Review

On Dermal Exposure Assessment

A Behroozy

Abstract

Hazardous chemicals may enter the body by inhalation, ingestion, injection or dermal absorption. These exposure routes constitute the overall exposure burden on the body. Most occupational exposure studies have focused on measurement of the concentration of airborne contaminants and other possible routes of exposure are often overlooked.

Several studies have already highlighted the importance of dermal absorption. However, less development occurred in the assessment of dermal exposures to occupational and environmental contaminants compared to air sampling techniques.

This paper intends to highlight the importance of dermal exposure and looks at the methods currently used for its assessment. Advantages and disadvantages of each method in the context of occupational dermal exposure assessment are also outlined. Dermal exposure models, as an easy-to-use and low-cost tool to predict dermal uptake, especially when few or no actual data are available, are also included in this review.

Keywords: Skin absorption; Workplace; Environmental monitoring; Hazardous substances; Humans; Occupational exposure

Department of Occupational Hygiene, School of Paramedicine and Public Health, Zanjan University of Medical Sciences, Zanjan, Iran

The Importance of Dermal Exposure Assessment

Health risks from occupational dermal exposure to hazardous substances may occur at many workplaces. In addition to the local effects that chemicals can directly have on the skin, the skin also acts as a pathway for hazardous chemicals to be absorbed into the body.[1] Exposures to soot, tar, and mineral oils, for example, have been known to cause skin cancer since decades ago. Dermal exposure is the process of contact between an agent and human skin at an exposure surface over an exposure period.[2,3] The US Environmental Protection Agency (US EPA) also defined dermal exposure as the amount of a chemical substance contacted by the outer layer of the skin, and being available for dermal uptake.[4] Dermal exposure is the direct contact of the skin with liquids, solids and splashes on the skin, or contact with contaminated working clothes or surfaces. It may also occur with aerosols, gases and vapors.[5]

New exposure levels are likely to be less than those seen previously, and they are therefore, more difficult to detect.[6] In addition, over the last few years, the emphasis in epidemiology has shifted from qualitative risk identification to quantitative risk assessment, which incorporates exposure-response relationships into the overall exposure assessment process and requires all exposures through multiple routes (*ie*, inhalation, dermal and oral) and from various sources (*ie*, occupational, environmental and dietary) be accurately assessed.[7] Therefore, valid and reliable exposure assessment methods are crucial in order to gain the right picture of a worker's overall exposure.

Correspondence to Ali Behroozy, PhD, Department of Occupational Hygiene, School of Paramedicine and Public Health, Zanjan University of Medical Sciences, Parvin Etesamee Ave, Zanjan 45157-86349, Iran
Tel: +98-241-727-3124, Fax +98-241-727-3153,
E-mail: abehroozy@zums.ac.ir

Received: Apr 8, 2013
Accepted: Jun 16, 2013

Cite this article as: Behroozy A. On dermal exposure assessment. *Int J Occup Environ Med* 2013;**4**:113-127.

The Current Dermal Exposure Measurement Methods

Similar to the assessment of inhalational exposure, a number of exposure parameters need to be measured for characterization of dermal uptake. The exposure intensity, exposed surface area, duration of skin contact, and the frequency of skin cleaning or repeated exposure should be measured to know the mass of substance likely to be entered the body.[8]

Proper dermal exposure assessment strategies depend on the study design and the health outcome under consideration. These two factors determine the locations where the measurements should be made. In the case of local effects like hand dermatitis, dermal exposure is important at the body location of interest, while for systemic effects, the total dermal exposure through all exposed areas is the key for estimating the absorbed dose.

Several dermal exposure evaluation methods have been developed in the past few decades. These methods broadly grouped into direct and indirect methods.

Direct methods

These methods basically assess what is deposited on the skin. Direct methods can be categorized into three subgroups including interception (or surrogate), removal, and visualization techniques.[2,9]

Interception methods

Interception techniques refer to placing dermal dosimeters in the form of patches/pads, gloves and whole body suits against the exposed skin or clothing to collect contaminants. When an interception sampler is worn or attached to the skin sampling zone, it receives the chemicals depositing on the skin of that part. Selection of the body parts for placing the dosimeters depends on the study design and the exposure scenario. For hand sampling, the cotton gloves may be used instead of patches. For whole-body sampling, a coverall may be used. If we need to sample the head as well, a coverall with a hood or a hat is used. All surrogate techniques assume that the collection medium captures and retains the chemicals in the same way as the skin does.[10] These methods can be grouped into three categories including patch, glove and whole body methods.

Patch method: Absorbent patches or dosimeters are attached to the different representative parts of body, either inside or outside the clothing (Fig 1). Patches with predetermined size are used to col-

TAKE-HOME MESSAGE

- Dermal exposure may occur through contact of the skin with liquids, solids and splashes on the skin, or contact with contaminated working clothes or surfaces. When inhalation exposure is well controlled, skin exposure can add up total body burden.
- A growing concern is currently on dermal uptake of pesticides and organic solvents. Occupational physicians, hygienists, epidemiologists and other interested parties are becoming more aware of the importance of dermal exposure.
- Over the past few years, several methods have been developed for dermal exposure measurement. The most commonly used methods are surrogate, removal, visualization, surface sampling, biomonitoring and exposure modeling.
- Exposure intensity, exposed surface area and the duration and frequency of exposure are the main exposure parameters required to quantify dermal exposure.
- In recent years, dermal exposure modeling techniques have been developed as easy- to-use and cost-effective tools
- Despite considerable developments in this field, the current knowledge is still limited, measurement methods are still fragmented and substance specific and there is still no dermal occupational exposure limits similar to OELs for inhalation exposure.

lect chemicals and surrogate for measuring the amount of contaminants coming into contact with the clothing or skin.[11] The quantities of contaminants on patches are then determined using suitable analytical techniques. The rate of clothing penetration may be determined using the difference between the amounts of chemicals deposited on the inside and outside clothing patches. The composition and size of the patches used in dermal sampling studies are important and need to be based on the physical and chemical properties of the contaminant and exposure conditions.

