 0.10)	—	ConsExpo

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$F_{trans\ fraction\ p}$	Distribution (on body part)	Transfer/contact factor (distribution) for the product (spray formulation) for spray application per body part ("i": hands, trunk or legs) (default provided by tool as percentage/fraction, determined by chosen application/spraying method)	—	United Kingdom POEM
$F_{trans\ fraction\ s}$	Transl	Proportion/fraction present on the surfaces assumed to be translodged onto skin	—	WHO operator / residential indoor
$F_{trans\ fraction\ s}$	Trans Factor/ Fraction $Transferred_{whole\ body/hands}$	Transfer factors to account for fractions of substance of interest transferred to hands, upper/lower body and feet (each covered/uncovered)	—	CARES
$F_{trans\ fraction\ s}$	F_{leach}	Transfer factor to account for the fraction of substance of interest that is leachable from the product (formulation) to be transferred ("migrate" according to ConsExpo) to the skin per unit amount of product (in decimal form as fraction: 10% w/w = 0.10)	—	ConsExpo
F_{unit}	CF	Correction factors for units (not further presented in this document)	—	CARES
$F_{use\ pat}$	Descriptor of use	PROC, application	—	ECETOC TRA (worker)
$F_{use\ pat}$	Pattern of use	Choice of the pattern of use (provided options: closed system, incorporation onto matrix or non-dispersion, wide dispersion)	—	EASE
$F_{use\ pat}$	Pattern of use	Adjustment factor to account for the pattern of use (options: "wide dispersive use", "non-dispersive use", "inclusion in matrix", "closed system without breaches")	—	MEASE
i (index)	BP (index)	Nine different body parts "i" are considered: head, upper or lower arms, hands, torso front or back, lower body part, lower legs, feet	—	DREAM

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$L_{s\ appl}$	R	Application rate	(kg a.i.)·ha^{-1}	EUROPOEM II
$L_{s\ appl}$	Application$_{Area\ treated}$	Amount (mass) of substance of interest used per unit of area treated	mg·m^{-2}	CARES
$L_{s\ appl}$	In tool, included in MR_s	Aimed target loading (concentration) of substance of interest on the wall (product specific)	g·m^{-2}	WHO operator / residential indoor
$L_{s\ appl}$	TC	Aimed target loading (concentration) of substance of interest on the wall (product specific)	g·m^{-2}	WHO operator / residential indoor
$L_{s\ appl}$	R	The use rate (application rate) of active substance	kg·ha^{-1}	German model
$L_{s\ res}$	$C_{surf,e}$	Transferable residue: available loading of substance of interest on the surface contacted on diary application (event) “e”	µg·cm^{-2}	SHEDS
$L_{s\ trans}$	Trans Residue	Transferable/dislodgeable residue: amount (mass) of substance of interest (pesticide) available for transfer from a treated surface at a specified time after application	mg·cm^{-2}	CARES
$L_{s\ trans}$	$F_{dislodge}$	Transferable/dislodgeable residue: amount (mass) of product that can be rubbed off per unit of surface area	mg·cm^{-2}	ConsExpo
$L_{s\ trans}$	DFR	Dislodgeable foliar residue	worst-case default: 1 or 3 µg·cm^{-2}·(kg a.i.)$^{-1}$·ha^{-1} multiplied by the application rate in (kg a.i.)·ha^{-1}	EUROPOEM II

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$L_{s\ trans}$	$DR_{surface\ k}$	Dislodgeable residue level of substance of interest on the surface of the microenvironment (varies as a function of the microenvironment)	$mg \cdot cm^{-2}$	LifeLine
$LR_{s\ flux}$	Flux Rate AI	Flux rate of substance of interest through impregnated material	$mg \cdot m^{-2} \cdot d^{-1}$	CARES
m_f	Concentration modifiers	Mass fraction of the substance in the product: > 1%, 1–5%, 5–25%, > 25%	—	ECETOC TRA (worker)
m_f	Fraction AI Formulation	Mass fraction of the substance of interest in the product (formulation) (e.g. 10% w/w = 0.10)	—	CARES
m_f	wf	Mass fraction of the substance of interest in the product (formulation) (e.g. 10% w/w = 0.10)	—	ConsExpo
m_f	C	Mass fraction provided as concentration of substance of interest in product/formulation (provided categories: <1%, 1–90%, >90% substance of interest; in tool, this parameter is included in $F_{s\ char}$)	—	DREAM
m_f	PI: Product ingredient fraction	Mass fraction of substance of interest in the product (formulation) or article	— ($mg \cdot mg^{-1}$)	ECETOC TRA (consumer)
m_f	Content in preparation	Mass fraction of the substance of interest in the product (formulation) (tool provides ranges to choose from: >1%, 1–5%, 5–25%, >25%)	—	MEASE
m_{fw}	Default concentration of the insecticide (weighted)	Fraction (called concentration) of substance of interest to the wall target loading ($L_{s\ appl}$) for surfaces with which inhabitants are in contact (10% of this contact with the walls, 90% with the floors and furniture)	0.15	WHO operator / residential indoor
$M_{prod\ skin}$	A_{prod}	Amount (mass) of product (formulation) directly applied to or in contact with skin	mg	ConsExpo

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$M_{s\ red}$	$MaxL_{b,e}$ $Abs_{b,e}$ HTM_e $Brush_{b,e}$ $Wash_{b,e}$ $Bath_{b,e}$	Reduction of dermal exposure (mass) to substance of interest on diary event "e" for: – being over maximum loading limit ($MaxL_{b,e}$) – absorption (binding) in stratum corneum on diary event "e" ($Abs_{b,e}$) – hand-to-mouth transfer of chemical on diary event "e" (HTM_e) – brush-off of loading on body part "b" on diary event "e" ($Brush_{b,e}$) – hand loading removal on diary event "e" by handwashing / bath or shower ($Wash_{b,e}$ / $Bath_{b,e}$)	µg	SHEDS
$MR_{prod\ appl\ skin}$	R	Use rate (application rate) of product applied directly to the skin	$mg \cdot s^{-1}$	ConsExpo
MR_s	ML	Mass (amount) of substance of interest (active ingredient) mixed and loaded per day and per spray operator, i.e.: $MR_s = c_{s\ in\ dilution} \cdot V_{spray\ day}$	$g \cdot d^{-1}$	WHO operator / residential indoor
$MR_{s\ appl}$	Use rate	Use rate	$kg \cdot min^{-1}$	RISKOFDERM
$MR_{s\ dep}$	R(t)	Deposition rate at time "t"	$mg \cdot s^{-1}$	SprayExpo
n_{appl}	$P_{E.BP}$, $P_{D.BP}$, $P_{T.BP}$	"Probability" (frequency) for transfer for body part "i" and exposure route "x": – for exposure route "emission" ($P_{E.BP}$) and "deposition" ($P_{D.BP}$): frequency of occurrence of the concerned exposure route – for exposure route "transfer" ($P_{T.BP}$): contact frequency with surfaces such as floor, worktables, machines and working tools (provided categories: unlikely, e.g. with $<1\%$ of task duration; occasionally; repeatedly; and almost constantly)	—	DREAM

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
n_{appl}	Contact level	Choice of the contact level (provided options: none, incidental, intermittent, extensive)	—	EASE
n_{appl}	FQ	Frequency of applications (tasks/events) per day	d^{-1} (default: 0.15–1)	ECETOC TRA (consumer)
n_{appl}	Contact level	Frequency of applications (tasks/events) per day (options: “none”; “incidental, i.e. one event per day, including splashes/spills; “intermittent”, i.e. 2–10 events per day; “extensive”, i.e. >10 events per day due to work where hands are part of process, e.g. transfer of wet objects)	—	MEASE
n_{appl}	Number of operations	Number of applications (operations) per day (default provided by tool, determined by chosen application method, volume and neck aperture width of container, application volume and dose, i.e. the final diluted formulation that is to be prepared in litres per hectare)	d^{-1}	United Kingdom POEM
n_{appl}	No. daily operations	Number of daily operations (corresponding to assumption that n_{tanks}, i.e. 12 tanks per day, are loaded) (in original tool, included in VF_{dermal})	d^{-1} (12)	WHO operator / residential indoor
$n_{contact}$	Frequency of (skin) contact	Frequency of skin contact: Light contact / More than light contact	—	RISKOFDERM
t_{exp}	Duration modifiers	Exposure duration: $<$15 min, 15–60 min, 60–240 min, $>$240 min	—	ECETOC TRA (worker)

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
t_{exp}	T_e	Duration of diary application (event) “e”	$h \cdot d^{-1}$	SHEDS
t_{exp}	Cumulative duration of the scenario in the shift	Exposure duration	min	RISKOFDERM
t_{exp}	T	Exposure duration: loading time or release / application duration	s	ConsExpo
t_{exp}	Duration of exposure	Exposure duration/contact with material (options: $<$15 min, 15–60 min, 60–240 min, $>$240 min)	min	MEASE
t_{exp}	t_R	Exposure duration	s	SprayExpo
t_{exp}	Duration of exposure (spraying)	Duration of exposure (spraying) (one application for whole exposure per day assumed)	h	United Kingdom POEM
t_{exp}	EF	Exposure duration (called “frequency”) (6 days per week, 6 weeks per treatment round, 2 rounds per year)	d (72)	WHO operator / residential indoor
t_{exp}	AT	Averaging time in days (1 year)	d (365)	WHO operator / residential indoor
t_{exp}, $t_{exp\ day}$	Exposure Duration	Exposure/application duration	h; $h \cdot d^{-1}$	CARES
$t_{exp\ day}$	t	Duration of work (application/task)	harvesting: 8 $h \cdot d^{-1}$, inspection tasks: 2 $h \cdot d^{-1}$	EUROPOEM II
$t_{exp\ day}$	ET_{jk}	Duration of the behaviour in the microenvironment (for residues on pets specified by user, for residues on surfaces)	$h \cdot d^{-1}$	LifeLine

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
$t_{exp\ ref}$	Reference Duration	Reference duration of exposure (generally 1 day for agricultural pesticides)	d	CARES
T_i	T	Numerical score for each determinant (option) for transport (mechanism) to the skin (score of 1–5 for each of the following options: transfer from previously contaminated surfaces, deposition, emission)	—	DERM
$T_{x\ i}$	E_{BP} D_{BP} T_{BP}	Transport mechanism (exposure route) to the skin per body part "i" with relevant index "x" corresponding to: $_{x=E}$: "emission": mass transport by direct release from a source $_{x=D}$: "deposition": mass transport from air that subsequently deposits $_{x=T}$: "transfer": mass transport from contaminated surfaces	—	DREAM
TC_s	$TC_{eff,b,e}$	Transfer coefficient: residue transfer rate of substance of interest to skin on diary application (event) "e" (may be calculated by SHEDS-Residential)	$cm^2 \cdot h^{-1}$	SHEDS
TC_s	TCj′	Age- and activity-specific transfer coefficient for substance of interest to skin, normalized to the individual's surface area (user-modifiable property of the relevant activity; for residues on pets, defined by both the area of the person that comes into contact with the pet and the size of the pet)	h^{-1}	LifeLine

