MILJA MÄKINEN

Dermal Exposure Assessment of Chemicals – an Essential Part of Total Exposure Assessment at Workplaces

Doctoral dissertation

To be presented by permission of the Faculty of Natural and Environmental Sciences of the University of Kuopio for public examination in Auditorium L23, Snellmania building, University of Kuopio, on Friday 19th December 2003, at 12 noon

Department of Environmental Sciences
University of Kuopio

2003

Distributor: Kuopio University Library
P.O. Box 1627
FIN-70211 KUOPIO
FINLAND
Tel. +358-17-163 430
Fax. +358-17-163 410
http://www.uku.fi/kirjasto/julkaisutoiminta/julkmyyn.html

Series Editors: Professor Lauri Kärenlampi, PhD
Department or Ecology and Environmental Science

Professor Jari Kaipio, PhD
Department of Applied Physics

Author's address: Kuopio Regional Institute of Occupational Health
P.O.Box 93
FIN-70701 KUOPIO
FINLAND
Tel. +358-17-201 211
Fax. +358-17-201 474
Email: milja.makinen@ttl.fi

Supervisors: Professor Pentti Kalliokoski, PhD
Department of Environmental Sciences
University of Kuopio

Professor Juhani Kangas, PhD
Kuopio Regional Institute of Occupational Health

Reviewers: Associate Professor Leena Nylander-French, PhD
University of North Carolina
Chapel Hill, North Carolina, USA

Professor Heikki Savolainen, MD
Ministry of Social Affairs and Health
Tampere

Opponent: Professor Matti Jantunen, PhD
National Institute of Public Health
Kuopio

ISBN 951-781-303-1
ISSN 1235-0486

Kopijyvä
Kuopio 2003
Finland

Mäkinen, Milja. Dermal Exposure Assessment of Chemicals – an Essential Part of Total Exposure Assessment at Workplaces. Kuopio University Publications C. Natural and Environmental Sciences 165. 2003. 88 p.
ISBN 951-781-303-1
ISSN 1235-0486

ABSTRACT

Skin is an important route of exposure for chemicals at workplaces, in addition to the better-described respiratory route. In order to increase the existing knowledge of dermal exposure, several studies have also been conducted in Finland, beginning in mid-90s. The aims of the dissertation were to experiment with different occupational hygiene sampling methods in various workplace conditions, and to determine how the measured data could be used in the modelling of exposure. Another objective was to characterise the existing predictive pesticide exposure models. A preliminary estimation was made of an exposure assessment strategy also covering the dermal route.

Dermal exposure was studied in plywood and paint manufacturing (phenol and xylenes, respectively), electroplating, the grinding of stainless and acid-proof steel (chromium) and during pesticide application in greenhouses (three pesticide products). The potential or actual dermal exposure was measured with different sampling methods. It was found that the exposure levels vary largely between the different processes and between individuals and body parts. It was also proven that it is not possible to predict dermal exposure levels by merely measuring breathing-zone concentrations. The advantages and limitations of the sampling methods applied were assessed. The results were also used in an attempt to find factors influencing exposure, but without complete success, thus requiring additional research.

The measurements done in electroplating and grinding have been included in European survey of occupational dermal exposure aimed at developing models for assessment of chemical risks at workplaces. The approach of allocation of work tasks into groups that can be treated as the basis for modelling was tested. The a priori developed groups (dermal exposure operation units) were shown to be too broad.

The European Predictive Operator Exposure Model, known as EUROPOEM has been developed for operator exposure assessment in pesticide application work. The number of indoor application data were to be increased with field sampling. It was clear, that increasing the number of data points and scenarios improves the model. Most importantly, with models like EUROPOEM, the assessor's expertise has a crucial significance on the result of the modelling.

A preliminary study of the European standard EN-689, and its concept of homogeneous exposure groups in incorporating dermal exposure, showed that the strategy is not practical at workplaces. This is due to the fact that applying EN-689 requires a large number of measurement data, which, especially in the case of dermal exposure is expensive and time consuming. A lack of assessment strategies for dermal exposure causes problems when total exposure to chemicals is assessed. New, more practical approaches should be developed.

Universal Decimal Classification: 331.436
National Library of Medicine Classification: WA 465
Medical Subject Headings: occupational exposure; skin; workplace; industry; hazardous substances; agrochemicals; pesticides; models, theoretical

YHTEENVETO (FINNISH SUMMARY)

Kemikaalialtistumista tapahtuu työpaikoilla usein paitsi hengitysteiden, myös ihon kautta. Lisäksi ihoon voi kohdistua paikallisia vaikutuksia. Suomessa ihoaltistumista on alettu tutkia määrätietoisesti vasta viimeisen vuosikymmenen aikana.

Tutkimuksen tarkoituksena oli testata erilaisia työhygieenisiä ihoaltistumisen mittausmenetelmiä käytännön kenttäolosuhteissa. Erityisesti haluttiin selvittää kerätyn mittaustiedon soveltuvuutta altistumisen mallintamiseen. Lisäksi pyrittiin selvittämään olemassaolevan torjunta-ainealtistumisen mallintamiseen luodun mallin käyttökelpoisuutta ja parantamaan sen luotettavuutta kasvihuoneolosuhteissa. Altistumisen arviointistrategioiden puute on tunnistettu, ja tutkimuksessa haluttiin myös alustavasti arvioida hengitystiealtistumisen arviointiin luodun, standardoidun strategian toimivuutta myös ihoaltistumisen arvioinnissa.

Ihoaltistumista tutkittiin vaneritehtaalla (fenoli), maalitehtaalla (ksyleenit), metallien pintakäsittelyssä (kromi), ruostumattoman ja haponkestävän teräksen hionnassa (kromi) ja torjunta-ainetyössä kasvihuoneissa (malationi, iprodioni ja deltametriini). Vaatteiden päälle tai paljaalle iholle tulevaa altistumista ja ihon altistumista suojavaatetuksen alla tutkittiin erilaisilla mittausmenetelmillä. Tutkimuksessa havaittiin, että altistumistasot vaihtelivat suuresti eri prosesseissa ja työntekijöiden sekä eri kehon osien välillä. Tutkimus todisti myös, että ihoaltistumista ei voida arvioida mittaamalla hengitystiealtistumista. Tutkimuksessa arvioitiin myös käytettyjen mittausmenetelmien etuja ja heikkouksia. Mittaustulosten avulla pyrittiin päättelemään mitkä tekijät prosessissa, työpaikalla tai työntekijän käyttäytymisessä vaikuttavat siten altistumiseen, että niitä voitaisiin käyttää altistumisen arvioinnin apuna sekä mallinnuksessa. Altistumiseen vaikuttavien, selkeiden tekijöiden löytäminen osoittautui vaikeaksi.

Pintakäsittely- ja hiontatyössä tehdyt mittaukset ovat osa eurooppalaista työperäisen ihoaltistumisen mittausprojektia, jossa on tarkoituksena luoda malleja ihoaltistumisen arvioimiseksi kemikaaliriskien arvioinnin osana. Lähestymistapana käytettiin työtehtävien jakoa ryhmiin, joissa altistuminen olisi samantyyppistä ja joissa altistumiseen vaikuttavat tekijät olisivat samanlaisia. Ryhmäjakoa käytettäisiin mallien pohjana. Tutkimuksessa havaittiin, että aiemman asiantuntemuksen ja kirjallisuustietojen perusteella tehty ryhmäjako ei sellaisenaan tule toimimaan mallinnuksessa, vaan sitä on tarkennettava huomattavasti.