Patches are usually made from surgical gauze, cotton gauze, clothing material, polyester-cotton cloth, absorbent paper, and polyurethane foam. These patches should be backed by an impervious material such as aluminum or plastic foil to reduce the potential of contamination of the patches by materials on the skin or clothing, and to prevent seepage of the contamination through the patch to the skin or clothing. The typical thickness for the patches is approximately 1 mm. The most commonly used patch size is 10×10 cm^2.[9] Using smaller patches generally fails to provide representative exposure data and should be avoided. A complete set of patches for each exposure period usually consists of 10–12 patches on the locations depicted in Figure 1. The number of patches used per worker varies from protocol to protocol. Organization for Economic Cooperation and Development (OECD) recommends the use of 13 patches covering 8% of body surface,[10] whereas the protocol of the World Health Organization (WHO) relies on six patches covering 3% of body area.[12]

Glove method: Gloves provide a technique for monitoring dermal hand exposure. Several light absorbent cloth gloves are commercially available. They can be used in place of, underneath or on top of the protective gloves. Physical durability of the sampling gloves is important; they should be capable of withstanding the mechanical forces exerted during the routine activities of the worker. Gloves should not become saturated, and they should be replaced if soaked. Participants are required to wash their hands in an appropriate solvent to remove background contaminants before wearing the sampling gloves. In the case of using protective gloves in work, sampling gloves should be worn underneath. Considerations should be given to avoid cross contamination. For example subjects should turn inside out from both hands, and then place the gloves into storage container. As with all dosimeters, gloves need to be pretested to ensure that they do not contain materials that might interfere with the contaminant under study.[13]

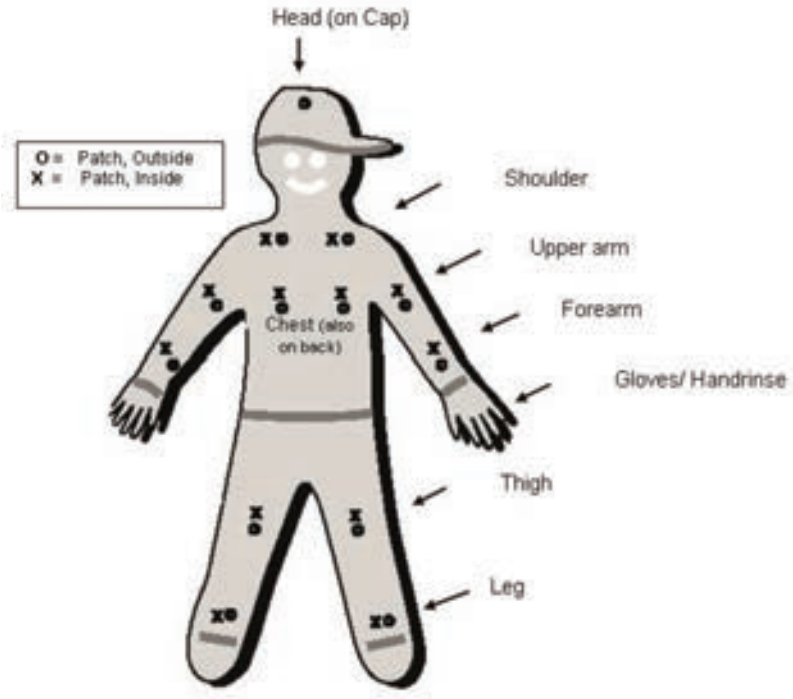

Figure 1: Body parts for dermal exposure measurement by absorbent patch

Whole body method: A whole body dosimeter, which is usually a type of cloth-

ing (including socks) is used for monitoring total dermal exposure. It should be made of suitable absorbent materials such as cotton or cotton/polyester.[12] Standard whole body dosimeters that are commercially available include white cotton socks, long-sleeved cotton T-shirts, and thermal underwear bottoms and tops. After exposure, dosimeters should be removed and sectioned for storage, extraction, and analysis. This procedure may be more suitable for liquids than dry contaminants, since powders may be lost in handling. Workers are required to wear whole body dosimeters underneath their normal work clothing to simulate the absorptive surfaces of bare skin protected by normal work clothing. As a result, work clothing may have the role of a potential source of cross contamination.[14]

Depending on the amount of contamination, whole body dosimeters are at least sectioned into arms, torso and legs. Whole-body suits seem to give more reliable data than patches. However, both techniques have their advantages and disadvantages (Table 1).

For lack of an impermeable barrier compared to patches, there is the potential for chemicals to penetrate through, which could result in underestimating exposure. Any measurements of dermal exposure that use surrogate skin sampling media such as patches, oversuits or gloves, raises the question of sampling efficiency and retention relative to the skin.

Removal methods

Removal techniques including washing, wiping, tape-stripping and suction remove chemicals from the skin (or surfaces). Collecting media are then analyzed by suitable techniques. Removal methods are particularly suitable for substances remaining on the skin for a long time, such as dusts and sticky low volatile substances. These techniques are often used to sample substances imposing local effects on the skin. Skin and surface sampling should be made before any hand washing or cleaning. These methods should not increase the risk by damaging the skin barrier or enhancing the penetration rate of the substance, *eg*, washing with solvents or using wipes soaked in solvents. These techniques, however, are not easily applicable to assess the total body exposure.[15]

Washing: Washing method is usually applied to the hands where a significant proportion of total dermal exposure occurs. For this purpose, the hand is placed in a sealable bag containing a known volume of a suitable solvent. Vigorous shaking then applied for a given period to wash out the chemicals from the surface of the skin. The resulting mixture subsequently analyzed by a suitable analytical method.