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
TC_s	Transfer Coefficient	Residue transfer rate of substance of interest to human skin during the completion of specific activities, calculated using concurrently collected environmental residue data	$cm^2 \cdot h^{-1}$	CARES
TC_s	TC	Transfer coefficient	$cm^2 \cdot ha^{-1}$ - vegetables: 2500 $cm^2 \cdot ha^{-1}$ - berries: 3000 $cm^2 \cdot ha^{-1}$ - tree fruit: 4500 $cm^2 \cdot ha^{-1}$ - ornamentals: 5000 $cm^2 \cdot ha^{-1}$ worst-case default: 30 000 $cm^2 \cdot ha^{-1}$	EUROPOEM II
TH	Film Thick	Film thickness of product (formulation) on dermal area	cm	CARES
TH	TL	Thickness of layer of liquid (product) in contact with skin	cm (default: 0.01; see also footnote in section A3.2.3.6)	ECETOC TRA (consumer)

Table A3.3 (continued)

Harmonized abbreviation	Original abbreviation	Definition	Unit/default	Model/tool
TH	In tool, included in $DV_{prod\ appl}$	Film thickness of a non-viscous liquid likely to be in contact with unprotected, immersed skin after runoff	cm (0.01)	WHO operator / residential indoor
$V_{p\ wall}$	In tool, included in MR_s	Volume of diluted spray formulation applied onto the walls	$l \cdot m^{-2}$	WHO operator / residential indoor
$V_{prod\ appl}$	Amount of Form Used	Amount (volume) of product (formulation) used	m^3	CARES
$V_{spray\ day}$	In tool, included in MR_s	Volume of (diluted) spray formulation used per day; i.e. $V_{spray\ day} = V_{tank} \cdot n_{appl}$	$l \cdot d^{-2}$	WHO operator / residential indoor
V_{tank}	In tool, included in MR_s	Volume of tank	l	WHO operator / residential indoor
ρ_{prod}	Density Formulation	Density of product (formulation)	$g \cdot cm^{-3}$	CARES
ρ_{prod}	D	Density of the product liquid	$g \cdot cm^{-3}$ (default: 1)	ECETOC TRA (consumer)
υ_{dep}	υ_{dep}	Deposition velocity: velocity of the deposition on the other parts of the body surface by turbulent diffusion	$cm \cdot s^{-1}$ (0.01)	SprayExpo
υ_{set}	υ_{set}	Settling velocity: velocity of sedimentation of sprayed aerosols (for details, see program: Koch, 2004; see also Hinds, 1999)	$cm \cdot s^{-1}$	SprayExpo

a.i., active ingredient; a.s., active substance

A3.3 EASE's logical criteria to assess dermal exposure

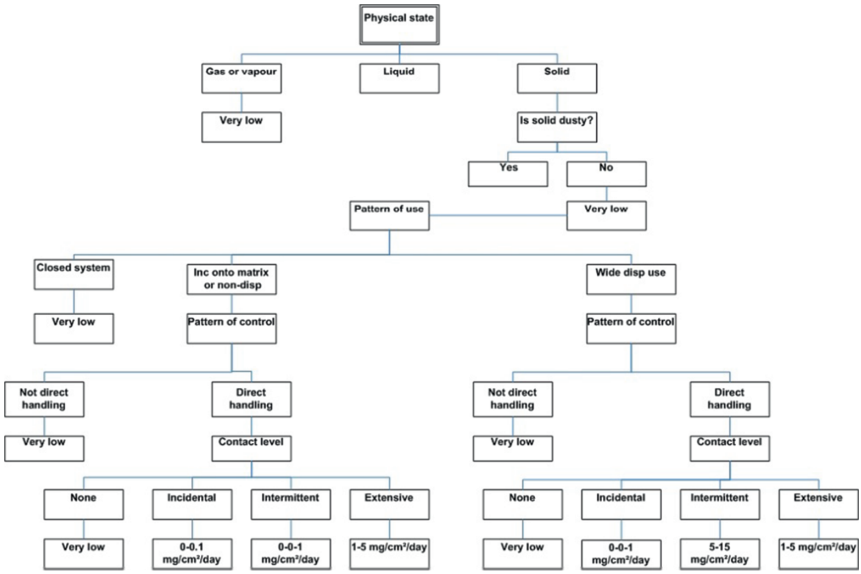


Fig. A3.1. Determination of dermal exposure in EASE (Cherrie et al., 2003).

A3.4 Valid ranges for continuous parameters and benchmark study on the validity of RISKOFDERM

For continuous parameters (use rate and duration), the valid ranges of the data set are provided in Table A3.5. Any estimates for higher use rates or longer durations than those found in the data set should be considered with special care, as these might lead to results that are above levels (per square centimetre) that are considered reasonable (TNO, 2006).

In TNO (2006), the results of a benchmark study are presented showing that, in general, the model appeared to be quite reasonable. In Table A3.6, the "percentage explained variance" indicates what part of the variation can be explained by the determinants used in the model (low percentage indicates determinants determining only a small part

Table A3.5. Valid ranges for continuous parameters (use rate and duration)[a]

Process	Use rate (l·min^{-1} or kg·min^{-1})		Duration (min)	
	Solids	Liquids	Solids	Liquids
Filling, mixing and loading	0.56–225	0.008–257	1–20	0.33–125
Wiping[b]	No data	0.0017–1.18	No data	5–35
Dispersion hand-held tools[b]	No data	0.0001–1.1	No data	1–445
Spraying[b]	0.02–0.12	0.04–50.4	4–90	3–600
Immersion	n.r.	n.r.	No data	4–483
Mechanical treatment	n.r.	n.r.	18–154	47–214

nr, not relevant, use rate is not a parameter in the model

[a] From TNO (2006).

[b] For these processes, there was also a boundary for the combinations of use rate and duration that did occur. High use rates generally do not occur with high durations.

of the variation, but this does not indicate that a model with a high percentage of explained variance leads to an accurate estimate). A model is assumed to perform well if it shows a high "percentage explained variance", a low geometric standard deviation (for the variation after correction for the determinants) and a small confidence interval for the intercept term. An evaluation of the relative performance of the model for different processes and the concluding remarks of the model builders are presented in Table A3.6.

Table A3.6. Performance of RISKOFDERM[a]

Process	Percentage explained variance	GSD		95% confidence interval for intercept	Remarks
		Body	Hands		
Filling, mixing and loading	61	—	5.4	0.06–1.73	Overall good performance
Wiping	50	5.8	3.5	453–1464	Overall good performance
Dispersion hand-held tools	75	5.9	11.2	20.4–181	High GSD for hands; other parameters reasonable to good
Spraying	31	6.0	6.0	14.7–39.3	Moderate percentage explained variance; other parameters good
Immersion	29	9.4	34.2	0.8–76.7	Poor performance in all of the parameters
Mechanical treatment	53	4.9	—	6.4–34.4	Overall good performance

GSD, geometric standard deviation

[a] From TNO (2006).

A3.5 Listing of the exposure determinants and their selectable options in the tools RISKOFDERM and BEAT

Table A3.7. Exposure determinants and their selectable options in RISKOFDERM and BEAT[a,b]

Determinant	RISKOFDERM		BEAT	
	DEO unit	Selectable options	DEO unit	Selectable options
Physical state of formulation (in BEAT, in addition, "particle size" and "particle wetness"; see columns to right)	1, 4, 6	*DEO 1*: Highly dusty solids (solid particles with high tendency to become airborne)† Low or moderately dusty solids* Liquid formulations† *DEO 4*: (just for transferring unit of result, not a fixed effect, no influence on resulting exposure magnitude): Solid Liquid *DEO 6*: Solid† Liquid*	1, 2, 3, 4, 5, 6	Physical state: Liquid Solid Particle size: Like flour Like sand Granules/pellets Particle wetness: Dry Damp Paste/slurry
Aerosol generation	1	Processes leading to significant aerosol generation† No aerosol generation*	1, 2, 3, 4, 5, 6	Included via particle size and wetness; see above
Viscosity	3	Similar to water* Similar to syrup/honey† Similar to oil†	1, 2, 3, 5, 6	Like solvent Like water Like oil/grease
Volatility	4	Highly volatile liquid formulations† Not highly volatile*	4	Low $<$1 Pa Medium 1–500 Pa High $>$500 Pa

Table A3.7 (continued)

Determinant	RISKOFDERM		BEAT	
	DEO unit	Selectable options	DEO unit	Selectable options
Work environment (confined/restricted space)	4	Work environment is outdoors† Work environment is indoors*	2, 3, 4, 6	Confined/restricted Open (selectable classifications in user interphase: indoor – large enclosures; indoor – small/medium; outdoor – restricted spaces; outdoor)
Automation	1	Automated or semiautomated processes† Manual process*	1, 5	Fully manual Partially automated Fully automated
Ventilation	1, 4, 5	*DEO 1*: Normal or good ventilation* Poor or no ventilation† *DEO 4, 5*: Adequate LEV / directed airflow away from the worker† No adequate LEV / not away from the worker (by ventilation system or by movement)*	1, 3, 4, 6	LEV / airflow away from worker General ventilation No airflow Airflow towards worker
Liquid-based dust control	—	Not included	6	Yes No
Kinetic energy	—	Not included	1, 6	Low-energy process High-energy process
Spray pressure	—	Not included	4	Showering Low/medium pressure High pressure Misting/fogging

Table A3.7 (continued)

Determinant	RISKOFDERM		BEAT	
	DEO unit	Selectable options	DEO unit	Selectable options
Segregation	4	Physical barrier separating worker from spray aerosol, e.g. a tractor cab† No physical barrier*	4, 6	No segregation Partial segregation Complete segregation/containment
Surface area of contact	2, 3, 4, 5	*DEO 2*: Extensive body contact[1] with treated surface† No extensive body contact with treated surface* *DEO 2, 3, 4, 5*: Exposure of the body, excluding hands (implemented automatically, no option within the tool)†	2	Whole front body Half front body Hands and forearms Whole hands only Fingertips only
Kind of skin contact	1	Light contact[2] (surfaces, limited deposition of dust and aerosols)† More than light contact (splashes and drops)*	—	Not included
Level of contamination	—	Not included	2	Invisible swipe (solid) / touch dry (liquid) Thin layer (solid) / damp (liquid) Thick layer (solid) / wet (liquid)
Frequency of contact	1, 6	*DEO 1*: Infrequent/rare contact[3]† Frequent/more than rare contact* *DEO 6*: Rare or irregular contact* Frequent or continuous contact[4]†	2	Rare Intermittent Frequent or continuous