EUROPOEM-malli on kehitetty torjunta-ainetyöntekijän altistumisen arvioimiseksi mm. torjunta-aineen levitystyössä. Tutkimuksen tarkoituksena oli tuottaa lisää kasvihuoneessa kerättyjä mittaustuloksia mallin pohjana olevaan tietokantaan. Mittaustulosten lisääminen paransi mallin tarkkuutta. Edelleen mallin käyttäjän asiantuntemus on erittäin tärkeää tulosten luotettavuuden kannalta.

Eurooppalaisessa standardissa SFS-EN-689 esitetään mittausstrategia hengitystiealtistumisen arvioimiseksi työpaikoilla. Väitöskirjatutkimuksessa selvitettiin alustavasti pilottimittakaavassa kyseisen strategian mahdollisuuksia toimia myös ihoaltistumisen arvioinnin pohjana. Strategian taustalla on työntekijöiden jakaminen homogeenisesti altistuviin ryhmiin tiettyjen tilastollisten perusteiden mukaisesti. Edes selkeästi hyvin samantyyppistä liimaustyötä tehneiden työntekijöiden ryhmä ei ollut homogeeninen standardin mukaisesti. Strategia ei osoittautunut käytännölliseksi työpaikoilla mm. suuren mittaustarpeen vuoksi. Ihoaltistumisen arviointistrategioiden puute vaikeuttaa ihoaltistumisen arviointia työpaikoilla. Uusia lähestymistapoja tarvitaan, jotta myös ihoaltistuminen voidaan tehokkaasti huomioida kokonaisaltistumista arvioitaessa.

ACKNOWLEDGEMENTS

This work was carried out at the Kuopio Regional Institute of Occupational Health in 1996-2003. I am grateful to Professor Jorma Rantanen, former Director General of the Finnish Institute of Occupational Health, and to Professor Harri Vainio, current Director General, for placing the excellent facilities of the Institute at my disposal.

I am greatly indebted to my supervisors, Professor Pentti Kalliokoski, Vice-rector of the University of Kuopio, and Professor Juhani Kangas, Director of the Kuopio Regional Institute of Occupational Health, for their collegial and critical comments and their untiring and friendly encouragement through out all phases of the study.

I express my thanks to Professor Leena Nylander-French and Professor Heikki Savolainen for their constructive criticism and expert review of the final manuscript. I also wish to thank Georgianna Oja, E.L.S. for the revision of the English text.

The invaluable contribution and ever-helpful attitude of my colleagues at the Kuopio Regional Institute of Occupational Health is cordially acknowledged. Especially I wish to mention the chief of our laboratory, Markku Linnainmaa, PhD, Anneli Tuomainen, PhD, Doc., Juha Laitinen, PhD and Professor Jyrki Liesivuori. In addition, without the excellent technical help of Pirjo Aholainen, Pirkko Ilkka, Juhani Rautiainen and Sirkka Roivainen, this study would not have been completed. Importantly, they always made the workdays great fun.

My kind appreciation is also due to Maria Hirvonen, MSc, for her statistical advice, and to Raija-Leena Pajula, MSc, for the library services. I also wish to thank the staff and the management of the workplaces participating this study for their cooperation.

Financial support was provided by the Finnish Work Environment Fund, the European Commission, The Ministry of Social Affairs and Health, and Finnish Occupational Hygiene Society, for which I am sincerely grateful.

Finally, I owe my warmest thanks to my partner Kari for his encouragement and loving care.

Kuopio, December 2003

Milja Mäkinen

ABBREVIATIONS

ACGIH	American Conference of Governmental Industrial Hygienists
AIHA	American Industrial Hygiene Association
AOEL	acceptable operator exposure level
ANOVA	analysis of variance
BEAT	Bayesian exposure assessment tool
CEC	Commission of the European Communities
CEN	Comité Européen de Normalisation (European Committee for Standardization)
DEO	dermal exposure operation unit
DOEL	dermal occupational exposure level
EASE	Estimation and Assessment of Substance Exposure
EC	European Community
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
EEC	European Economic Community
EN	norme européenne (European standard)
EUROPOEM	European Predictive Operator Exposure Model
EPA	Environmental Protection Agency
HEG	homogeneous exposure group
HTP	haitalliseksi tunnettu pitoisuus (occupational exposure limit)
ILSI RSI	International Life Sciences Institute, Risk Science Institute
JMP	Joint Medical Panel
LD_{50}	lethal dose 50%
NOAEL	no-observed adverse effect level
OECD	Organization for Economic Co-operation and Development
OEL	occupational exposure limit
OEL_{int}	internal occupational exposure limit
PHED	Pesticide Handlers Exposure Database
RISKOFDERM	Risk Assessment for Occupational Dermal Exposure to Chemicals
RTECS	Registry of Toxic Effects of Chemical Substances
SEG	similarly exposed group
STM	Sosiaali- ja terveysministeriö (Ministry of Social Affairs and Health)
WHO	World Health Organization

LIST OF ORIGINAL PUBLICATIONS

This dissertation is based on data presented in five articles. In the text, these sources are referred to by their Roman numerals:

I. Mäkinen M., Kalliokoski P. and Kangas J. (1999) Assessment of total exposure to phenol-formaldehyde resin glue components in plywood manufacturing. *International Archives of Occupational and Environmental Health*. 72: 309-314.

II. Mäkinen M. and Linnainmaa M. (2003) Dermal exposure to chromium in electroplating. *Annals of Occupational Hygiene.* (in press)

III. Mäkinen M. and Linnainmaa M. (2003) Dermal exposure to chromium in the grinding of stainless and acid proof steel. *Annals of Occupational Hygiene.* (in press)

IV. Tuomainen A., Mäkinen M., Glass R. and Kangas J. (2002) Potential exposure to pesticides in Nordic greenhouses*. Bulletin of Environmental Contamination and Toxicology*. 69:342-349.

V. Mäkinen M., Kangas J. and Kalliokoski P. (2000) Applicability of homogeneous exposure groups for exposure assessment in the chemical industry. *International Archives of Occupational and Environmental Health*. 73:471-478.

In addition, some unpublished data are presented.

CONTENTS

1. INTRODUCTION

Even though the first cases of work-related illness reported in association with the dermal absorption of chemicals, scrotum cancers of chimney sweeps, were identified as early as 1775 by Sir Percival Pott in England (Waldron, 1983), dermal exposure has generally been recognised as an occupational hazard only since the end of the 19th century. Even today, dermal exposure assessment is not a priority in the field of occupational hygiene. However, a considerable awakening occurred in the 1980s, and a systematic characterisation of this field began with the formalisation of the definitions of dermal exposure, its pathways and mechanisms, and the designing of sampling methods and strategies (Fenske, 2000).