Several types of solutions including various types of aqueous surfactant solutions like water, water with surfactant, and water-alcohol mixture to neat isopropanol or ethanol may be used to collect hand rinse samples. Selection of the solvent depends on the physical and chemical properties of the contaminant being studied. For example, if a chemical is water soluble, then an aqueous surfactant solution should be used instead of a neat alcohol. Water used for preparing aqueous solutions should be distilled and deionized. Two consecutive washings can be used to achieve better removal; however, washing may affect the integrity of the skin, and make it more penetrable.[16] The handwashing procedure has been standardized to ensure operator independency in pesticide applications.[17]

Wiping: This method can be carried out dry or using absorbent materials soaked in an appropriate solvent like water, alcohol or other solvents, providing these solvents do not damage the skin, or increase penetration of the chemicals. For water-soluble chemicals, a wipe pad

Table 1: Advantages and disadvantages of dermal exposure measurement methods

Method	Advantages	Disadvantages
Patch method	Easy to use, low costs Can be used to assess local effects and the effectiveness of personal protective equipment (PPE). The dosimeter is backed with a protective impermeable layer.	Extrapolation from patch to body area needs to be made. Assumption of uniform distribution for contaminant Adherence of the contaminant to the patch and real skin may differ.
Glove method	More applicable Simple to use	It measures the loading available at the time of sampling. Its application is limited to the hands
Whole body suits	It overcomes the problem posed by the assumption of uniform deposition in patch method. There is no need to extrapolate from patches to larger body regions It can be used concurrently with biological monitoring to measure absorbed dose. It is less likely to miss areas of body where exposure may occur.	Expensive analysis It requires large volume of solvent for extraction of the chemical. Due to the lack of an impermeable backing layer chemicals may penetrate through.
Hand washing	Simple to use Low costs	Some solutions may be hazardous to the hands It is limited for repeated sampling. It does not recover residues absorbed into the skin. Limited use when the substance is highly volatile or rapidly absorbed by the skin. Removal efficiency varies depending on loading, time of sampling, number and duration of hand washings It is not applicable for whole body measurement. There are uncertainties in the removal efficiency.
Wiping	It can be used to take samples from the skin, work surfaces and work tools	There is no standard protocol for the number of wipes and the amount of force.
Tape stripping	It measures percutaneous absorption rather than exposure. Simple to use	It is subject to operator variation.
Visualization	There is no need for chemical analysis It provides instant results It measures actual skin loading.	A tracer needs to be added whose behavior may differ from the chemical substance understudy. It needs skilled operator and it is expensive. Tracer may bind to skin and limits the application of this method.
Biological monitoring	This method measures actual internal dose. It integrates all routes of exposure. It is useful in assessing the effectiveness of PPE.	Exposure routes and causes cannot be distinguished. Human pharmacokinetic studies are required for validation. Not relevant to local skin effects Only a few biological exposure limits are available. More interference is required to collect samples Potential problems in using invasive techniques to collect specimens

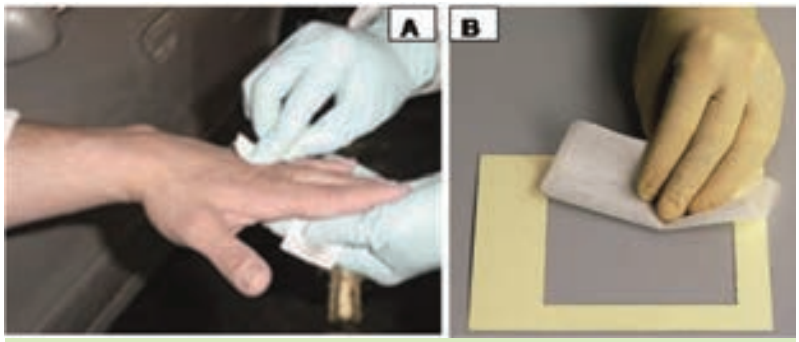

Figure 2: A) Skin wiping; B) Template with a known size for wipe sampling

moistened with deionized water can be used to wipe the skin. The best procedure is generally to allow employees to use a wipe pad to clean their skin surface, and then putting the wipe pad into a clean container. This sampling method may be used to take samples from the skin, work surfaces and work tools. By taking samples from predetermined areas (Fig 2), it is possible to make comparisons between samples taken at different times or from different surfaces. Several wipes such as cotton balls, cotton pads, filter papers and wet wipes are currently used for this purpose. There is currently no standard protocol describing the number of wipes and the amount of force needed to be applied in collecting samples.[18]

Figure 3: Tape stripping

Tape stripping: Tape stripping removes a thin layer of the outer surface of the skin for determining the amount of the chemicals deposited on the skin. This method is more invasive than surrogate and other removal methods. This technique is also used to take samples from surfaces such as tools, work benches and personal protective equipment (Fig 3).

It is a good method for compounds with low volatility and long retention time on the skin.[19] However, it has been argued that tape stripping, as wipe sampling, may not be as accurate as washing method due to the larger variation caused by the operator performing the sampling.[20]

Visualization techniques

These techniques rely on measuring fluorescent materials deposited or retained on the skin or other surfaces under ultraviolet light by suitable detection or imaging systems.[18] Fluorescence might be produced by the chemical itself or by a tracer added to the chemical. The most commonly used fluorescent tracers are Uvitex, Tinopal and Calcoflur.

The use of fluorescent compounds is coupled with video imaging measurements to produce exposure estimates. This requires pre- and post-exposure images of the skin surfaces under long-wave ultraviolet illumination, development of a standard curve relating dermal fluorescence to skin-deposited tracer, and sampling the chemical residue to quantify the relationship between the tracer and the chemical substance deposited on the skin. A portable tracer detection system is shown in Figure 4.