Table A3.7 (continued)

Determinant	RISKOFDERM		BEAT	
	DEO unit	Selectable options	DEO unit	Selectable options
Application/use rate	1, 2, 3, 4	Rate at which the formulation is handled or dispersed ($l \cdot min^{-1}$ or $kg \cdot min^{-1}$), implemented linearly	1, 3, 4	$l \cdot min^{-1}$ or $kg \cdot min^{-1}$
Distance to source (Proximity)	3, 4, 5, 6	*DEO 4, 6*: $>$100 cm from primary source of exposure (more than one arm's length)† $<$100 cm from primary source of exposure (within one arm's length)* *DEO 3*: $>$30 cm from primary source of exposure* $<$30 cm from primary source of exposure† *DEO 5*: $<$30 cm from primary source of exposure† $>$30 cm but $<$100 cm from primary source of exposure* $>$100 cm from primary source of exposure†	4, 6	$<$30 cm 30–100 cm $>$100 cm
Length of tool handle	See above	See above	3	Hand held ($<$30 cm) Long handled ($>$30 cm)

Table A3.7 (continued)

Determinant	RISKOFDERM		BEAT	
	DEO unit	Selectable options	DEO unit	Selectable options
Orientation	3, 4	*DEO 3, 4*: Level or overhead* Downwards† *DEO 4*: Level* Overhead† Downwards†	3, 4	Overhead Level Downwards
Duration	1, 2, 3, 4, 5, 6	Duration of exposure (min), implemented linearly	1, 2, 3, 4, 5, 6	Duration of exposure (min), implemented linearly

DEO, dermal exposure operation; LEV, local exhaust ventilation

[a] From Warren et al. (2006); BEAT (2011).

Notes:

* Determinants marked with an asterisk (*) are included in $\alpha 0$ (the mean (log) potential dermal exposure for the DEO). Deviations from this condition ($\alpha 0$) are implemented as fixed effects or otherwise (duration and application rate). Hand exposure is also included in $\alpha 0$, whereas body exposure is implemented via a fixed effect, which is not optional but is calculated automatically for each DEO unit where it is possible.

† Fixed effects.

Definitions for types of contact provided in the tool RISKOFDERM:

1 Extensive: worker tends to lean against wet surfaces or has to work in areas with extensive contact with freshly wiped surfaces. Otherwise select Not extensive.

2 Light: touching contaminated surfaces and/or limited deposition of dust or aerosol.
More than light: splashes and drops. Part of the worker is in direct contact with stream of substance.

3 Frequent/>rare: happens on average once or more per scenario.
Infrequent/rare: happens sometimes but on average less than once per scenario.

4 Frequent: contact happens with a high frequency, prolonged or constantly or has a clear regular pattern.
Rare or irregular: contact happens with a low frequency and without a regular pattern.

A3.6 Phillips & Garrod's (2001) indicative distribution approach (integrated in BEAT)

In the indicative distribution approach of Phillips & Garrod (2001), empirical distributions of dermal exposure data sets for biocide uses have been studied to seek commonalities for a large number of data sets (mainly based on patch method and cotton sampling gloves beneath protective gloves). Potential dermal exposure is influenced by various parameters related to the emission profiles and physical properties of the formulation and by the workplace conditions. The levels of dermal exposure (called "contamination") measured for each individual exposure studied were normalized over time to generate a rate of contamination (in-use formulation per unit of time), and the distribution parameter, median and geometric standard deviation of the non-zero values were determined. These statistical values of dermal exposure were assigned to four deposition levels and three idealized distribution profiles, resulting in a simple 12-box matrix (Table A3.8) of indicative values for potential dermal exposure (mass rate).

The authors stated that the values provided apply specifically to the category of jobs from which they were drawn and the key interpreted data on which they were based: non-agricultural pesticides, mixing

Table A3.8. Indicative values for biocide deposition rate of an in-use formulation[a,b]

Distribution profile		Deposition level ($mg \cdot min^{-1}$)			
		4 (low)	20 (medium)	100 (high)	500 (very high)
Narrow (GSD = 2.45)	Median	4	20	100	500
	P75	7 (9)	37 (46)	180 (225)	920 (1150)
	P95	18 (30)	87 (150)	440 (750)	2200 (3750)
Medium (GSD = 3.36)	Median	4	20	100	500
	P75	8 (12)	45 (60)	230 (300)	1100 (1500)
	P95	29 (60)	150 (300)	730 (1500)	3700 (7500)
Wide (GSD = 6.04)	Median	4	20	100	500
	P75	14 (15)	67 (75)	340 (375)	1700 (1850)
	P95	77 (100)	390 (500)	1900 (2500)	9700 (12 500)

GSD, geometric standard deviation; P75, 75th percentile; P95, 95th percentile

[a] From Phillips & Garrod (2001).

[b] The corresponding indicative distributions according to BEAT (2011) are provided in parentheses.

Table A3.9. Approximations of HSE empirical models to fit into the framework of Phillips & Garrod (2001)

Distribution profile	Deposition level ($mg \cdot min^{-1}$)			
	4 (low)	20 (medium)	100 (high)	500 (very high)
Narrow	Timber pretreatment (solvent), cabbed orchard spraying	Antifouling (mixing paint and ancillary tasks)[a]	x	x
Medium	x	Public hygiene, insecticide spraying, timber pretreatment (aqueous)	Antifouling paint sprayer	x
Wide	x	x	Remedial biocide spraying (including mixing and loading), uncabbed orchard spraying	Sheep dipping

HSE, Health and Safety Executive of the United Kingdom

[a] Remark for narrow profile / medium deposition level: The median value was 49 $mg \cdot min^{-1}$, but the profile of the result was concluded to be narrow by the authors.

and loading and spraying of antifouling paints (spraying ships), timber pretreatment, the use of public hygiene insecticides and remedial sheep dipping (see Table A3.9). However, these profiles (magnitude and spread) can be used to predict likely contamination for similar exposure situations where few or no data are available. An exposure situation can be described by the task itself or the technique used.

The worker actually spraying is expected to achieve a higher exposure rate than the ancillary workers who may tend the paint reservoir, manage the trailing paint lines or move the platform from which the painter operates. Additionally, the spread ("distribution") of exposure is broader for the spraying worker than for the ancillary workers. Exposure is higher when using water-based formulations in contrast to organic solvent–based formulations (surface tension and volatility may be important). Fine, low-pressure, aqueous spraying

processes result in lower rates than high-pressure spraying. High-pressure solvent-based spraying leads to deposition rates similar to those for medium-pressure spraying, but the spread of the data was less.

Many other variables may affect the deposition level and/or the spread of exposure, such as wind speed, the proximity to the coated surface or the confinement of the job (e.g. beneath the bottom of a vessel). The model does not incorporate further information as to the patterns of use, the concentration of the contaminant in the formulation or the frequency or duration of exposure.

Generally, it is concluded that discrete and well-defined jobs give rise to "narrow" exposure distributions, and the more variables that affect the distribution, the wider it becomes.

A3.7 Uncertainty factors (UF) used in BEAT

Table A3.10. Uncertainty factors for individual exposure determinants in BEAT[a]

Determinant	DEO unit	Description	UF body		UF hands	
Viscosity	1, 2, 3, 5, 6	Like organic solvent/water vs like oil	5		5	
		Like organic solvent/water vs like syrup	10		10	
		Like organic solvent/water vs like grease	10		10	
		Like oil vs like syrup	5		5	
		Like oil vs like grease	10		10	
		Like syrup vs like grease	5		5	
Particle size and wetness	1, 2, 3, 4, 5, 6	Like dry flour vs like dry sand	3		3	
		Like dry flour vs like dry granules	10		10	
		Like dry sand vs like dry granules	4		4	
		Like dry flour/sand/granules vs like paste/slurry	20		20	
Automation	1, 5	Manual process vs semiautomated process	10		10	
		Manual process vs automated process	50		50	
		Semiautomated process vs automated process	10		10	
Ventilation	1, 3, 4, 6		*DEO 1, 3*	*DEO 4, 6*	*DEO 1, 3*	*DEO 4, 6*
		LEV / airflow away from worker vs general ventilation	3	5	2	3
		LEV / airflow away from worker vs no airflow	3	5	2	3
		LEV / airflow away from worker vs airflow towards worker	10	10	5	10
		General ventilation vs no airflow	1	1	1	1

Table A3.10 (continued)

Determinant	DEO unit	Description	UF body		UF hands	
		General ventilation vs airflow towards worker	3	5	3	3
		No airflow vs airflow towards worker	3	5	3	3
Kinetic energy	1, 6	Low-energy process vs high-energy process	*DEO 1* 7	*DEO 6* 10	*DEO 1* 5	*DEO 6* 10
Use rate[b]	1, 3, 4	Ratio of use rates <50 Ratio of use rates >50	$r^{0.6}$ 50		 50	
Restricted spaces	2, 3, 4, 6	Open vs restricted spaces	10		5	
Frequency of contact	2	Rare contact vs intermittent contact Rare contact vs frequent or continuous contact Intermittent contact vs frequent or continuous contact	7 50 10		7 50 10	
Extent of contact	2	Fingertips only vs whole hands Fingertips only vs hands and forearms Fingertips only vs whole body Whole hands vs hands and forearms Whole hands vs whole body Hands and forearms vs whole body	1 50 100 20 100 10		10 10 10 1 1 1	
Contamination of objects	2	Touch dry vs damp Touch dry vs wet or saturated Damp vs wet or saturated	10 50 10		10 50 10	

Table A3.10 (continued)

Determinant	DEO unit	Description	UF body	UF hands
Length of tool handle	3	<30 cm (hand held) vs 30–100 cm (arm's length)	4	5
		<30 cm (hand held) vs >100 cm (beyond arm's length)	10	10
		30–100 cm (arm's length) vs >100 cm (beyond arm's length)	3	3
Orientation	3, 4	Downwards vs level	2	2
		Downwards vs overhead	7	5
		Level vs overhead	4	3
Volatility	4	High vs medium	3	3
		High vs low	5	5
		Medium vs low	2	2
Segregation	4, 6	No segregation vs partial segregation	10	10
		No segregation vs complete segregation/containment	100	100
		Partial segregation vs complete segregation/containment	10	10
Distance to source	4, 6	<30 cm (hand held) vs 30–100 cm (arm's length)	4	5
		<30 cm (hand held) vs >100 cm (beyond arm's length)	10	10
		30–100 cm (arm's length) vs >100 cm (beyond arm's length)	3	3

Table A3.10 (continued)

Determinant	DEO unit	Description	UF body	UF hands
Spray type	4	Showering/sprinkling vs surface spraying	2	2
		Showering/sprinkling vs space spraying	5	5
		Showering/sprinkling vs misting/fogging	5	5
		Surface spraying vs space spraying	5	5
		Surface spraying vs misting/fogging	5	5
		Space sprayings vs misting/fogging	1	1
Liquid-based dust control	6	No liquid-based dust control vs liquid-based dust control	5	5

LEV, local exhaust ventilation; UF, uncertainty factor

[a] From BEAT (2011).