Agricultural pesticides have long been an exception to the lack of recognition given to dermal exposure to chemicals. For them, the dermal route of exposure has been noticed to be predominant for some 50 years (van Hemmen & Brouwer, 1995). Batchelor & Walker published the first scientific report on dermal exposure measurements for pesticides in 1954 (Ness, 1994). Pesticides still remain the only group of chemicals with a standardised international guidance protocol for measuring dermal exposure (WHO, 1986; Fenske, 1993; OECD, 1997).

Currently, the key issue in dermal exposure research is the need to develop biologically relevant monitors that would mimic skin properties and measure concentration rather than mass (Cherrie & Robertson, 1995; van Hemmen & Brouwer, 1995; Schneider et al., 1999; Soutar et al., 2000). Numerous researchers and institutions have pointed out the complexity of measuring dermal exposure and the discrepancies observed with of current methods, e.g., US EPA, 1992; Fenske, 1993; Cherrie & Robertson, 1995; van Hemmen & Brouwer, 1995; OECD, 1997; Schneider et al., 1999; Sartorelli, 2002; McDougal & Boeniger, 2002; to mention a few.

The growing concern for dermal exposure led to a meeting of investigators funded by the European Commission to discuss dermal exposure and related issues. This meeting produced the idea of networking researchers of this field to help fill in the recognised data gaps (Dost, 1995). The practical outcomes of the network have been, for example, a theme issue of dermal exposure assessment in the *Annals of Occupational Hygiene* (44/2000) and a programme called the RISKOFDERM (Risk Assessment for Occupational Dermal Exposure to Chemicals, QLK4-CT-1999-01107), funded by the European Commission (RISKOFDERM, 1999).

Developing valid predictive models for dermal exposure is another important aim in Europe. Such development is needed to meet the requirements of chemical legislation, such as chemical agents directive, new and existing substances legislation, plant protection products directive and biocidal product directive (EC, 1967; EC, 1991; EC, 1994; EC, 1998a and b), of the European Union, which requires the assessment of worker exposure by all relevant routes, including the skin. So far, the development has been the most rapid for pesticide operator exposure (EUROPOEM II, 2003). Nevertheless, for example, the EASE model (Estimation and Assessment of Substance Exposure), recommended by the European Commission, that has been developed to assess exposure to new and

existing chemicals is insufficient, especially with respect to dermal exposures (CEC, 1996; Benford et al., 1999).

In order to assess risks related to systemic effects caused by dermal exposure, it is necessary 1) to determine the amount of contaminant on the surface of the skin, 2) to assess systemic uptake, and 3) to evaluate potential health effects (Benford et al., 1999; McDougal & Boeniger, 2002, Sartorelli, 2002). This dissertation concentrates on the questions related to the first category.

2. RELEVANCE OF CHEMICAL DERMAL EXPOSURE AT WORKPLACES

The work environment is a complex entity with potential to induce exposure via multiple routes and pathways. In order to assess total exposure to chemicals effectively, all these pathways, including the skin, must be taken into account (Figure 1) (Mulhausen & Damiano, 1998).

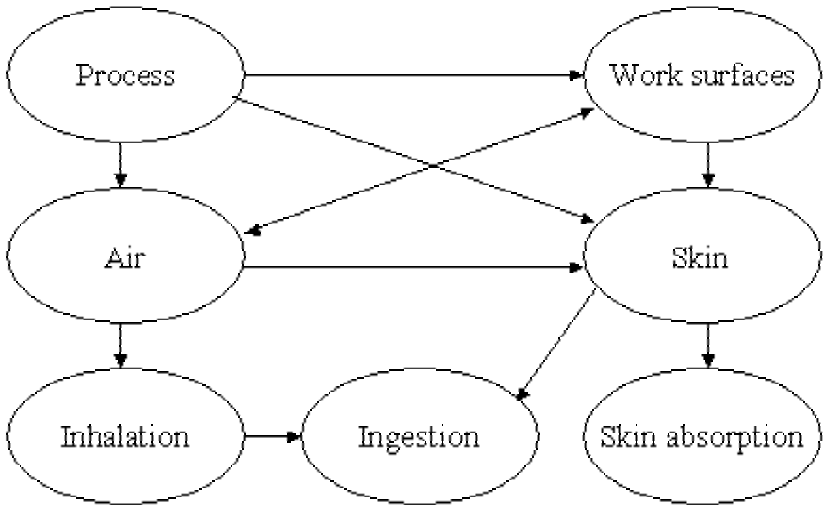

Figure 1. Model of exposure pathways in work environment (adapted from Mulhausen & Damiano, 1998).

The adverse effects caused by skin exposure can occur locally within the skin or systemically due to absorption through the skin and dissemination via the vascular and lymphatic systems (Cherrie & Robertson, 1995; van Hemmen & Brouwer, 1995). Dermal exposure can also lead to oral uptake due to eating, smoking, and the like with contaminated hands. Through contact, contaminated hands can redistribute substances to other parts of the body, such as the eyes or genital areas. Contaminated work clothing can also lead to exposure at home (van Hemmen & Brouwer, 1995). The assumption that personal protective garments, such as gloves, totally prevent dermal uptake has proven to be untrue. For example, the reluctance to wear protective equipment (cultural and climatic issues), the permeability of some types of garments, contaminant deposition on unprotected areas of the skin, and contamination of the inner layer of clothing may reduce the effectiveness of personal protection (Benford et al., 1999). It has also been noted that, sometimes, the correlation between occupational hygiene sampling and biological monitoring is poor. This poor correlation may be due to differences in the hygienic behaviour of workers. However, when the results of biological monitoring were compared with visual observations of the behaviour (work habits, personal hygiene, etc.) of chromium platers and grinders, the correlation was good (Lumens et al., 1993).

2.1 Systemic exposure

Many compounds are known to penetrate skin. Health hazards caused by the dermal uptake of pesticides, amines, and phenols have been known already for a long time (Fiserova-Bergerova, 1993). In a handbook of occupational dermal exposure, almost 300 substances are listed as relevant with respect to skin permeability in occupational or environmental settings according to United States regulatory agencies and scientific publications (Ness, 1994).

The significance of dermal exposure has increased in relation to that of respiratory exposure as permissible inhalation exposures have decreased (Fiserova-Bergerova, 1993; Benford et al., 1999). Occupational exposure limits (OELs) have been reduced even by orders of magnitude, and, therefore, chemicals with skin penetration rates high enough to contribute significantly to total exposure currently constitute a large part of the widely used compounds. They clearly account for over 30% of the agents provided with skin notation in OEL lists (Fiserova-Bergerova, 1993). On the other hand, it has been shown that reducing the sources of airborne contaminants also reduces dermal exposure (Vermeulen et al., 2000a).