Computer analysis of the image can be used to provide a quantitative estimate of the mass of fluorescent compound on the skin and the exposed area. Fenske, *et al*, developed the Video Imaging Technique to Assess Exposure (VITAE), which transformed qualitative observations of the

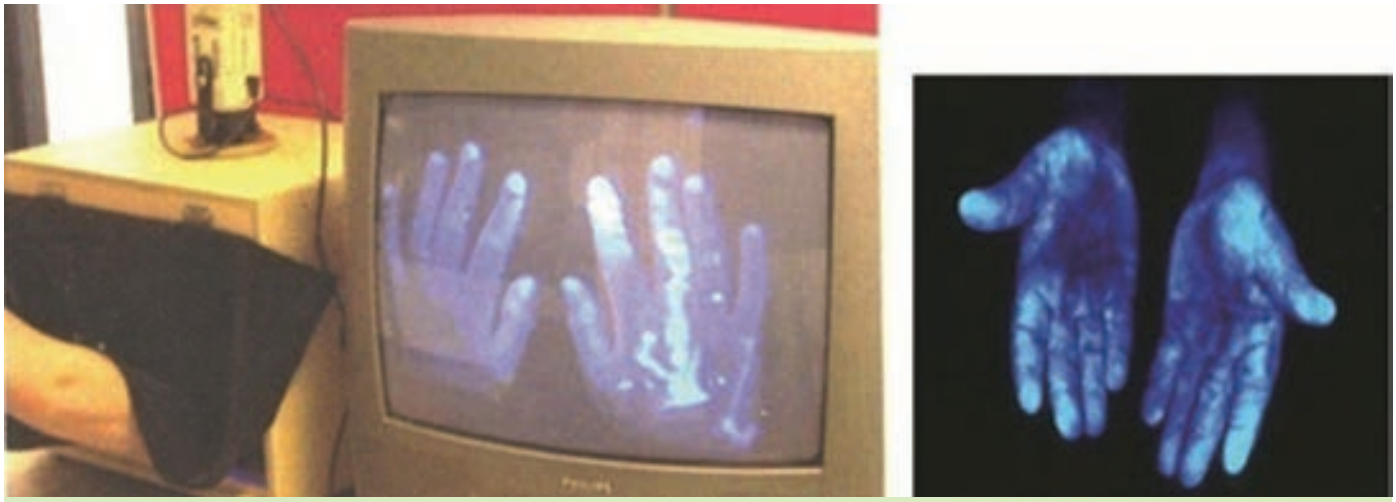

Figure 4: A portable system for detection of the traces on the skin and surfaces[18]

fluorescent skin images into quantitative data by means of a computer software.[21] Another visualization technique is Fluorescent Interactive Video Exposure System (FIVES). These techniques allow uniform illumination of the body surface and provide information on the area exposed and the amount of substance deposited on the skin.[22]

Indirect methods

Indirect methods primarily refer to measuring a biologic response such as cholinesterase activity in blood or urinary excretion. Measuring contaminants on an accessible surface and dermal exposure modeling also fall into indirect methods group. The main concern in indirect methods is defining a relationship between biological indices or surface contamination, and dermal exposure levels. The availability of the skin absorption data is crucial for this purpose.

Surface sampling methods (non-human)

The most common method used to assess potential exposure from a contaminated surface is wipe sampling (Fig 2). Materials used as wipe samplers for chemicals include glass fiber, filter paper, cotton swab, surgical gauze, paper tissues and cloth.[23]

While wipe sampling provides information about the mass of the contaminant on a surface, the method suffers from a lack of standardized protocol and fails to relate the mass of contaminant on the surface to the mass transferred into the skin. The accuracy and precision of wipe sampling depend on surface characteristics, contaminant loading, type of sampling material, and the procedures used.[9]

Suction: Suction method is mainly used to collect particulate matter on surfaces. In this method the contaminant particulates are drawn to the collecting medium using a small vacuum pump (Fig 5). Compared to other removing methods, this technique is more costly, complicated and prone to errors.

Biomonitoring

Biological monitoring is the assessment of human exposure through the measurement of internal chemical markers of exposure, such as the chemical agent itself, one of its metabolites, or an exposure-related change in human biological samples, related or unrelated to disease.[24]

Figure 5: Collecting particulates from a surface using a suction pump

This method is useful in determining dermal uptake, especially when dermal exposure is a significant contributor to the employee's overall uptake. Because of the difference between animal and human metabolisms, human pharmacokinetic studies are required to validate the results obtained from biological monitoring. Ideally, surface and dermal sampling should be done concurrently with air and biological monitoring. By this approach, not only the true dose of an individual is assessed, but also the sources of exposure are identified. Biomarkers of exposure potentially reflect the internal dose and have the advantage that they integrate the exposure through all routes including the skin. However, for most chemicals, no biomarkers of the internal dose are available.[25] As a result, substances absorbed through the skin will require separate exposure estimates for dermal exposure.

For chronic health outcomes, the cumulative exposure is generally considered as the most appropriate measure of exposure. It is also important to note that biological monitoring has no relevance when local skin effects are being considered.

The advantages and disadvantages of the methods already discussed in this paper are provided in Table 1.

Dermal exposure modeling

Dermal exposure assessment to hazardous substances can be expensive and time-consuming. It also requires a considerable degree of professional expertise and judgment. Furthermore, technical information from a wide range of scientific and professional disciplines is needed. The great degree of random variability between individuals and workplace situations, and the practical and economic constraints of gathering sufficient data should also be taken into account to make reliable judgments. Therefore, any means to ease the complexity of the exposure assessment process, and making it more structured and formalized is desirable. With use of a standardized methodology, exposure predictions can be made with some degree of uniformity and reliability. Validating such a method against real exposure data can then lead to refined and more accurate predictive systems called models.