[b] For DEO 1: Use rate applicable only if both scenarios are manual processes.

A3.8 POEM default values

Table A3.11. Default values for potential dermal exposure volume[a] on hands during mixing and loading per operation without gloves for liquid pesticide formulations[b]

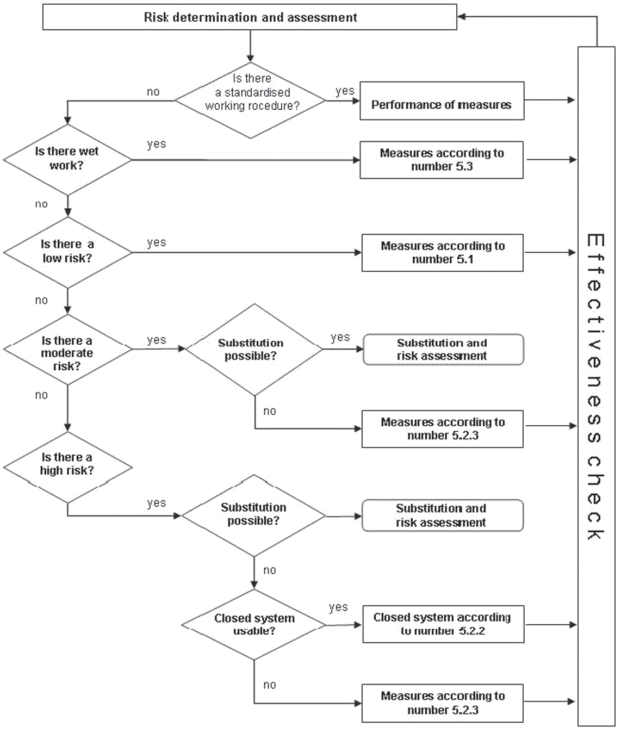
Size of container and diameter of opening	Dermal exposure volume[a] of non-diluted pesticide formulation (ml)
1 litre, any closure	0.01
2 litres, any closure	0.01
5 litres, narrow closure	0.2
5 litres, 45 or 63 mm closure	0.01
10 litres, narrow closure	0.5
10 litres, 45 mm closure	0.1
10 litres, 63 mm closure	0.05
20 litres, narrow closure	0.5
20 litres, 63 mm closure	0.05

[a] Called “potential contamination of hands”.

[b] From WHO (2011d).

APPENDIX 4: ADDITIONAL INFORMATION ON CHAPTER 8: METHODS FOR EXPOSURE PREVENTION AND REDUCTION

A4.1 Hierarchy of exposure control



5.1 General hygiene measures
5.2.2 Closed system
5.2.3 General hygiene measures, technical and organisational measures, eventually personal protective measures
5.3 General hygiene measures, technical and organisational measures, personal protective measures

Fig. A4.1. Procedure for laying down protective measures where there is skin contact (BAuA, 2011a).

Reprinted from TRGS 401, page 39, Ausschuss für Gefahrstoffe – Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA), www.baua.de.

A4.2 Selection guides/aids for gloves

STEP 1: Administrative Information	
Company	Department
Completed by	Section
Task details	
Task Location	Date Prepared
STEP 2: Control Information	
Control Measures (in place)	Reason for using gloves
	Residual risk
	Short duration work
	Interim measure
Safe Working Distance Measures	Temporary failure
	Emergency work
	Controls at source – not reasonably practical
	In case of control measures failure

STEP 3: Substances/Product Information		
Substances (used in the task)	Amount used Small (g or ml) Medium (kg or l) Large (Tonnes)	Forms encountered during the task (Solids - low dust, medium dust, high dust; Liquid - free flowing, viscous)
1		
2		
3		

Liquid Medium Water-based	Solvent based	oil based	other: water/solvent mix; water/oil mix

STEP 4: Work Related Information	
Task duration (minutes)	Task frequency/day
Dermal exposure pathways Immersion Direct contact Splashes Surface contact Deposition	
Dexterity requirement Low Medium High	Grip requirements Low High
Abrasion potential Low High	Cut potential Low High
Tear potential Low High	Puncture potential Low High
Humidity in the area where gloves are used Dry Wet	Temperature at which gloves are to be used (°C)
STEP 5: Wearers Related Information	
Likely exposure areas Hands Wrists Forearms	Glove exposure pattern Intermittent use Change after each use Regular use
Glove sizes required 6 7 8 9 10 11	Inner liner required (to absorb excess sweat) Yes No
Types of inner liner required:	
Any Other Relevant Information (e.g. hot spatter may land on the skin; paper work during the task; pH) Seek individual wearer information: e.g. (i) Missing fingers; (ii) known allergies or skin conditions.	

Fig. A4.2. "Glove selector" to provide supplier of gloves with suitable recommendations for protective gloves (Sithamparanadarajah, 2008).

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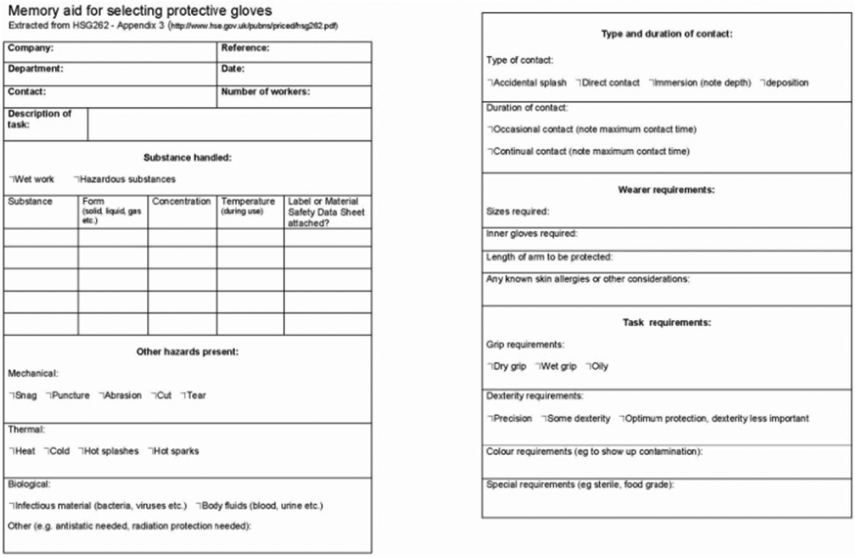

Memory aid for selecting protective gloves

Extracted from HSG262 - Appendix 3 (http://www.hse.gov.uk/pubns/priced/hsg262.pdf)

Company:	Reference:
Department:	Date:
Contact:	Number of workers:
Description of task:	

Substance handled:

¬Wet work ¬Hazardous substances

Substance	Form (solid, liquid, gas etc.)	Concentration	Temperature (during use)	Label or Material Safety Data Sheet attached?

Other hazards present:

Mechanical:

¬Snag ¬Puncture ¬Abrasion ¬Cut ¬Tear

Thermal:

¬Heat ¬Cold ¬Hot splashes ¬Hot sparks

Biological:

¬Infectious material (bacteria, viruses etc.) ¬Body fluids (blood, urine etc.)

Other (e.g. antistatic needed, radiation protection needed):

Type and duration of contact:

Type of contact:

¬Accidental splash ¬Direct contact ¬Immersion (note depth) ¬deposition

Duration of contact:

¬Occasional contact (note maximum contact time)

¬Continual contact (note maximum contact time)

Wearer requirements:

Sizes required:

Inner gloves required:

Length of arm to be protected:

Any known skin allergies or other considerations:

Task requirements:

Grip requirements:

¬Dry grip ¬Wet grip ¬Oily

Dexterity requirements:

¬Precision ¬Some dexterity ¬Optimum protection, dexterity less important

Colour requirements (eg to show up contamination):

Special requirements (eg sterile, food grade):

Fig. A4.3. "Memory aid for selecting protective gloves" (HSE, 2013a).

A4.3 Skin protective products

Table A4.1. SPP by allergen[a]

Allergen	Active agent or product name	Comment	Reference	Availability
Urushiol	Quaternium-18 bentonite	Very effective, absent or very reduced dermatitis	Liu et al. (2000)	http://www.ivyblock.com
	Stokogard	52% reduction in dermatitis severity	Bauer et al. (2001)	Not available
	Hollister moisture barrier	52% reduction in dermatitis severity	Not provided	http://www.hollister.com
	Hydropel	48% reduction in dermatitis severity	Not provided	Not available

Table A4.1 (continued)

Allergen	Active agent or product name	Comment	Reference	Availability
	Teflon-like polymer in perfluoroalkyl-polyether	Highly effective	Marks et al. (1995)	Not available
Epoxy resins	Kerodex 77 and Dermotect	Decreased intensity of reaction	Grevelink et al. (1992)	http://www.arsima.dk http://www.procar.nl
	Nobecutane and Organon	Methacrylate wound spray, decreased reaction intensity/area	Not provided	Not provided
Nickel	EDTA	Various EDTA formulations are effective	Vidmar & Iwane (1999)	Compounded cream
	5-Chloro-7-iodoquinolin-8-ol (clioquinol)	Most effective nickel ligand; is a potential neurotoxin	Not provided	Various formulations are commercially available
	Cream based on ion exchange resin	Very effective	Not provided	Not available
	Spray containing dexamethasone and isopropyl myristate	Very effective	Not provided	Not available
	DTPA	Oil-in-water emulsion; 96% reduction of positive reaction in patch test	Kalimo et al. (1999)	DTPA compounded with Hydrocream HY/Excipial
Potassium dichromate	1.8% Na_2H_2EDTA + 5.4% $CaNa_2EDTA$	Effective in reducing dermatitis	Vidmar & Iwane (1999)	Compounded cream
	Cream compound: silicone, glyceryl lactate, glycine, tartaric acid and base	60% effective in 60 workers	Macan et al. (2002)	Compounded cream

Table A4.1 (continued)

Allergen	Active agent or product name	Comment	Reference	Availability
Cobalt	DTPA	70% effective in patch test trial	Kalimo et al. (1999)	DTPA compounded with Hydrocream HY/Excipial
Copper	DTPA	64% effective in patch test trial	Kalimo et al. (1999)	DTPA compounded with Hydrocream HY/Excipial

DTPA, diethylenetriaminepentaacetic acid; EDTA, ethylenediaminetetraacetic acid

[a] Adapted from Schalock & Zug (2007).