Skin consists of two to three layers, depending on the definition: 1) the epidermis, 2) the dermis and 3) the hypodermis. The *epidermis* is a non-vascular layer formed by layers of living (so-called viable epidermis) and dead cells, the layer of dead cells, the s*tratum corneum,* acting as the diffusion barrier on the epidermis. The *dermis* is composed of elastic and collagen tissue and it also contains the sweat glands, hair follicles, sebaceous glands, blood vessels and nerves. Blood perfusion of the dermis accounts for about 3% of cardiac output. The *hypodermis*, which is not always categorised as a skin layer at all, consists mainly of connective tissues and fat. It is perfused by 2.2% of cardiac output. In order to be circulated in blood, a chemical needs to penetrate through the stratum corneum to the perfused layers (US EPA, 1992; Fiserova-Bergerova, 1993; Ness, 1994). The transport processes in the stratum corneum include intercellular, transcellular, and transappendageal (penetration via skin appendages) diffusion. According to Fick's law of diffusion, the total mass uptake at steady state, or flux, is proportional to the concentration gradient across the skin barrier, the area exposed, and the duration of exposure (Equation 1) (U.S.EPA, 1992).

Equation 1.	Flux (cm/h) = chemical diffusivity (cm^2/h) x [concentration difference between outer and inner surface of stratum corneum (mg/cm^3) / thickness of stratum corneum (cm)]

The main factors influencing dermal absorption are 1) the physicochemical properties of the chemical (solubility and chemical structure), 2) skin differences (e.g., between body parts), and 3) differences in exposure (production and worker-related factors) (Fiserova-Bergerova, 1993; Leung & Paustenbach, 1994). Loss processes such as evaporation from the surface, metabolism, and binding determine the amount absorbed through the layers. The thickness of the stratum corneum varies largely between different body parts, as shown in Table 1 (US EPA, 1992).

Table 1. Regional variation in the thickness of human stratum corneum (from EPA, 1992)

Body area	Thickness of stratum corneum (µm)
Abdomen	15
Forearm (interior)	16
Back	11
Forehead	13
Scrotum	5.0
Back of hand	49
Palm of hand	400
Sole of foot	600

In addition, hairiness, presence of glands, amount of perspiration, environmental conditions (temperature and humidity), and vehicle of the chemical have also an effect on penetration (Fiserova-Bergerova, 1993). Furthermore, the condition of the skin affects its barrier function. The permeability of the skin can increase considerably if the skin is excessively hydrated (prolonged contact with aqueous media or sweating), the skin and the contaminant are occluded, dermatological diseases occur, if the skin is damaged by abrasion, trauma or corrosive chemicals, or lipids are removed by organic solvents, soaps or other detergents (Grandjean, 1990). Specifically, in industrial settings, the most important factors related to dermal absorption are exposure duration, surface area of the exposed skin, form of the chemical in question, physical activity of the worker, and skin temperature (Fiserova-Bergerova, et al., 1990).

Chemicals can end up on to the skin in all physical forms: liquid, solid, vapour, or aerosol (McDougal & Boeniger, 2002). Liquid substances are considered the most important causes of dermal exposure in occupational and environmental settings (US EPA, 1992; McDougal & Boeniger, 2002). Liquids can be pure substances, mixtures, or aqueous solutions. Important determinants of liquid exposure are evaporation, the ability of the liquid to change skin condition, and, as a consequence, penetration (McDougal & Boeniger, 2002). The bioavailability of chemicals depends of the matrix (Leung & Paustenbach, 1994).

Exposure to solids (usually particles) can result in their adherence to the skin, where they persist until washed off. Exposure-determining factors include particle size and solubility. The importance of dermal exposure to solids is not generally well known (Schneider et al., 1999; McDougal & Boenigier, 2002).

For vapours, uptake through the skin is generally negligible when compared with inhalation uptake, as the total skin surface area of the body is about 1.8 m^2, whereas the surface area of the lungs is up to 90 m^2 (van Hemmen & Brouwer, 1995). Therefore, only the liquid portion is usually significant with respect to volatile chemicals and their dermal uptake (Cohen & Popendorf, 1989). In a recent study of the uptake of solvent vapours, in which groups of volunteers were exposed to OEL concentrations, it was noted that, for xylene, toluene and tetrahydrofuran, dermal route contributed only about 1-2% of the total body burden, and, for methyl ethyl ketone, it was 3.0-3.5%. However, for a glycol ether (1-methoxypropan-2-ol), 5-10% of the total uptake was obtained via the dermal

route (Brooke et al., 1998). In another volunteer study, the effect of environmental conditions (temperature, humidity, clothing) on the dermal uptake of 2-butoxyethanol was assessed. It was shown, as predicted, that, with higher temperatures and humidities, the uptake increased. Surprisingly, the clothing (T-shirt and shorts vs. Tyvek® coveralls) had very little effect on dermal absorption. When the volunteers were exposed to conditions of an "industrial scenario" with a high temperature and high humidity, while wearing coveralls, the dermal uptake was reported to cause 39% of the total uptake. In all the other experiments, the proportion absorbed dermally was between 10% and 15% (Jones et al., 2003). In the fibreglass-reinforced polyester industry, it has also been shown that percutaneous styrene absorption is not important when compared with respiratory exposure (Limasset et al., 1999).

2.1.1 Percutaneous penetration data for regulatory purposes

If no data are available on percutaneous absorption, a default value of 100% of dermal absorption is often used as the worst-case scenario in regulative risk assessment, even though it is not even close to a realistic assumption (Benford et al., 1999). In RTECS (Registry of Toxic Effects of Chemical Substances of the United States National Institute for Occupational Health and Safety) database search, 16 times more oral toxicity studies were available than dermal studies, and there were four times as many inhalation studies as dermal studies. For risk assessment, therefore, in many cases, route-to-route extrapolations must be used (McDougal & Boeniger, 2002). As a result, percutaneous absorption data produced in real exposure conditions could have a large impact on regulatory risk assessment (Benford et al., 1999; McDougal & Boeniger, 2002). For this purpose, an improved protocol has been proposed for regulative toxicity studies of pesticides in order to enhance the relevancy of toxicological data in assessing occupational risks (Ross et al., 2001).

In order to generate such data, results from human volunteer studies would be appropriate. For example, for pesticides, the generation of such data has been strongly encouraged (Woollen, 1993). In vivo data can also be produced with animals. In vitro methods, using human skin as the membrane, are commonly used. Both methods have their advantages and disadvantages, but they both offer a better option for risk assessors than the use of defaults like 100% (Benford et al., 1999). Biological mathematical modelling to predict internal dose has also been increasing lately (McDougal & Boeniger, 2002).

2.1.2 Dermal exposure levels

The risk assessment process related to dermal exposure is complex. With current knowledge, it is not possible to compare exposure levels with health-based OELs, as there are large gaps in the needed knowledge, for instance, a lack of dermal absorption data relevant for the realistic exposure scenarios (Benford et al., 1999). In the next few sections, the current approaches and developments are introduced.

2.1.2.1 Skin notations

Skin notations have been adopted in the OEL lists of several countries. Skin notations indicate the chemicals for which evidence exists for skin absorption. If a chemical does not have a skin notation, it does not automatically mean that the dermal route is not relevant, but, instead, that not enough knowledge is available on the issue (McDougal & Boeniger, 2002). The basic purpose of skin notation is to attract attention to the dermal route. Skin notations do not indicate the degree of hazard (Sartorelli, 2002). They are also only applied to chemicals that have a respiratory exposure limit (Packham, 2003).