Models are used to assess occupational dermal exposure particularly in cases when few or no actual data are available. They can also serve as tools in epidemiological studies.[6] Some of the currently used models for dermal exposure are described as follows:

Conceptual model for dermal exposure: Dermal contamination may occur from the deposition of aerosols, by direct immersion into a chemical substance (liquid or powder) due to spills and splashes, through vapor penetration, or by direct contact with contaminated surfaces. Dermal exposure can be considered as an interactive process between a source of contamination and the body with sev-

eral compartments and processes. A conceptual model of the processes leading to exposure from the source of a hazardous substance to the surface of the skin, and the intermediate compartments has been proposed by Schneider, *et al*.[26] Pathways between six compartments and two barriers are described along with eight mass transport processes (Fig 6). The identified compartments are source, air, surface contaminant layer, outer and inner clothing contaminant layers separated by the clothing fabric barrier having a buffer capacity, and the skin contaminant layer, which is separated from the perfused tissue by the stratum corneum that acts as a rate-limiting barrier. The mass transfer processes include emission (E), deposition (D$_p$), resuspension/evaporation (E$_r$), transfer (T), removal (R), redistribution (R$_d$), decontamination (D$_c$), and penetration/permeation (P).

The transport process of the contaminants through the skin layers is generally driven by the concentration gradient between the dermal surface concentration and the concentration within the perfused tissue. There is no active transport mechanism involved in this process. This model provides a valid framework for uniform terminology, and increases the awareness about the exposure routes and factors. This multi-compartment model is more concerned with what happens rather than why it happens. All compartments are assumed to be well mixed and operating in parallel.

Estimation and Assessment of Substance Exposure (EASE): EASE model was developed by the Health and Safety Executive (HSE) in the UK for assessing exposure to new and existing chemicals in the EU. In this model, various factors, which would influence exposure, were systematically examined and coded, and the initial model was set up. The obtained data were subsequently compared with data contained in HSE's National Exposure Database (NEDB), and refined to produce the eventual model. This model ranks the workplaces in broad bands of exposure and thus, it always assumes homogeneous exposure within the workplace.[6] EASE is essentially a series of decision trees. For any substance, this model asks a number of questions about the physical properties of the substance, the circumstances of its use, and the measures used to control exposure. For any question, the user must select from a number of representative categories. Once all the questions have been answered, the exposure prediction is determined by integration of the choices made.

RISKOFDERM: The RISKOFDERM dermal exposure model was developed for estimating potential dermal exposure, *ie*, the total amount of a substance coming into contact with the protective clothing, work clothing and exposed skin. It is based on statistical analysis of data gathered in the RISKOFDERM project, an European project on dermal exposure contributed by 15 European institutes/organizations from 10 European member states in order to develop a validated/benchmarked predictive model for estimating dermal exposure. The model originally consists of a set of equations, which have been entered into a user friendly MS Excel® spreadsheet. This model is used to estimate potential dermal exposure to a product or substance used for, or handled in a separate process or task within a workday.[27]

European Predictive Operator Exposure Model (EUROPOEM): EUROPOEM was developed at the request of the European Commission for predicting pesticide handlers' exposure (EUROPOEM I). The number of field data in the first version was limited and unrepresentative for certain exposure scenarios and