Table A4.2. Selection of SPP[a]

	Duration/extent of skin contact			
	Short term		Longer term	
	Small area	Large area	Small area	Large area
Unclassified substances	Depending on the risk assessment			
Working in a wet environment	+			
R66	+	+	+	+
R38	+	+	+	–
R21	+	–	–	–
R34, R35	–	–	–	–
H	–	–	–	–
R24, R27	–	–	–	–
R40, R45, R46, R48	–	–	–	–
R60, R61, R62, R63	–	–	–	–
R68	–	–	–	–
R43, R42/43	–	–	–	–
Sh, Sah	–	–	–	–

+, use of skin protection agents possible; –, use of skin protection agents not possible

H, possible dermal absorption; Sh, substance with skin sensitizing properties; Sah, substance with skin sensitizing properties and respiratory allergen (see section 8.2.2)

[a] Annex 9 to TRGS 401 (BAuA, 2011a).

A4.4 Test methods

A4.4.1 In vitro methods

The need for standardized test methods for evaluation of the performance of protective gloves has long been recognized, and numerous national and international standards for efficacy testing of gloves have been developed (Zimmerli, 1996; Henry, 2005; Mellström & Carlsson, 2005). In addition to the review of common in vitro and in vivo test methods provided here, other standardized leakage tests and their limitations have been reviewed by Carey et al. (1989).

A4.4.1.1 Degradation testing

Degradation is defined as a deleterious change in one or more physical properties of a protective clothing material due to contact with a chemical (ASTM F739-12). The immersion test has been traditionally used by manufacturers to assess the chemical resistance of protective gloves. During the test, pieces of the glove material are immersed in different chemicals and subsequently visually inspected. Resistance properties are rated as excellent, good, fair or not recommended. Besides the qualitative nature of this rating, the test results are deemed to be frequently misleading, as both sides of the material are simultaneously exposed to the chemical (Boman et al., 2005). A modification of the test allows for exposure of only the external side of the material and grading according to the change in the weight after some exposure period. Although there are currently no established standards, degradation testing can be used as a screening procedure during the development of protective materials.

A4.4.1.2 Permeation testing

Permeation is the process by which a chemical migrates through the protective material on a molecular level. It involves the sorption of the chemical onto the external surface of the test material, molecular diffusion through it and desorption of the molecules from the internal surface of the sample (Boman et al., 2005).

Standards for permeation testing of protective materials have been established in the USA and Europe. These standards have been

Table A4.3. Standards for permeation testing of protective materials

Standard	Description
ASTM F739-12	Standard test method for permeation of liquids and gases through protective clothing materials under conditions of continuous contact
ASTM F1383-12	Standard test method for permeation of liquids and gases through protective clothing materials under conditions of intermittent contact
EN 374-3:2003	Protective gloves against chemicals and microorganisms. Part 3: Determination of resistance to permeation by chemicals
ISO 6529:2013-02	Protective clothing—Protection against chemicals—Determination of resistance of protective clothing materials to permeation by liquids and gases

adopted by other countries as well, and an international ISO standard has been developed (Table A4.3). EN 374:2003 specifies conditions for permeation testing of protective gloves by both liquid and solid chemicals, whereas ISO 6529:2013-02 deals with permeation of protective clothing by liquid substances. ASTM F739-12 and ASTM F1383-12 describe procedures for testing of gases under conditions of continuous and intermittent contact.

As most elements of the testing procedures are similar between the different standards, description of the method is based on ASTM F739-12. Permeation tests are performed in a specially designed two-compartment flow-through system of standard dimensions (see section A4.4.1.3). Samples are cut from the palms of gloves and placed between the two compartments of the permeation cell. The first compartment contains the test chemical, which is in contact with the outer surface of the glove. Air or water is passed through the second compartment of the cell to collect any chemical that has migrated to the inside surface of the sample. Resistance to permeation is assessed by measuring the breakthrough time (the time between the initial application of the chemical and its detection on the other side of the sample) and the permeation rate (mass of the chemical passing through the test material per unit of time and per unit of area) (in $\mu g \cdot min^{-1} \cdot cm^{-2}$).

Standard method EN 374-3:2003 employs the same permeation cell and test procedure as ASTM F739-12, except that the flow rate of the collection medium is different. For an open-loop system, the flow rate

of the gaseous collection medium should be equivalent to five volume changes of the collection chamber per minute (i.e. 500 ml·min^{-1}). The resistance of a protective glove is determined by the normalized breakthrough time when a permeation rate of 1 mg·cm^{-2}·min^{-1} is detected. ISO 6529 specifies the permeation cell and flow rate of the collection medium similar to those of EN 374-3:2003. Further similarities and differences between these standards are reviewed in Boman et al. (2005).

Established breakthrough times depend to a large extent on the test conditions (e.g. temperature, stretching of glove, duration of exposure, selection of test method). Hence, they give only a rough indication of how long a glove can be used before the chemical will permeate through it. EN 374-1:2003 includes a protection index based on breakthrough times from tests with various combinations of gloves and test chemicals (Table A4.4). Usually, glove manufacturers publish information on breakthrough times of their products and a list of chemicals against which they have been tested. The "chemical resistant" pictogram must be accompanied by a three-digit code, referring to the code letters of 3 chemicals (from a list of 12 standard defined chemicals) for which a breakthrough time of at least 30 minutes has been obtained.

It should be noted, however, that testing the barrier properties of chemical gloves under the above conditions does not sufficiently represent the situation of real workplace exposures. Elevated temperature inside the glove due to body heat, mechanical stretching, duration and

Table A4.4. Classification of protective gloves based on chemical permeation test results according to EN 374:2003

Protective index	Breakthrough time (min)
1	>10
2	>30
3	>60
4	>120
5	>240
6	>480

pattern of exposure, as well as exposure to a single chemical or to a chemical mixture, may have a significant impact on the real protection time of gloves.

A4.4.1.3 Penetration testing

Penetration is defined as chemical flow through material pores, closures, seams, pinholes or other imperfections of the protective material on a non-molecular level. Penetration testing is performed to evaluate the penetration of liquids through gloves and other protective materials on a non-molecular level. Standard penetration tests are used as a quality control measure to ensure that gloves are free from holes (tests for leakage). The ASTM and EN test procedures shown in Table A4.5 have been standardized.

During the water leak test in EN 374-2:2003, the glove is filled with 1000 ml of water and visually examined for leaks. Any detectable water on the outside of the glove before or after a 2-minute observation time indicates a failure of the test. Both water leak tests in EN 374-2:2003 and EN 455-1:2000 use similar procedures and are well suited for quality control, as they utilize the whole glove and not only parts of it. Overall, the "1000 ml water leak test" has been considered as the best combination of utility and performance when compared with other leakage tests (Schroeder et al., 2005). In the air leak test, the glove is inflated under water with air of predetermined pressure and then inspected for the release of air bubbles.

Table A4.5. Standards for penetration testing of protective materials

Standard	Description
ASTM F903-10	Standard test method for resistance of materials used in protective clothing to penetration by liquids
EN 374-2:2003	Protective gloves against chemicals and microorganisms. Part 2: Determination of resistance to penetration (including methods for air and water leak testing)
EN 455-1:2000	Medical gloves for single use. Part 1: Requirements and testing for freedom from holes

In standard test ASTM F903-10, part of the glove is mounted in a penetration test cell and challenged with liquid under defined pressure. Observation of visible water on the outside of the membrane after a predefined time indicates failure of the test. A viral penetration test for elastomeric materials is implemented in ASTM F1671/F1671M-13. The test uses phi-X174 bacteriophage and offers a good combination of utility and performance.

Degradation, permeation and penetration testing is a valuable means for the assessment of gloves' protective effect. Several other standardized leakage tests and their limitations have been reviewed by Carey et al. (1989). It should be noted that standard test methods are designed to provide reproducible results for laboratory testing and are not intended to represent the complexity of workplace use situations. In addition, the permeation test results will depend to a certain extent on minor variability in test conditions, such as design of the test cell, choice, volume, temperature and flow rate of collecting medium, sampling strategy, sensitivity of analytical equipment and qualification of testing personnel. Combined with results from other tests and considering all relevant factors, data from standardized permeation and penetration testing offer the best basis for glove selection.

A4.4.2 In vivo testing of protective gloves

In vivo methods for glove testing are a good supplement to in vitro permeation and penetration testing and provide valuable information on the maximum protection time under conditions of practical use. In vivo tests can be performed in experimental animals or humans; however, they are more time consuming than in vitro tests and subject to substantial ethical considerations.

A4.4.2.1 Animal studies

Animal studies are usually performed with guinea-pigs. Prior to actual testing, the hair on the back of the animal is removed, and a catheter is inserted into the animal's carotid artery to allow for blood sampling during the subsequent chemical exposure. The glove under investigation is fixed on a glass ring, the chemical is added and the

ring is attached to the skin. Blood samples are drawn regularly during a predefined exposure period. The method measures the cumulative effect of both penetration and absorption into the systemic circulation and does not provide any insights on the processes that take place at the dermis or epidermis. Compared with in vitro testing, this animal model is a closer approximation to the real-life situation, where different biological factors, such as the effect of occlusion and compromised skin barrier, can be considered. However, this model does not account for possible variations found in real workplace conditions and provides no means to assess biologically significant responses, such as the development of contact dermatitis.

A4.4.2.2 Patch testing with allergens

Patch tests can be performed in already sensitized individuals during clinical examination of suspected contact dermatitis. When a patient is tested for different workplace allergens and a sensitizer is identified, the potential protective effect of gloves can also be evaluated. During the patch testing, the allergen is applied on the outer surface of a glove piece, which is then fixed on the back of the patient. Application time under occlusion is usually 2 days, and the setup requires the parallel evaluation of a positive control (the substance without glove material) as well as a negative control (the glove material alone). This experimental design, however, does not sufficiently represent the actual everyday use of protective gloves in various work situations. Patch testing has been applied for some photography chemicals, epoxy resin components and glyceryl monothioglycolate (Svedman & Bruze, 2005).