The basis for skin notations differs between policy-making organisations. The traditional method of assigning them has been to base the criteria on acute dermal toxicity studies (dermal LD_{50} on rabbits or rats). American Conference of Governmental Industrial Hygienists (ACGIH) assigns the skin notation based on the potential for a significant contribution to the overall exposure by the cutaneous route. The chemical may receive a skin notation if its dermal LD_{50} is smaller than 1 g/kg. Furthermore, ACGIH recommends that biological monitoring should be used to determine the relevant contribution of dermal absorption to the systemic dose (ACGIH, 2000).

In the Finnish list of OELs, 165 skin notations can currently be found. This number corresponds to about 27% of all substances listed for OELs. In Finland, a skin notation is assigned to substances that can be absorbed through the skin and can cause health effects, which cannot therefore be evaluated only according to their air concentrations (STM, 2002).

In Sweden, a skin notation indicates that the substance can easily be absorbed percutaneously. About 23% of the chemicals listed for OELs have a skin notation (Sartorelli, 2002).

In the United Kingdom, skin notations are assigned to substances that can penetrate intact skin and contribute to systemic toxicity. Data requirements consist of available or predicted information on showing a substantial contribution to body burden or possible systemic effects (Sartorelli, 2002).

According to German regulations, substances that can penetrate the skin have skin notations, for which specific protective health and safety measures, such as biological monitoring, must be arranged. A substance is considered to be absorbed through the skin according to (in order of decreasing significance) surveys and field studies, in vivo animal studies, in vitro penetration studies, and theoretical models (Sartorelli, 2002).

In Italy and France, there are no official systems for skin notations, and, for the most part, occupational hygienists use ACGIH notations (Sartorelli, 2002).

The Dutch Expert Committee on Occupational Standards approach is based on the comparison of dermal uptake with respiratory uptake. In The Netherlands, a skin notation should be assigned when the amount absorbed by the arms and forearms in an hour is more than 10% of the amount absorbed by inhalation during exposure equalling the OEL concentration for 8 hours. This approach has been criticised, however, as it has been noted that also other more permeable areas of the skin may be

highly relevant for dermal absorption, even though the external exposure is not as high (de Cock et al., 1996). The OELs may also be defined according to effects not relevant to internal dose, such as respiratory irritation or discomfort (Fiserova-Bergerova et al., 1990; de Cock et al., 1996).

2.1.2.2 Banding approach

The Health and Safety Executive in the United Kingdom has proposed a banding approach to control risks, especially those in small enterprises. Chemicals are categorised by their hazardous characteristics into bands of acceptable exposure, and, as a consequence, into corresponding concentration ranges. Safety data sheets are used as the main source of information. The combined risk phrases of the chemical determine into which band the chemical is placed (Brooke, 1998; Maidment, 1998). The approach has been described as conservative with a default value of 100% for dermal absorption. However, it provides more information than skin notation for controlling dermal risks (McDougal & Boeniger, 2002).

2.1.2.3 Dermal occupational exposure levels

The need to develop quantitative dermal occupational exposure levels (DOELs) has been expressed by several authors (e.g., Fenske, 1993; Bos et al., 1998; Brouwer et al., 1998). Fenske (1993) suggested that dermal exposure levels could be controlled from the following three aspects of the exposure: 1) biological measures of exposure, 2) levels of contamination on clothing, or 3) levels of deposition on skin or surfaces of the workplace. In the Dutch approach (Bos et al., 1998; Brouwer et al., 1998), it is suggested that a DOEL should represent the maximum amount of substance deposited on the skin during a period of time (usually a workshift) without adverse effect. Exposure levels could also be set for surface contamination. The proposed DOEL can have units of area (maximum skin surface area that can be exposed without exceeding the internal OEL) or mass (acceptable dermal surface density over exposed skin area), depending on the measurements used for the calculations.

DOEL may be calculated with a two-phase approach. First, an internal health-based occupational exposure limit (i.e., a maximum dose absorbed without leading to adverse systemic effects [OEL_{int}]) is calculated. Second, this OEL_{int} value is used to derive an external DOEL on the basis or flux rate or the percentage of absorption (Bos et al., 1998; Brouwer et al., 1998; McDougal & Boeniger, 2002). In conclusion, the DOELs developed by Bos et al. (1998) can be used to define the maximum skin surface area to be exposed for a given time period (workshift). This approach can be used if a flux derived under occupationally relevant exposure conditions is available. In this case, if the exposed area is smaller than the maximum area defined, no health risk is indicated for dermal exposure. If there is no flux derived, or exposed area is larger than the maximum area, the DOEL is to be interpreted as the product of dermal area dose and area exposed. Then, if the area decreases, the dose can be allowed to increase. Therefore, for a specific substance, the DOEL can be set at different levels depending on the actual surface area of exposed skin (Bos et al., 1998).

The major uncertainties with this approach are the lack of validated techniques for measuring dermal exposures, the difficulties in evaluating the areas of contamination, the variation in skin permeability, the lack of dermal absorption data, and between-worker variation. In addition, the calculation process is complex, as different scenarios lead to different units of exposure. These issues lead to simplifications in risk assessment, but such is also the case in calculations of gastrointestinal or respiratory uptake (McDougal & Boeniger, 2002; Sartorelli, 2002). In addition, it has been recently demonstrated that, contrary to common belief, the variability of between-worker exposure is not larger for dermal exposures than for respiratory exposures (de Cock et al., 1998; Kromhout & Vermeulen, 2001).

2.2 Skin diseases

Dermatological illnesses are the most important group of occupational diseases reported in many industrialised countries (Cherrie & Robertson, 1995; Jolanki et al. 1998; Lushniak, 2003). Occupational skin diseases are an important public health problem. In addition to being common, they usually have a poor prognosis, and they cause considerable economic loss due to sick leave. Skin disorders are also often restricting and annoying for the individual (Diepgen & Coenraads, 1999; Lushniak, 2003).

The incidence rate of occupational contact dermatitis is approximately 0.5 – 1.9 cases per 1000 full-time workers per year (Diepgen & Coenraads, 1999). In Finland, 21% of all occupational diseases registered in the year 2001 were dermatoses (Ammattitaudit 2001).

Irritant dermatitis is reported to account for about 70% of all cases of occupational dermatological illnesses. The common causes are repetitive wet work, mechanical irritation, and certain chemicals. Allergic contact dermatitis is caused by a hypersensitivity response to a contact allergen due to sensitisation to the parent compound or reactive metabolite. Important factors influencing the development of allergic contact dermatitis are exposure time, type of exposure, concentration of allergen, and genetic susceptibility (Basketter et al., 1999).

Dose-response characteristics in contact sensitisation have been under extensive research. This research has led to the determination of safe concentrations or thresholds for allergens, expressed as dose per unit surface skin area or as release from surface (Wass & Wahlberg, 1991; Nethercott et al., 1994; Kimber et al., 1999). For consumer products, an ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) task force has published allowable concentrations of deposition for chromium, nickel, and cobalt (Basketter et al., 2001). In conclusion, this approach could serve as a tool in risk assessment and management in occupational settings (Nethercott et al., 1994).