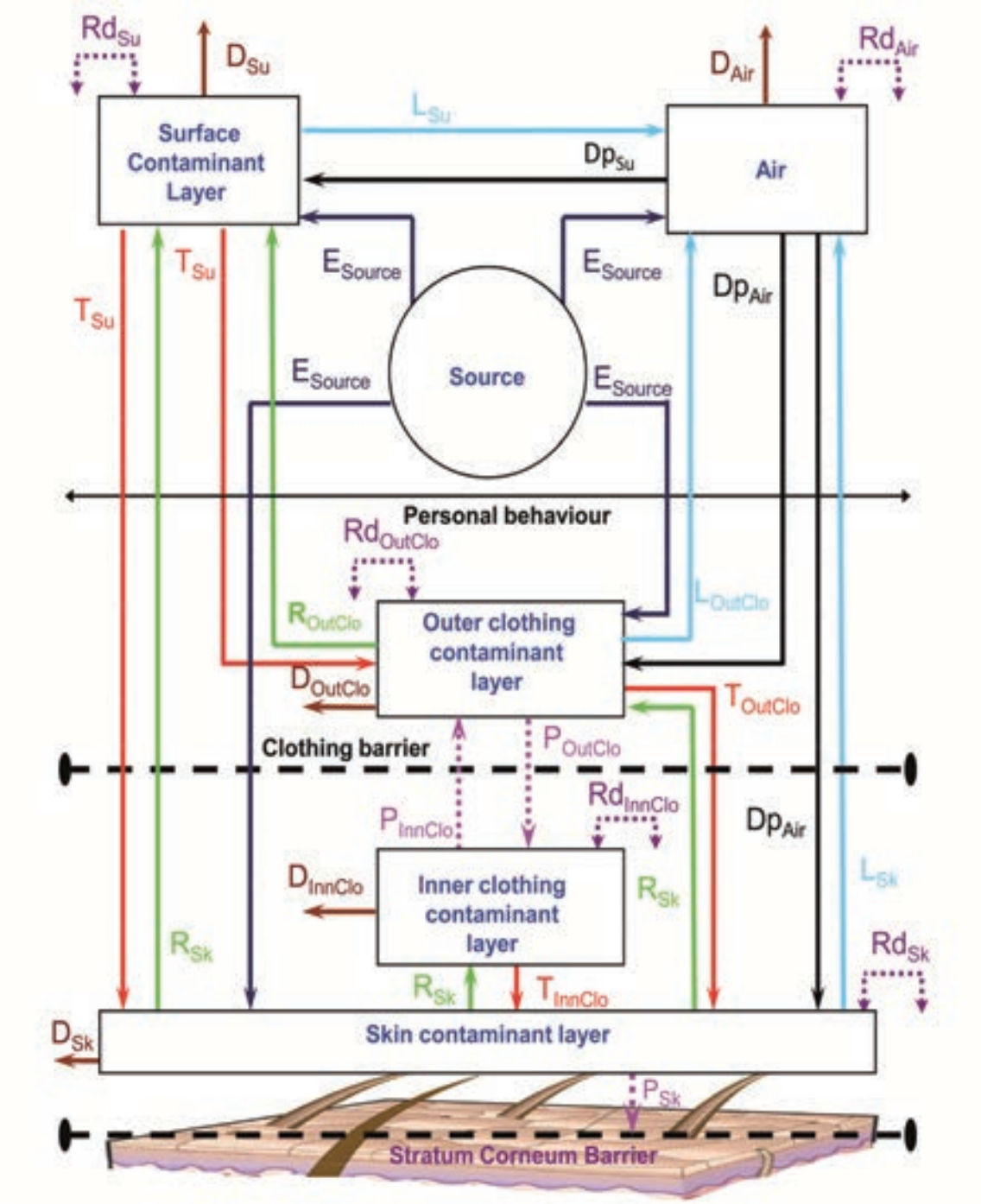

Figure 6: The conceptual model of dermal exposure showing 6 compartments and 8 mass transfer processes. The 6 compartments include source, air, surface contaminant layer (Su), skin contaminant layer (Sk), outer clothing contaminant layer (OutClo) and inner clothing contaminant layer (InnClo). The 8 mass transfer processes are E: Emission, Dp: Deposition, Rd: Redistribution, D: Decontamination, P: Penetration/Permeation, L: Resuspension/Evaporation, R: Removal, and T: Transfer (adapted with permission from Schneider, *et al*. 1999[26]).

thus, a more validated and enlarged model was subsequently developed (EUROPOEM II). In addition, the EUROPOEM I did not contain a model to predict the exposure of re-entry workers or bystanders. These features were also developed in the new version. The surrogate exposure levels for each scenario are compared with an acceptable operator exposure value (AOEL) derived from relevant toxicological data, usually the no-observed adverse effect level of a sub-chronic study. When the ratio of exposure and the AOEL is below 1, the exposure in that scenario is considered acceptable. Exceeding the AOEL leads to further assessment.[28] The field sampling of both versions followed the protocol approved in an OECD guidance document.[8] The accuracy of the model increased in the updated second version, as it contains more field data obtained from modern pesticide use scenarios and more work has been done to validate the default values, such as protection factors of personal protective equipment and clothing.[29]

Control banding: Control banding is a system used to assess and manage workplace risks. It is a process that matches a control measure (*eg*, ventilation, engineering controls, containment, *etc*) to a range or "band" of hazards and exposures (*eg*, skin/eye irritation, very toxic, carcinogenic, *etc*) It is intended to minimize workers' exposures to hazardous chemicals in the workplace and particularly to help small- and medium-sized enterprises (SMEs) by providing an easy-to-understand and practical approach to control hazardous exposures at work.

Chemicals are categorized by their hazardous characteristics into bands of exposure concentrations and consequently, into corresponding control strategies. Safety data sheets are used as the main source of information. This system then determines a set of useful controls that will prevent harm to workers. It provides more information than skin notation for controlling dermal risks.[30]

Much of the current concept of the control banding derives from the Control of Substances Hazardous to Health (COSHH Essentials) package developed by the UK HSE. It was designed to assist SMEs in complying with the UK chemical safety regulations. The scheme uses the risk phrases (R) that in the Europe must be assigned to potentially harmful chemicals by the manufacturer of the chemical. Risk phrases describe the most important harmful effects of a chemical and have also been adopted in many non-European countries. These phrases have been grouped by experienced toxicologists into five hazard groups. The user finds the R phrases for the chemical by referring to the label or material safety data sheet supplied by the chemical supplier and looking for the R phrases in the list of hazard groups; the full list and precise meaning of each of these risk phrases are available at: *www.hse.gov.uk/chip/phrases.htm*. The hazard group for the chemical is then selected using this grouping system.

Once a chemical has been assigned to a particular hazard group, it is necessary to consider the assessment of the potential exposure in the workplace. The combination of the hazard classification of the chemical and assessment of the exposure potential will allow understanding of the level of risk, which leading to the selection of an appropriate control method. Table 2 shows R phrases for dermal exposure. The relative rankings for systemic toxicity (through the skin) are consistent with the rationale for inhalation hazard ranking and include all health hazards.

Stoffenmanager: A Web-based tool called *stoffenmanager* (meaning "materials manager," online version available at: *www.stoffenmanager.nl*) was initially developed in the Netherlands as

Table 2: Relevant risk phrases for the skin exposure

Risk No.	Phrase
Exposure via the skin	
R 21	Harmful in contact with the skin
R 24	Toxic in contact with the skin
R 27	Very toxic in contact with the skin
Exposure of the skin	
R 34	Causes burns
R 35	Causes severe burns
R 38	Irritating to the skin
R 43	May cause sensitization by skin contact
R 66	Repeated exposure may cause skin dryness or cracking
Exposure of the eyes	
R 36	Irritating to the eyes
R 41	Risk of serious damage to eyes

a tool allowing SMEs to prioritize their health risks to hazardous substances and finding effective control measures. The core of this tool is actually a risk banding scheme. The *stoffenmanager* classifies the hazards of a product on the basis of the R phrases of a product according to the COSHH Essentials scheme (Table 2). The *stoffenmanager* inhalation exposure algorithm is based on an exposure model originally presented by Cherrie and Schneider.[31] The dermal exposure model is based on the RISKOFDERM toolkit.[32]