A4.4.2.3 Open chamber system

The open chamber system for glove testing has been developed to closely imitate the practical use of the glove while remaining relatively safe for the patient. The model allows for in vivo testing in humans, taking into consideration various individual factors, such as skin condition and temperature, occlusion and humidity. The testing device consists of three open circular stainless steel chambers placed in a flexible acrylic plate. The examined glove material is fixed to the

chambers such that it constitutes the bottom of the chamber and the contact surface with the skin (Svedman & Bruze, 2005). During the test, the acrylic plates with the chambers are fixed to the skin, typically on the back or the forearm of the patient, and a standardized volume of the test product or chemical is applied to the bottom of the chambers. Uncovered chambers can be used as a positive control, whereas glove material with known protection against the test chemical can constitute the negative control. Exposure times should be selected to closely mimic the workplace situation, and positive controls should be of limited duration to prevent severe skin damage. Evaluation of the test results is based on the transient eczematous reaction of the skin in response to the chemical passed through the glove material. Testing with some acrylates has demonstrated the ability of this test to discriminate between the protective effects of several different glove types (Svedman & Bruze, 2005).

RÉSUMÉ

L'exposition dermique a été reconnue comme un mode d'exposition important, la population s'exposant directement ou indirectement à divers produits et substances, au travail, au domicile ou dans les installations publiques. Il s'agit d'un processus complexe de contact entre une substance et la peau pendant un certain temps. Les maladies qui résultent de cette exposition (et de l'absorption qui s'ensuit) peuvent avoir un impact important sur la santé. La meilleure méthode pour gérer les risques associés à l'exposition dermique consiste à identifier les dangers à prendre en compte (produits chimiques et autres), les sources et les voies d'exposition, à faire une évaluation quantitative de l'exposition (soit en la mesurant, soit en la modélisant) pour approfondir l'estimation du risque et, finalement, à éliminer ou au moins réduire et limiter l'exposition.

1.1 Sources et voies d'exposition

En milieu professionnel, les expositions dangereuses dépendent en général soit de l'activité, soit du profil de toxicité d'un produit. Les expositions dermiques résultent le plus souvent d'éclaboussures, de déversements accidentels ou de traînées (principalement au cours du mélange ou du chargement), pendant l'application elle-même ou par le biais de surfaces contaminées, comme des machines ou feuilles diverses. Par conséquent, les conditions du scénario général d'exposition étant influencées par les réglementations nationales sur la sécurité et les normes au travail, les principaux déterminants entraînant une exposition dermique pourraient être différents dans les pays développés et ceux en développement (par exemple le travail à mains nues, l'utilisation d'un équipement qui fuit et le fait de travailler avec des contraintes réglementaires de sécurité moins strictes dans les pays en développement). Les pesticides, les solvants organiques et les liquides pour la transformation des métaux sont tous considérés comme contribuant de manière importante aux maladies professionnelles. Le contact prolongé ou répété avec l'eau (travaux humides) peut également être nocif pour la peau, un effet pouvant être renforcé

par la présence d'autres agents irritants (par exemple dans des secteurs comme la coiffure ou la métallurgie).

Bien que la manipulation directe et l'application sur la peau puissent être considérées comme les sources d'exposition dermique les plus directes, des études ont établi que d'autres voies ou procédés peuvent être souvent les plus significatifs. Il faut donc aussi considérer les voies indirectes d'exposition (comme le contact avec des substances déposées ou adsorbées sur des surfaces). Des exemples en sont le fait de retourner dans un champ après l'épandage de pesticides, le contact avec des matières contaminées ou des résidus, comme le plomb des peintures dans les poussières ou les sols. De plus, il arrive que les travailleurs vivent près des installations où ils sont employés et qu'ils ramènent en outre (volontairement ou non) des produits dangereux à leur domicile, parfois pour les entreposer. Les agents ou travailleurs eux-mêmes ainsi que leur famille ont alors une exposition supplémentaire à leur domicile, celle-ci pouvant affecter particulièrement les jeunes enfants et les personnes âgées, qui peuvent être plus sensibles. Les facteurs contribuant aux expositions de ce type sont le manque de formation et de connaissances sur les produits et méthodes spécifiques (par exemple pour le contrôle des pesticides), ainsi que la facilité d'accès à des produits très toxiques peu coûteux.

Hors cadre professionnel, la population peut être exposée par voie dermique à des produits chimiques de diverses classes en utilisant toute une gamme de produits de consommation, notamment les produits d'hygiène personnelle et les cosmétiques, les textiles (et les chaussures) et les produits ménagers, soit en raison des conditions d'utilisation, soit du fait des profils toxicologiques. Par exemple, l'utilisation des produits d'hygiène personnelle et des textiles entraîne un contact direct avec la peau, prolongé, parfois répétitif (utilisation quotidienne), très souvent sur une grande partie de la surface corporelle. Si, pour de tels produits, des substances critiques pour la voie dermique (par exemple des allergènes nouveaux ou inhabituels) sont utilisées, des effets négatifs peuvent survenir, comme des réactions allergiques par contact.

Les parfums et les conservateurs sont les allergènes les plus fréquemment utilisés dans les produits d'hygiène personnelle, les cosmétiques, les produits ménagers, ainsi que les textiles, les jouets

d'enfants et les désodorisants. La composition des produits change fréquemment et les réglementations et définitions nationales pour leur innocuité varient selon le pays. Il existe de plus une diversité internationale des produits commercialisés et certains peuvent être utilisés depuis longtemps (par exemple pour des raisons culturelles). C'est ainsi que l'on a observé que certains produits cosmétiques traditionnels entraînaient une exposition dermique à des métaux lourds (par exemple le khôl pour les yeux) ou des allergies sévères (par exemple le henné noir pour les tatouages temporaires).

Il faut faire spécialement attention à l'exposition dermique des enfants en raison de leur activité particulière (pendant la journée, ils sont couchés, ils rampent, ils touchent à tout et ont tendance à tout mettre à la bouche) et de leur plus grande surface corporelle par rapport au poids comparé aux adultes. De plus, les jouets et d'autres produits dans leur domicile peuvent renfermer diverses substances empruntant la voie de l'exposition dermique (par exemple les produits ignifuges, les hydrocarbures aromatiques polycycliques, les phtalates, les plastifiants).

1.2 Méthodes analytiques pour estimer l'exposition dermique

Différentes méthodes peuvent être utilisées et l'on peut les classer grossièrement en méthodes directes et indirectes. Les méthodes directes peuvent être subdivisées en trois groupes : interception, enlèvement et in situ. Les techniques d'interception impliquent d'utiliser des dosimètres ou des patches remplaçant la peau pour la collecte des substances ou produits déposés. Les techniques d'enlèvement comportent des méthodes d'échantillonnage fréquemment utilisées – essuyage, lavage des mains, application de ruban adhésif – ainsi que les méthodes plus rarement employées comme l'aspiration et l'immersion. La technique in situ la plus importante est l'imagerie par vidéo.

Les trois méthodes d'échantillonnage se fondent sur des conceptions techniques différentes, aboutissant à des caractéristiques ou limitations spéciales. Par exemple, pour les techniques d'interception, le matériel évite en général le processus potentiel d'absorption. Les techniques d'enlèvement ne prélèvent que la substance disponible sur

la surface cutanée et l'on ne peut évaluer celle qui a été absorbée pendant l'exposition. Pour les images vidéo, on se sert d'un traceur et c'est la similitude entre lui et la substance qui détermine l'exactitude de la mesure. Des différences supplémentaires dans les résultats analytiques peuvent être dues à la voie d'exposition. Certaines lacunes ont été identifiées; elles concernent la validation analytique des procédures d'échantillonnage, l'absence d'études comparatives et le manque de procédures harmonisées au plan international.

Les méthodes indirectes soit analysent les processus avant l'exposition dermique (méthodes par migration et transfert), soit mesurent les concentrations de produits dans les liquides ou les tissus de l'organisme après absorption (surveillance biologique). Les mesures de la migration déterminent la quantité de substance pouvant migrer dans un liquide (par exemple la sueur) par unité de surface. La vitesse de migration dépend principalement de la combinaison substance-matrice. Dans la méthode par transfert, les paramètres de transfert (coefficients ou taux) décrivent le processus de transfert vers la peau et dépendent de l'activité étudiée, de même que de la combinaison substance-matrice.

La surveillance biologique est un outil très utile pour évaluer le risque, en particulier lorsqu'il faut prendre en compte plusieurs voies d'exposition. Pour l'exposition dermique, elle suppose la connaissance de la toxicocinétique afin de pouvoir extrapoler la quantité initiale de l'exposition dermique. De plus, les autres voies d'exposition, inhalation et voie orale, doivent être négligeables pour pouvoir évaluer l'exposition dermique.

Actuellement, la conception des études utilisées pour estimer l'exposition dermique est principalement orientée sur des aspects pratiques. Il n'y a pas de méthodes applicables en toute circonstance, et il est impossible de fournir un guide pour aider à choisir celle qui convient dans une situation particulière. Pour combler les lacunes actuelles dans les connaissances, des études comparatives sont nécessaires. Elles devraient aider à comparer l'utilité des méthodes, à déduire des protocoles harmonisés et, en fin de compte, à améliorer notre compréhension des processus et des déterminants sous-jacents de l'exposition dermique.

1.3 Modèles et outils pour estimer l'exposition dermique

En l'absence de valeurs mesurées ou lorsque des mesures ne sont pas faisables, on considère que la modélisation est une méthode utile pour évaluer l'exposition dermique. On utilise cette technique à différentes fins, souvent motivées par des besoins réglementaires, comme l'estimation de l'exposition dans une population en particulier, l'évaluation de l'efficacité des mesures de réduction du risque ou la détermination des limites pour les substances dans les produits. On a mis au point des modèles décrivant les processus physiques ainsi que des modèles empiriques, et on peut mettre en œuvre un ou plusieurs modèles dans des logiciels ou d'autres outils (feuille de calcul, par exemple) pour en simplifier l'utilisation.

Plusieurs modèles et outils, mis au point pour différents objectifs, sont présentés. Le concept semi-quantitatif DREAM est conçu pour évaluer les déterminants de l'exposition et fournir des informations liées à l'activité pour des stratégies de mesure analytique. DERM a pour vocation d'être un outil pratique « facile d'emploi » (par exemple pour les programmes éducatifs dans les pays en développement). RISKOFDERM se base sur la notion de créer des modèles à partir de groupes déterminés d'après les tâches en utilisant les mesures disponibles. BEAT donne l'option de rechercher des scénarios similaires d'exposition avec les données mesurées pouvant être combinés avec un modèle hiérarchique bayésien pour des prévisions de probabilité. ECETOC TRA a été mis au point comme outil de criblage pour l'évaluation du risque, MEASE est conçu pour l'exposition des travailleurs aux métaux et autres matières inorganiques, ConsExpo couvre plusieurs activités liées aux consommateurs et SprayExpo s'intéresse à diverses applications en pulvérisation. Bien que les deux méthodes portent sur les pesticides, les modélisations de l'Union européenne (modèles allemands et néerlandais, POEM et EUROPOEM) diffèrent des modèles orientés sur le récepteur que l'on trouve aux États-Unis d'Amérique (Calendex, CARES, LifeLine, PHED, SHEDS), ces derniers rendant compte de l'exposition dermique cumulée par de multiples voies.