3. CONCEPTS AND PATTERNS OF DERMAL EXPOSURE

Skin contamination can occur from the deposition of aerosols, via direct immersion into a chemical substance (liquid or solid), as a result of spills and splashes, through vapour penetration, or from contact with contaminated surfaces (Fenske, 1993; Ness, 1994; van Hemmen & Brouwer, 1995). Dermal exposure has been described as an interactive process between a source of contaminants and the body with several loading, transfer, and decontamination processes (van Hemmen & Brouwer, 1995).

Dermal exposure is often divided into potential dermal exposure and actual dermal exposure. The definition of these concepts vary in different sources. In this thesis, these terms are used based on the definitions presented in the glossary of terms in the OECD guidance document for pesticide studies (OECD, 1997). In the document, the potential dermal exposure is defined as "the total amount of pesticide coming into contact with the protective clothing, work clothing and skin." The term actual dermal exposure refers to "the amount of pesticide coming into contact with bare (uncovered) skin and the fraction transferring through protective and work clothing or via seems to the underlying skin, and which is therefore available for percutaneous absorption." These definitions are also used throughout the RISKOFDERM project. Both potential and actual dermal exposure in this context refer to external exposure. Another approach is to define actual exposure as the internal dose.

A more-detailed conceptual model describing the pathways leading to dermal exposure and the intermediate compartments of the contaminants has been presented to define consistent terminology and to ensure that the most appropriate variables are taken into account when dermal exposure situations are described and dermal exposure is assessed (Figure 2). The model describes the transport of contaminant mass from the source of a hazardous substance to the surface of the skin. Pathways between six compartments (source, air, surface contaminant layer, outer clothing contaminant layer, inner contaminant layer and skin contaminant layer) and two barriers (clothing and stratum corneum) are described with eight mass transport processes (emission, deposition, resuspension or evaporation, transfer, removal, redistribution, decontamination, and penetration and permeation) (Schneider et al., 1999). This model acts as a framework for uniform terminology and increases the awareness of exposure routes and factors. It should lead to greater consistency across the field of dermal exposure, and allow studies to be compared (Soutar et al., 2000), and lead to the development of more standardised dermal exposure assessment strategies (Vermeulen et al., 2000b).

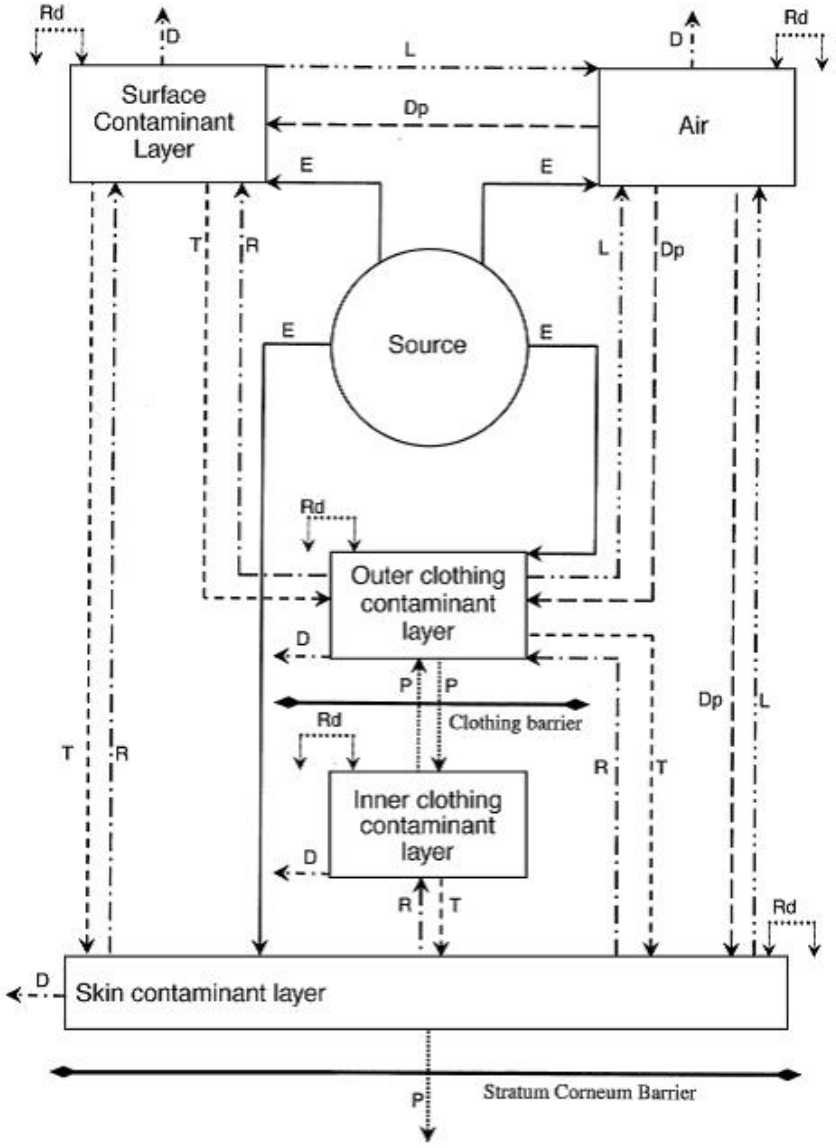

Figure 2. The conceptual model proposed by Schneider et al. (1999). Systematic presentation of the overview, compartments and transport processes. E = emission (———), Dp = deposition (– – –), L = resuspension/evaporation (– ·· – ·· –), T = transfer (- - - -), R = removal (– · – · –), Rd = redistribution (····), D = decontamination (– · – · –), P = penetration/permeation (····).

3.1 Dermal exposure measurement methods

There are several reasons for measuring dermal exposure. First, measurement data are needed for defining the exposure pathways, quantifying the extent and magnitude of skin contamination, and evaluating variability. In some obvious cases, visual observation may already provide sufficient information. A second rationale is to evaluate the efficacy of protective clothing, which cannot be reliably assessed with mere laboratory testing. The performance of protective clothing also depends on such matters as worker behaviour and material degradation. Thirdly, dermal exposure measurements are important when the skin is the main contributor of total exposure. Especially when there are no valid biological monitoring methods available, occupational hygiene measurements are necessary (Fenske, 1993). It must also be noted that biological monitoring has no relevance when local skin effects are considered (van Hemmen & Brouwer, 1995).

An ideal dermal exposure assessment method would 1) measure the amount available for penetration through the skin, 2) estimate skin deposition and loading unbiased by duration and sampling time, 3) enable repeated sampling, 4) be applicable to all anatomical regions, 5) mimic various processes of loading and removing, and 6) have high resolution and low detection limits - and it would be validated sufficiently (van Hemmen & Brouwer, 1995).

The uptake rate of chemicals via skin is dependent on the concentration of the material on the surface of the skin rather than on its mass (Cherrie & Robertson, 1995; Schneider et al., 1999). In the conceptual model of dermal exposure, the concentration on the skin is defined as the mass of hazardous material on the skin surface divided by the sum of the hazardous material and the mass of all other liquid substances, like sweat, skin oil, and possible barrier cream (Schneider et al., 1999). However, all current assessment methods for dermal exposure still measure the mass deposited on the skin, rather than concentration. During the past few years, this shortcoming has been discussed thoroughly (Brouwer et al., 2000a; Cherrie et al., 2000; Soutar et al., 2000). In a situation in which the concentration of the hazardous substance is constant, it has been suggested that uptake could be proportional to the product of the area exposed and the duration of exposure. This alternative exposure metric could be used as a surrogate approach and is practically achievable with the use of a fluorescent tracer (Brouwer et al., 2000b; Cherrie et al., 2000).