This toolkit is based on a large number of measurements of dermal exposure in real work situations and is considered a valid tool for assessing dermal exposure. The tool combines hazard information of a substance or product with an inhalation and/or dermal exposure assessment to calculate a risk score. These risk scores are assigned to exposure bands. The comparison of exposure bands and hazard bands leads to a risk band or priority band (Table 3). Relevant control measures can be subsequently put into an action plan. The tool has several other functionalities regarding registration and storage of products. *Stoffenmanager* generally estimates exposure well and is sufficiently conservative, but it needs more adaptations for specific scenarios.[33]

Conclusion

The skin exposure is a relatively new area of concern in the field of occupational and environmental risk assessment. Occupational dermal exposure and uptake can have an important role in worker's total exposure and is very likely to occur in many different situations and for all sorts of chemicals.

Many published cases are found in the literature that demonstrate the skin route as an important means of exposure, resulting in adverse health consequences. For example, phenol poisonings due to percutaneous absorption have been recognized as an occupational health hazard as early as 1880,[34] and the introduction of tetraethyllead as a gasoline additive in the 1920s with its ability to enter blood after contact with skin, resulted in multiple fatalities due to occupational skin exposure.[35] Dimethylformamide (DMF) has been shown to cause hepatic disease even if its air occupational exposure limit is respected, because accidental skin contact with liquid DMF can significantly increase its uptake.[36] These are just a few of the published examples where skin contact resulted in disease. It is very likely that many other cases have occurred, which have not been documented in the literature. In spite of these dramatic events, dermal exposure assessment remained undeveloped for most of the 20th century, until the 1990s when the systematic characterization of dermal exposure initiated.

The importance of dermal exposure

and uptake has already been highlighted by six international conferences on Occupational and Environmental Exposure of the Skin to Chemicals (EESCs: 2002 USA, 2005 Sweden, 2007 USA, 2009 UK, 2011 Canada, and 2013 Netherlands) and several national seminars and courses such as Derm ex international course which was held three times in the UK, the Netherlands and Sweden, focused on the various issues related to occupational skin exposure.

Much of our current understanding of dermal exposure and uptake has come from investigations on the health effects of pesticides. There is also currently growing concern on the dermal uptake of organic solvents. Our knowledge of the factors influencing dermal exposure and uptake of chemicals through this route is increasing; there are also more data available relating to dermal absorption of chemicals. Furthermore, interested groups such as occupational physicians, hygienists, and epidemiologists are becoming more aware of the importance of dermal exposure when taking history of patients or facing dermal exposure scenarios in the workplaces.

With decreased OELs values for inhalation exposures and increased understanding of the importance and mechanisms involved in dermal uptake of chemicals in the workplace, more questions have raised in this field and further studies are required to address these questions. Dermal exposure assessment is changing to one of the most important and challenging areas of research in occupational and environmental hygiene. The future of dermal exposure assessment is likely to provide more opportunities for collaborative and multidisciplinary research among interested researchers. It also seems there is great potential for new developments in dermal measurement methodologies.

Taken together, it is now clear that dermal exposure assessment has broadened to include a more detailed knowledge of the skin anatomy and physiology, dermal uptake, skin sensitization, and the potential for skin contact to initiate a more common sense among researchers and general public. Knowledge of genetic variability and susceptibility related to the skin is also likely to grow rapidly in the next few years. Advances in these areas will in turn lead to more complete and accurate models of risk, and ultimately to improved protection for both workers and the general population.

However, the current knowledge in this field is still limited and assessing the risk of dermal exposure remains a challenge for interested groups. Measurement methods are still very fragmented, unstandardized and often substance-specific. Each of the current methods has its own advantages and disadvantages, and there is still no international consensus on Dermal Occupational Exposure Limits (OELs).

Table 3: Priority bands in the *stoffenmanager*. Hazard band from A: lowest to E: highest and exposure band from 1: lowest exposure to 4: highest exposure level. Overall result, from 1: highest priority to 3: lowest priority (adapted with permission from Marquart, *et al*, 2008[33]).

Exposure band	Hazard band				
	A	B	C	D	E
1	3	3	3	2	1
2	3	3	2	2	1
3	3	2	2	1	1
4	2	1	1	1	1

Acknowledgments

The author sincerely thanks Dr. Sean Semple for his valuable comments on an earlier draft of the manuscript.

Conflicts of Interest: None declared.