Il est impossible de dire quels modèles ou quels outils sont les plus exacts dans des circonstances déterminées, lesquels donnent

des résultats comparables et ceux dont on devrait recommander l'utilisation, du fait que leur portée, leurs caractéristiques et leurs limitations sont variables. Pour des situations très similaires d'évaluation de l'exposition, différents modèles et outils peuvent être utilisés selon les organisations. Il en résulte que l'évaluation et la description de l'applicabilité des modèles et outils sont sous l'influence de divers facteurs, comme l'objectif initial ayant dirigé leur mise au point (souvent dans un contexte réglementaire), les descriptions de leur tâche, leur base de données et l'usage approprié des valeurs fournies par défaut, ainsi que les étapes pour l'extrapolation. Le présent document constitue une première tentative de donner un aperçu général et comparatif de l'applicabilité, des caractéristiques et des limitations des différents modèles. De plus, un appendice donne les algorithmes sous-jacents des modèles et outils présentés sous une forme synchronisée et condensée afin de faciliter la comparaison des principes de base et des déterminants de l'exposition retenus dans les différents modèles.

1.4 Dermatoses associées à l'exposition dermique

L'exposition dermique peut entraîner des lésions locales et/ou des effets systémiques après le franchissement de la barrière cutanée, et l'on observe un risque émergent de développement de dermatoses susceptibles d'avoir des répercussions critiques sur la santé et l'économie des personnes qui travaillent comme du grand public. Les dermatoses les plus courantes sont décrites, de même que les situations typiques qui les provoquent. La plus importante est l'eczéma (ou dermite) de contact (inflammation localisée), provoqué par un contact direct de la peau avec des irritants ou des allergènes externes. Il y en a deux types, irritatif ou allergique. Dans le cadre professionnel, la plus importante est la dermite de contact irritative, qui représente 50 à 90 % des dermatoses dues au contact avec des produits chimiques ou au travail en milieu humide. La part des dermatoses professionnelles est d'environ 10 % sur l'ensemble des maladies professionnelles en Europe et aux États-Unis, avec une prévalence (mesure de la fréquence de la maladie) pouvant atteindre 65 % des personnes employées dans certains secteurs comme la coiffure, la peinture ou le nettoyage. Par contre, la dermatose la plus répandue dans la population générale est l'eczéma de contact allergique, avec une prévalence de 21,2 % (dermite de contact résultant de l'exposition à au moins un

allergène) dans les populations d'Amérique du Nord et d'Europe de l'Ouest. D'autres maladies cutanées et des effets directs (par exemple l'irritation, l'urticaire, l'acné, des cancers et la phototoxicité) sont également présentés.

1.5 Méthodes de prévention et de réduction de l'exposition

Un bref aperçu des mesures législatives prises pour protéger les travailleurs et les consommateurs ainsi que les méthodes générales d'identification des dangers sont présentés. Il y a ensuite une explication des méthodes utilisées pour réduire l'exposition en les hiérarchisant.

Dans de nombreux pays, la législation porte sur la manipulation sans danger des substances sur le lieu de travail. Les lois concernant le consommateur traitent fréquemment de l'étiquetage et du conditionnement. Les avertissements des dangers et des précautions à prendre conformes au Système général harmonisé de classification et d'étiquetage des produits chimiques alertent les travailleurs et les consommateurs des dangers et leur conseillent l'utilisation correcte. De plus, plusieurs institutions calculant les limites de l'exposition professionnelle fournissent également des notations pour la peau, indiquant le potentiel d'absorption dermique d'un produit chimique. Enfin, les limites de l'exposition dermique professionnelle se veulent des mesures quantitatives de l'exposition maximale acceptable.

L'élimination ou la substitution sont les méthodes préférées de prévention de l'exposition dermique. Les autres mesures pour la réduire sur le lieu de travail comportent les contrôles techniques, les mesures prises au niveau de l'organisation et, enfin, l'équipement de protection individuel. Les contrôles techniques comportent des méthodes de séparation (par exemple l'enfermement, le confinement ou l'isolement), des changements de produits ou de procédé (par exemple des produits moins concentrés, des liquides ou des granulés au lieu de poudres, le conditionnement dans de plus petits récipients). Les mesures au niveau organisationnel définissent les pratiques et procédures au travail et couvrent la formation du personnel professionnel et les conséquences du non-respect. L'équipement de protection individuel doit être envisagé « en dernier ressort » si

d'autres mesures ne peuvent être mises en pratique. Les critères de sélection pour l'utilisation de ce type d'équipement sont récapitulés; les facteurs influant sur l'efficacité des équipements (par exemple les caractéristiques du matériel, les conditions d'utilisation et de travail, l'acceptation, l'utilisation et l'entretien corrects par l'utilisateur) sont décrits de manière plus détaillée.

Hors cadre professionnel, on peut obtenir une prévention et une réduction de l'exposition en introduisant des changements modifiant les produits, en donnant des instructions ou en communiquant sur l'usage sans danger ou en prenant des mesures administratives. On considère que la mesure la plus efficace est de changer les produits (par exemple en autorisant une concentration maximale ou en modifiant la forme: pastilles ou granulés par exemple au lieu de poudres). Les mesures administratives (par exemple la fixation de valeurs limites, des restrictions à la commercialisation ou une interdiction), ainsi que la nécessité d'améliorer l'étiquetage des produits dangereux pour sensibiliser le public aux risques potentiels sont également exposées.

Enfin, il y a une présentation des différences d'efficacité de plusieurs réglementations.

RESUMEN

Ya sea en el trabajo, en el hogar o en establecimientos públicos, la población está expuesta, directa o indirectamente, a gran diversidad de sustancias y productos. Por ello, se ha señalado que una importante vía de exposición es la exposición cutánea, un complejo proceso de contacto temporal entre la sustancia implicada y la piel. Las enfermedades derivadas de la exposición —y la consiguiente absorción— cutánea pueden tener considerables repercusiones en la salud humana. El mejor modo de gestionar los riesgos de la exposición cutánea consiste en identificar los peligros (sustancias y productos químicos) y las fuentes y vías de exposición pertinentes, evaluar cuantitativamente la exposición (midiéndola o calculándola mediante un modelo) para refinar la evaluación del riesgo y, finalmente, eliminar o, al menos, reducir y controlar la exposición.

1.1 Fuentes y vías de exposición

En el entorno laboral, generalmente, las exposiciones peligrosas están condicionadas por el tipo de actividad profesional o el perfil de toxicidad de un producto. La exposición cutánea tiene lugar principalmente como consecuencia de salpicaduras, derrames o difusión del producto (en especial durante los procesos de mezcla y carga), en el transcurso de su aplicación o por contacto con superficies contaminadas, como maquinaria o material vegetal. Dado que algunas de las circunstancias que rodean a cualquier tipo de exposición están sujetas a los reglamentos de seguridad y las normas laborales de cada país, es posible que los principales factores que determinan la exposición cutánea no sean los mismos en los países desarrollados y en los países en desarrollo. En estos últimos cabe mencionar, por ejemplo, el uso de las manos como herramientas de trabajo, la utilización de equipos no estancos y una regulación menos estricta de la seguridad laboral. Los plaguicidas, los disolventes orgánicos y los líquidos de metalistería contribuyen notablemente a la morbilidad laboral. También el contacto prolongado o repetido con el agua puede resultar perjudicial para la piel, y este efecto puede verse potenciado por la presencia de otras

sustancias irritantes (por ejemplo, en profesiones como la peluquería o la metalistería).

Si bien la manipulación directa y la aplicación sobre la piel se consideran las fuentes más inmediatas de exposición cutánea, en diversos estudios se ha observado que, con frecuencia, son otras vías u otros procedimientos los principales implicados. Así, también deben tenerse en cuenta las vías indirectas de exposición cutánea, como el contacto con sustancias depositadas o adsorbidas sobre una superficie. Algunos ejemplos son el acceso a un campo de cultivo tras la aplicación de un plaguicida y el contacto con materiales contaminados o con otros residuos, como el plomo de pinturas presente en el polvo doméstico o en la tierra. Por otra parte, puede que los trabajadores vivan cerca de su lugar de trabajo y que, además, involuntaria o intencionadamente, transporten sustancias peligrosas a sus hogares o las almacenen en ellos. De ese modo, los trabajadores u operarios estarían expuestos también en el interior de sus casas, al igual que sus familias. La exposición doméstica puede afectar especialmente a los niños pequeños y a los ancianos, dada su mayor vulnerabilidad. Entre los que factores que contribuyen a estos tipos de exposición sobresalen la falta de formación adecuada y el desconocimiento de los productos y métodos específicos (por ejemplo, para el control de plagas), así como la facilidad de acceso a productos baratos y de gran toxicidad.

En entornos no laborales, la utilización de diversos productos de consumo supone la exposición cutánea a sustancias químicas de distintas clases. En este sentido, cabe destacar, bien por sus condiciones de uso o por su toxicidad inherente, los productos de cuidado personal, los cosméticos, los textiles (incluido el calzado) y los productos domésticos. En el caso de los productos de cuidado personal y textiles, su utilización implica un contacto directo con la piel que, a menudo, abarca una gran parte de la superficie corporal, es de larga duración y ocurre repetidamente (con el uso cotidiano). Si estos productos contienen sustancias potencialmente perjudiciales por vía cutánea (por ejemplo, alérgenos nuevos o inusuales), pueden provocar efectos adversos tales como reacciones alérgicas de contacto.

Las fragancias y los conservantes son los alérgenos más habituales en productos de cuidado personal, cosméticos y productos domésticos,

así como en productos textiles, juguetes y ambientadores. Los ingredientes de los productos se cambian con frecuencia, y los reglamentos y las definiciones de seguridad varían de un país a otro. También varían los productos que se comercializan en cada país, y algunos pueden utilizarse durante largo tiempo (por ejemplo, por motivos culturales). Tal es el caso de algunos cosméticos tradicionales, cuyo uso conlleva la exposición cutánea a metales pesados (por ejemplo, el *kohl* o *surma* como cosmético para los ojos) o puede producir reacciones alérgicas graves (por ejemplo, la alheña o *henna* negra para tatuajes temporales).