The direct techniques for assessing dermal exposure can be divided into three main categories (Fenske 1993). These methods include surrogate skin techniques, removal techniques, and fluorescent tracer techniques. In addition, surface sampling can be used to assess dermal exposure indirectly. Biological monitoring can also be applied to assess dermal exposure, even though it does not distinguish the exposure routes (Fenske 1993). Most of the methods currently used to assess dermal exposure originate from pesticide studies. These methods have been reviewed, for example, by Davis (1980), Nigg & Stamper (1985), and Worksafe Australia (1995). The presentation of methods in the next sections is not exhaustive, but it covers the main approaches generally used.

3.1.1 Surrogate skin techniques

Surrogate skin techniques, also called the pseudo-skin approach, refer to placing collection medium against the skin or clothes and subsequently analysing it for its chemical content. The methods include patch sampling, during which the patches cover small surface areas, and garment samplers or overalls, which cover entire body regions or even the whole body (Fenske, 1993; van Hemmen & Brouwer, 1995).

All surrogate skin techniques assume that the collection matrix captures and retains chemicals in the same manner as the skin, but this is not the case with the current materials used. Laboratory and field efficiencies, recoveries, and stabilities must be tested thoroughly for any patch or garment method used (Soutar et al., 2000).

3.1.1.1 Patch methods

The number of patches used per worker varies between protocols. The protocol most applied especially in pesticide studies, developed by the Organization for Economic Co-operation and Development (OECD) recommends the use of 13 patches (OECD, 1997), whereas the protocol of the World Health Organization (WHO) relies on six patches (WHO, 1986). In addition, the size of the patches varies considerably between published studies and protocols. The most commonly applied, traditional patch size is 10 x 10 cm. (Fenske, 1993). Usually, only one or two patches are attached under the clothing layer to measure actual exposure (Soutar et al., 2000). After the sampling and analysis, the measured amount is related to the surface area of the corresponding body part. Materials used for patches include surgical gauze, alpha-cellulose paper, charcoal, cotton gauze, polyurethane, and polypropylene (e.g., Nigg & Stamper, 1985; Cohen & Popendorf, 1989; McArthur, 1992; van Rooij et al., 1994; US EPA, 1996; OECD, 1997; Tucker et al. 2001). Generally, when liquid exposures are being assessed, the patch material should be absorbent enough to retain all the liquids contacting it. For particle sampling, the porosity of the material is the key issue (OECD, 1997; Soutar et al., 2000).

Patch sampling assumes 1) uniform exposure (i.e., the deposition rate on the patch is representative over the whole body part) or 2) worst-case exposure (i.e., the patch has been located at the point of highest exposure potential for the body part in question). Dermal exposure of a certain body region is calculated by multiplying the contamination found (mass/cm^2) by the corresponding skin surface area. For example, a patch of 100 cm^2 represents less than 2% of the total surface for the chest region (Fenske, 1990). Extrapolation can, however, sometimes lead to underestimation (droplets missing the patch when spraying) or overestimation (splash directly on the patch) (Soutar et al., 2000). When large databases of dermal exposure measurements (pesticides and industrial chemicals) have been studied to estimate the causes of variability, it has been shown that the largest component of variability is the between-body-location component (de Cock et al., 1998; Kromhout & Vermeulen, 2001). In a study of dermal exposure to polycyclic aromatic hydrocarbons, it was noted that the exposure estimate calculated with six patch samplers was 4.5-fold lower than that achieved with a whole body method (van Rooij et al., 1994). In another study, patch samplers

underestimated the exposure to copper by 28% to 82% when compared with the whole-body method (Wheeler & Warren, 2002). It is possible to decrease the potential error by increasing the size of the patch. Careful observation of work processes during sampling is also essential. If the limitations are accepted and taken into account, then patch sampling is a cost-effective and simple method for basic hazard evaluation and control (Soutar et al., 2000).

Another approach is to find the most efficient and representative location for a single patch. In a study of rubber manufacturers' exposure to cyclohexane-soluble matter, it was found that one patch attached to a worker's wrist had the high correlation of 0.89 with total body exposure. This approach allows more subjects to be studied, with same resources, and this aspect is important in processes with high between-worker variation (Vermeulen et al., 2000b).

3.1.1.2 Whole-body methods

The assumption of uniform exposure can be overcome by using garment or whole-body methods, with which lightweight disposable overalls, cotton overalls, and the like are used as samplers. The most important disadvantage of the method is the difficult and time-consuming extraction of the contaminant (Fenske, 1993; Soutar et al., 2000). The variation in the fit of the garment between different sized workers may also cause errors (van Rooij et al. 1994). The actual exposure and efficiency of protective clothing can be measured with underclothing as a monitor (van Hemmen & Brouwer, 1995; de Vreede et al., 1998). In a recent pesticide study, potential exposure was measured with cotton overalls, which were used both as a protective garment and as a monitor. Penetration through the overalls and the actual exposure were estimated with a Tyvek® coveralls worn under the cotton garments (Machera et al., 2003). The normal clothing of workers has also been used as monitors. This approach has the advantage of being suitable in conjunction with biological monitoring, as it does not add an extra layer to interfere with the normal process of skin contamination (Chester, 1995).

3.1.1.3 Glove method

An important application of garment sampling is the use of absorbent gloves, usually cotton liners, to measure the exposure of hands. They can be used in place of, underneath, or on the top of the protective gloves. Gloves are easy to use in the field, and they efficiently collect residues that would otherwise be absorbed into the skin during the sampling period. In some tasks, the gloves may interfere with normal work and their absorption characteristics inevitably differ from those of the skin. Gloves should not become saturated, and they should be replaced if soaked. (Ness, 1994). In most comparative studies (glove method vs. hand washing), it has been noted that the glove method produces higher estimates of exposure (Davis et al., 1983; Fenske et al., 1989; Fenske et al., 1999). However, underestimation has been also reported (Zweig et al., 1985).

3.1.2 Removal techniques

3.1.2.1 Washing and wiping

The most common removal methods are washing and wiping. Washing with water, water with surfactant, a water-alcohol mixture, or pure alcohol has been used to assess hand exposure, while wiping has also been applied to larger skin surfaces (Fenske, 1993; Brouwer et al., 2000a). Washing and wiping techniques are not, however, easily applicable to the assessment of total body exposure (van Hemmen & Brouwer, 1995; Brouwer et al. 2000a). The handwashing procedure has been standardised to ensure operator independency (CEN 1996). Skin wiping is not operator independent (Fenske, 1993; Brouwer et al., 2000a), but the variation can be reduced by limiting the number of operators within a study (Brouwer et al., 2000a). Wiping has also been reported to underestimate exposure. In a comparative study of wipe sampling, hand washing, and the glove method, it was noted that wipe sampling underestimated the exposure by 10-fold (Fenske et al., 1999). However, much better recoveries were found in another study, in which 2-propanol was used as the solvent instead of a water-surfactant mixture. In this study, it was also concluded that hand wiping is a more applicable approach in residential settings when the exposure of children is being assessed (Geno et al., 1996).