References

1. Demierre AL, Peter R, Oberli A, *et al*. Dermal penetration of bisphenol A in human skin contributes marginally to total exposure. *Toxicol Letters* 2012;**213**:305-8.
2. Semple S. Dermal exposure to chemicals in the workplace: just how important is skin absorption. *Occup Environ Med* 2004;**61**:376-82.
3. Brouwer D. Dermal exposure: harmonization of terminology. Proceeding of the 6th International Occupational Health Association Conference (IOHA), September 19-23, **2005**. Pilanesberg, South Africa.
4. US-EPA. *Exposure Factors Handbook. National Center for Environmental Assessment.* Office of Research and Development. US Environmental Protection Agency. Washington DC, **1997.**
5. Jones K, Cocker J, Dodd LJ, *et al*. Factors Affecting the Extent of Dermal Absorption of Solvent Vapours: A Human Volunteer Study. *Ann Occup Hyg* 2003;**44**:511-18.
6. Vermeulen R, Stewart P, Kromhout H. Dermal exposure assessment in occupational epidemiologic research. *Scand J Work Environ Health* 2002;**28**:371-85.
7. Vermeulen R, Heideman J, Bos RP, *et al*. Identification of dermal exposure pathways in the rubber manufacturing industry. *Ann Occup Hyg* 2000;**44**:533-41.
8. Cherrie JW, Robertson A. Biologically relevant assessment of dermal exposure. *Ann Occup Hyg* 1995;**39**:387-92.
9. Fenske RA. Dermal exposure assessment techniques. *Ann Occup Hyg* 1993;**37**:687-706.
10. OECD. Guidance Document for the Conduct of Studies of Occupational Exposure to Pesticides During Agricultural Application, OECD Series on Testing and Assessment, No. 9, OECD Publishing, Paris, France. Available from *www.oecd-ilibrary.org/environment/guidance-document-for-the-conduct-of-studies-of-occupational-exposure-to-pesticides-during-agricultural-application_9789264078079-en* (Accessed March 1, 2013).
11. Wassie F, Spanoghe P, Tessema DA, *et al*. Exposure and health risk assessment of applicators to DDT during indoor residual spraying in malaria vector control program. *J Expo Sci Environ Epidemiol* 2012;**22**:549-58.
12. WHO. Field surveys of exposure to pesticides: Standard protocol. Pesticide Development and Safe Use Unit. Division of Vector Biology and Control, WHO Headquarters, Geneva. *Toxicology Letters* 1986;**33**:223-35.
13. Cavallari JM, Osborn LV, Snawder JE, *et al*. Predictors of dermal exposures to polycyclic aromatic compounds among hot-mix asphalt paving workers. *Ann Occup Hyg* 2012;**56**:125-37.
14. Lesmes-Fabian C, Garcia-Santos G, leuenberger F, *et al*. Dermal exposure assessment of pesticide use: The case of sprayers in potato farms in Colombian highlands. *Sci Total Environ* 2012;**430**:202-8.
15. Brouwer DH, Boeniger MF, van Hemmen JJ. Hand wash and manual skin wipes. *Ann Occup Hyg* 2000;**44**:501-10.
16. Marquart H, Brouwer DH, van Hemmen JJ. Removing pesticides from hands with simple washing procedure using soap and water. *Occup Environ Med* 2002;**44**:1075-82.
17. CEN. Chemical disinfectants and antiseptics. Hygienic handwash. *Test Method and Requirements* (Phase 2/Step 2). Final draft prEN 1499. European Committee for Standardization (CEN). Brussels, Belgium, **1996**.
18. Rajan B. *Controlling skin exposure to chemicals and wet-work*. West Midlands, UK: RMS Publishing, **2008**.
19. Roff MW. A novel lighting system for the measurement of dermal exposure using a fluorescent dye and image processor. *Ann Occup Hyg* 1994;**38**:903-19.
20. Kammer R, Tinnerberg H, Eriksson K. Evaluation of a tape-stripping technique for measuring dermal exposure to pyrene and benzo(a)pyrene. *J Environ Monit* 2011;**13**:2165-71.
21. Fenske RA, Leffingwell JT, Spear RC. A video imaging technique for assessing dermal exposure. I. Instrument design and testing. *Am In Hyg Assoc J* 1986;**47**:764-70.
22. Cherrie JW, Brouwer DH, Roff M, *et al*. Use of qualitative and quantitative fluorescence techniques to assess dermal exposure. *Ann Occup Hyg* 2000;**44**:519-22.
23. EPA . A literature review of wipe sampling

methods for chemical warfare agents and toxic industrial chemicals. 2007, Available from *www.epa.gov/nhsrc/pubs/600r07004.pdf* (Accessed March 1, 2013).

24. ACGIH. Threshold Limit Values for chemical substances and physical agent & Biological Exposure Indices, American Conference of Governmental Industrial Hygienists, Cincinnati, Ohio, **2011**.
25. Van Hemmen JJ, Brouwer DH. Assessment of dermal exposure to chemicals. *Science of Total Environment* 1995;**168**:131-41.
26. Schneider T, Vermeulen R, Brouwer D, *et al.* Conceptual model for assessment of dermal exposure. *Occup Environ Med* 1999;**56**:765-73.
27. van Hemmen JJ, Auffarth J, Evans PG, *et al*. RISKOFDERM: risk assessment of occupational dermal exposure to chemicals. An introduction to a series of papers on the development of a toolkit. *Ann Occup Hyg* 2003;**47**:595-8.
28. Fiserova BV. Relevance of occupational skin exposure. *Ann Occup Hyg* 1993;**37**:673-85.
29. Van Hemmen JJ. EUROPOEM: a predictive occupational exposure database for registration purposes of pesticides. *Appl Occup Environ Hyg* 2001;**16**:246-50.
30. McDougal JN, Boeniger MF. Methods for assessing risks of dermal exposures in the workplace. *Critical Rev Toxicol* 2002;**32**:291-327.
31. Cherrie JW, Schneider T. Validation of a new method for structured subjective assessment of past concentrations. *Ann Occup Hyg* 1999;**43**:235-45.
32. Goede HA, Tijssen SC, Schipper HJ, *et al.* Classification of dermal exposure modifiers and assignment of values for a risk assessment toolkit. *Ann Occup Hyg* 2003;**47**:609-18.
33. Marquart H, Heussen H, Feber M, *et al*. Stoffenmanager: a Web-based control banding tool using an exposure process model. *Ann Occup Hyg* 2008;**52**:429-41.
34. Hamilton A, Reznikoff P, Burnham GM. Tetraethyl lead. *J Am Med Assoc* 1925; **84**:1481-86.
35. Diechmann WB. Local and systemic effects following skin contact with phenol: a review of the literature. *J Ind Hyg Toxicol* 1949;**31**:146-54.
36. Fiorito A, Larese F, Molinari S, *et al*. Liver function alterations in synthetic leather workers exposed to dimethylformamide. *Am J Ind Med* 1997;**32**:255-60.