Se presta especial atención a la exposición cutánea de los niños, debido a sus pautas específicas de actividad (tumbarse, gatear, tocar objetos y llevárselos a la boca) y a que presentan una mayor relación entre la superficie corporal y el peso que los adultos. Asimismo, los juguetes y otros productos de su entorno doméstico pueden contener diversas sustancias potencialmente perjudiciales por vía cutánea (pirorretardantes, hidrocarburos aromáticos policíclicos, ftalatos o plastificantes, entre otros).

1.2 Métodos analíticos de evaluación de la exposición cutánea

Para valorar la exposición cutánea se emplean diferentes métodos que, en líneas generales, pueden clasificarse como directos o indirectos. A su vez, los métodos directos se dividen en tres grupos: las técnicas de interceptación, las técnicas de eliminación y las técnicas *in situ*. Para la interceptación se emplean dosímetros de cuerpo entero o parches, que recogen los productos o sustancias que se depositarían en la piel. Las técnicas de eliminación incluyen métodos de muestreo de uso frecuente —el frotamiento, el lavado de manos y las tiras de cinta adhesiva— o infrecuente, como los métodos de succión o inmersión. La técnica *in situ* más importante es la visualización en video.

Estas tres modalidades de muestreo están basadas en diseños técnicos distintos, y por ello sus características y sus limitaciones son diferentes. Por ejemplo, en el caso de las técnicas de interceptación, el material empleado suele impedir el posible proceso de absorción. Mediante las técnicas de eliminación únicamente pueden recogerse muestras de la sustancia presente en la superficie de la piel, pero no se puede determinar la sustancia absorbida durante la exposición. Para

la visualización en video se utiliza un marcador, y la exactitud de la medición depende de la similitud entre este y la sustancia. Otras diferencias en los resultados analíticos pueden deberse a la vía de exposición. Las deficiencias detectadas se refieren a la validación analítica de los procedimientos de muestreo, la falta de estudios comparativos y la ausencia de procedimientos armonizados de ámbito internacional.

Los métodos indirectos permiten estudiar los procesos antes de que se produzca la exposición cutánea (métodos de migración y de transferencia) o medir las concentraciones de la sustancia en los líquidos o los tejidos corporales tras la absorción (vigilancia biológica). Mediante el método de migración se determina la cantidad de la sustancia que puede migrar a un líquido corporal artificial (por ejemplo, sudor) por unidad de superficie del producto. La tasa de migración depende fundamentalmente de la combinación sustancia-matriz. Mediante el método de transferencia se describe el proceso de transmisión a la piel a través de parámetros tales como coeficientes o tasas, que dependen de la actividad evaluada y de la combinación sustancia-matriz.

La vigilancia biológica resulta muy útil para evaluar el riesgo, en particular cuando se estudia la exposición por diferentes vías. Si se conoce la toxicocinética de la sustancia, la vigilancia biológica permite cuantificar por extrapolación la exposición cutánea original, siempre que las demás vías de exposición —la inhalación y la vía oral— sean insignificantes.

Hoy por hoy, los estudios de evaluación de la exposición cutánea tienen un enfoque eminentemente práctico. No hay ningún método que pueda emplearse en todas las circunstancias, ni se pueden ofrecer orientaciones que ayuden a elegir un método adecuado para unas circunstancias determinadas. Para cubrir las lagunas existentes en esta materia se requieren estudios comparativos que permitan contrastar la utilidad de los distintos métodos, elaborar protocolos armonizados y, en última instancia, mejorar nuestra comprensión de los procesos subyacentes a la exposición cutánea y de sus factores determinantes.

1.3 Modelos e instrumentos para la estimar la exposición cutánea

La elaboración de modelos (modelización) se considera un valioso método para evaluar la exposición cutánea cuando no se dispone de datos de mediciones o estas no resultan factibles. La modelización de la exposición cutánea se utiliza para fines diversos—generalmente relacionados con necesidades normativas—, como calcular la exposición en una población determinada, evaluar la eficacia de las medidas de reducción de riesgos o establecer los límites de concentración de las sustancias en los productos. Se han elaborado modelos que describen procesos físicos y modelos empíricos, y algunos de ellos pueden aplicarse mediante programas informáticos u otros recursos (por ejemplo, hojas de cálculo) que permiten simplificar su uso.

En este documento se presentan varios modelos e instrumentos, desarrollados con distintos objetivos. El método semicuantitativo DREAM tiene por finalidad evaluar los factores determinantes de la exposición y obtener información adicional relativa a la actividad para su empleo en la medición analítica. DERM es un instrumento que pretende ser práctico y de fácil manejo y podría utilizarse, por ejemplo, en programas educativos en países en desarrollo. RISKOFDERM está concebido para elaborar modelos a partir de agrupaciones de tareas, utilizando para ello los datos procedentes de las mediciones. BEAT permite buscar situaciones de exposición similares con sus correspondientes mediciones, que pueden combinarse con un modelo jerárquico bayesiano para efectuar predicciones probabilísticas. ECETOC TRA es un instrumento de cribado para evaluar el riesgo, MEASE está orientado a la exposición profesional a metales y otras sustancias inorgánicas, ConsExpo abarca varios aspectos de la exposición de los consumidores y SprayExpo se ocupa de diversos tipos de aplicación por pulverización. En cuanto a los modelos referentes a la aplicación de plaguicidas, los de la Unión Europea (modelos alemán y holandés, POEM y EUROPOEM) difieren de los utilizados en los Estados Unidos de América (EE. UU.) (Calendex, CARES, LifeLine, PHED, SHEDS), que están centrados en los receptores y permiten evaluar la exposición cutánea acumulada por distintas vías.

No es posible indicar qué modelos o instrumentos son los más exactos en unas circunstancias determinadas, si los resultados de los modelos o los instrumentos son comparables o qué modelos o instrumentos deben recomendarse, ya que su ámbito de uso, sus características y sus limitaciones varían de uno a otro. Para situaciones muy parecidas, diferentes organizaciones pueden emplear distintos modelos e instrumentos de evaluación de la exposición. Diversos factores influyen en la determinación y la evaluación de las aplicaciones de los modelos e instrumentos; entre otros, la finalidad para la que se desarrollaron (frecuentemente en un contexto normativo), sus descripciones de tareas, sus bases de datos, sus valores por defecto y sus procedimientos de extrapolación. En este documento se ofrece una primera tentativa de comparación de las diferentes aplicaciones, características y limitaciones de los distintos modelos e instrumentos. Asimismo, en un apéndice del documento se recogen, de manera ordenada y condensada, los algoritmos en que se basan los modelos e instrumentos presentados, para facilitar la comparación de sus principios rectores y de los factores determinantes incluidos en los diferentes modelos.

1.4 Enfermedades de la piel debidas a la exposición cutánea

La exposición cutánea puede provocar lesiones en la piel o efectos sistémicos tras atravesar la barrera cutánea, con el consiguiente riesgo de que se desarrollen dermopatías que pueden comportar graves repercusiones para la salud y la economía, tanto de los trabajadores como del resto de la población. Se describen aquí las enfermedades más habituales de la piel, así como las circunstancias típicas que las originan. La enfermedad cutánea más importante es la dermatitis de contacto (inflamación localizada), que se produce por el contacto directo de la piel con sustancias irritantes o alérgenos externos. Existen dos tipos de dermatitis de contacto: la irritativa y la alérgica. La dermatitis irritativa de contacto es la dermopatía laboral más importante, ya que el 50%-90% de las enfermedades cutáneas se deben al contacto con sustancias químicas o a la exposición prolongada al agua. Las dermopatías de origen laboral representan aproximadamente el 10% de las enfermedades profesionales en Europa y los EE. UU., con una prevalencia (una medida de la difusión de una enfermedad) de hasta el 65% entre los trabajadores de sectores como la peluquería, la imprenta o la limpieza. Por el contrario, la enfermedad cutánea más

importante en la población general es la dermatitis alérgica de contacto, cuya prevalencia es del 21,2% (en el caso de la exposición a uno o más alérgenos) en las poblaciones de Norteamérica y Europa occidental. También se incluyen en este informe otras enfermedades cutáneas y efectos directos, como la irritación, la urticaria, el acné, el cáncer y la fototoxicidad.

1.5 Métodos de prevención y reducción de la exposición

Se ofrece un breve repaso de las medidas legislativas encaminadas a la protección de los trabajadores y consumidores y de los métodos generales de identificación de peligros. A continuación se describen y clasifican los métodos empleados para reducir la exposición.

En muchos países, la legislación establece las condiciones de seguridad para la manipulación de sustancias en el lugar de trabajo. Las leyes relativas a los consumidores suelen abordar el etiquetado y el envasado. Las indicaciones de peligro y prudencia acordes con el Sistema Mundialmente Armonizado de Clasificación y Etiquetado de Productos Químicos advierten a trabajadores y consumidores de los peligros e instruyen sobre el uso correcto. Asimismo, varias instituciones dedicadas a la determinación de los límites de exposición profesional proporcionan notaciones relativas a la piel, que indican el potencial de absorción cutánea de una sustancia química. Los límites de exposición cutánea profesional están concebidos como medidas cuantitativas de la exposición máxima aceptable.

El método preferido de prevención de la exposición cutánea es la eliminación o sustitución. Otras medidas adoptadas para reducir la exposición en los lugares de trabajo son los controles técnicos, las medidas organizativas y los equipos de protección personal. Los controles técnicos incluyen procedimientos de separación (por ejemplo, el cierre, la contención o el aislamiento) y modificaciones de los productos o los procesos (por ejemplo, la reducción de la concentración en los productos, la sustitución de polvos por líquidos o gránulos y la utilización de envases de menor tamaño). Las medidas organizativas se centran en las prácticas y los procedimientos de trabajo, en la formación del personal y en las consecuencias del incumplimiento de las normas. Los equipos de protección personal deben contemplarse como

último recurso, en el caso de que otras medidas no resulten prácticas. Se resumen los criterios de selección que se aplican a los equipos de protección personal y se describen detalladamente los factores que determinan la eficacia global de dichos equipos (por ejemplo, las características de los materiales, las condiciones de uso y de trabajo, y la aceptación, el uso correcto y el mantenimiento de los equipos por parte de los usuarios).

En entornos no laborales, la exposición puede evitarse o reducirse mediante modificaciones del producto, instrucciones o información sobre su uso seguro, o medidas administrativas. Las modificaciones del producto (fijar una concentración máxima o variar su presentación —por ejemplo, sustituyendo el polvo por glóbulos o gránulos—) se consideran la medida más eficaz. También se mencionan las medidas administrativas (como el establecimiento de valores límite y las restricciones o la prohibición de comercialización) y la necesidad de etiquetar mejor las sustancias peligrosas para aumentar la percepción del riesgo por parte de la población.

Por último, se comentan las diferencias observadas en la eficacia de varias normas.