Conceptually, these methods measure the amount removable from the skin rather than the skin loading (Schneider et al., 1999). The removal efficiency must be studied a priori as a part of quality assurance (Fenske, 1993; Fenske & Lu, 1994; Brouwer et al., 2000a). Sampling efficiency studies should mimic the relevant exposure process (i.e., the field conditions and exposure patterns, relevant time of residence of the contaminant on the skin and relevant levels of skin loading present) (Brouwer et al., 2000a). In a study of removal efficiency of an organophosphorous insecticide called chlorpyrifos, it was found that ethanol removed 30% and an isopropanol-water mixture removed 43% when the skin loading was about 7 – 12 $\mu g/cm^2$. At lower skin loadings (0.1 – 1 $\mu g/cm^2$), the removal efficiency was even lower. Increasing time between exposure and washing also lowered the removal efficiency in some cases (Fenske & Lu, 1994). When the efficiency of a water and soap mixture in removing pesticide residues from hands was compared in field conditions and in the laboratory, the efficiencies were high and the variation between subjects was low in the laboratory compared with the measurements done in field conditions. Two consecutive washings can be used to achieve better removal (Marquart et al., 2002). However, washing may affect the integrity of the skin, and it becomes more penetrable. This characteristic decreases the opportunities to repeat the washing during the study period (van Hemmen & Brouwer, 1995). Using soap and water instead of organic solvents can largely prevent this increase in penetrability. In addition, a soap and water mixture usually removes the contaminants as efficiently as solvents (Marquart et al., 2002).

In a review article on handwashing and skin wiping procedures, in which 28 and 19 pieces of sampling efficiency data were reported, respectively, the efficiency ranged from 23% to 96% (median 73%) for hand washing and from 36% to 104% (median 5 %) for wiping (Brouwer et al., 2000a).

3.1.2.2 Tape stripping

A novel method for dermal exposure assessment for compounds of low volatility and long retention on the skin is the tape stripping of outer cell layers of the stratum corneum. It has been applied for multifunctional acrylates (Surakka et al., 1999 and 2000; Nylander-French, 2000) and metals (Cullander et al., 2000). Until today, these methods have only been used to assess hand and forearm exposure. It has been claimed that tape stripping, as wipe sampling, may not be as accurate as washing methods due to the larger variation caused by the operator performing the sampling (Roff et al., 2001).

3.1.2 Image processing with fluorescent tracers

Methods based on the fluorescence of substances enable the mass of a contaminant on the surface of skin and the area of skin exposed to be assessed simultaneously. It has been proposed that, together with recording the exposure time, an exposure estimate predicting dermal uptake could be derived (Cherrie et al., 2000). The method is also applicable for assessing the efficiency of protective garments (Fenske, 1988b; Archibald et al., 1994c; Fenske et al., 2002) and may serve as valuable tool for worker education and training (Fenske, 1993). The fluorescent tracer method has also been used to study the transfer and adherence of a chemical compound to the skin on a hand in contact with a contaminated surface (Brouwer et al., 1999). It has proven useful in finding exposure pathways and sources (e.g., contaminated surfaces) (Kromhout et al., 2000). The method has even been found to be practical and easily manoeuvrable in difficult field conditions (Kallunki et al., 2003).

Some compounds, such as polycyclic aromatic hydrocarbons, are inherently fluorescent, and dermal exposure can be assessed directly with luminoscopic methods (Vo-Dinh, 1987). Usually, it is necessary to introduce fluorescent tracer compounds into a process, but such a procedure is not possible for all industrial processes. The method has been successfully applied in studies of agricultural pesticides (Archibald et al., 1994a and 1995; Black & Fenske, 1996; Bierman et al., 1998), chlorophenols in timber mills (Fenske et al., 1987), spray painting (Brouwer et al., 2000b), and oils and biological fungicides used in timber harvesters (Kallunki et al., 2003).

Together with image-processing systems, like video imaging, it is possible to estimate whole-body exposure quantitatively (Fenske, 1988a; Roff, 1994) The method does not need any distributional assumptions, it measures actual skin loadings, and it is possible to find unrecognised exposure pathways and secondary sources of exposure (Cherrie et al., 2000). Technical progress in data and image processing has improved the equipment along with the methodology during the past several years (Fenske et al., 1986a and b; Fenske, 1990; Roff, 1994; Archibald et al., 1994b; Fenske & Birnbaum, 1997; Roff, 1997b; Ojanen et al., 2001).

The behaviour of the contaminants studied and the tracer applied to the process is not always similar due to the lack of homogeneity of the suspended tracer in the solution and its different adherence to skin and surfaces. This lack of similarity may cause problems when the results are

interpreted (Roff, 1994; Brouwer et al., 2000b). The results from a tracer study have been compared with those of a chemical analysis in two studies. In the first study, a large variation between the methods (fluorescent tracer vs. analysis of coveralls) appeared, but in the second study (fluorescent tracer vs. washing of skin), the correlation was good. However, both research groups came to the conclusion that the accuracy of the fluorescent tracer method is not as good as that of chemical analysis at low exposure levels. Nevertheless, the ability to determine accurately the exposed areas and the possibility to collect large data sets easily are highly important advantages of these methods (Roff, 1997b; Brouwer et al., 2000b).

3.1.3 Surface sampling techniques

Surface sampling techniques, like wipe sampling or vacuuming of surfaces may serve as a predictor of dermal exposure to chemicals. Traditionally, surface contamination sampling has been used in the sampling of radioactive agents (Fenske, 1993). Materials used as wipe samplers for chemicals include glass fibre, filter paper, cotton swab, surgical gauze, Kleenex-paper®, and cloth. Reported solvents include water and various organic solvents. Dry wipes have also been used (McArthur, 1992). After the terrorist attack on 11 September 2001 Gaborek et al. (2001) reported that they had applied surface wiping for polychloride biphenyls, dioxins, furans, and lead in Pentagon headquarters to ensure the safety of emergency response and remediation crews, and returning workers. For solid substances, adhesive tapes (e.g., Scotch Tape® and forensic tape) have also been used. They have proven to be more efficient for solids than wipe sampling (Wheeler & Stancliffe, 1998).

The accuracy and precision of wipe sampling depend on surface characteristics, contaminant loading, sampling material, and procedures (Fenske, 1993). For estimating the transfer of the contamination during contact, it is difficult to determine the contact area, the exposure time and the cohesive forces related to the degree of transfer (van Hemmen & Brouwer, 1995). For example, wiping pressure is operator-dependent, and no standard devices and methods are used (McArthur, 1992; Fenske, 1993). The reliability of surface wiping or washing for estimating dermal exposure has generally been considered poor (McArthur, 1992; van Hemmen & Brouwer, 1995).

In most cases, a 100% removal of the contaminant is not desirable. A transferable residue is the proportion of the contaminant likely to be transferred to human skin (Fenske, 1993). An application of this approach is also the concept of dislodgeable foliar residue used to assess re-entry workers' exposure to pesticides. It has been proven that the dislodgeable foliar residue, which is determined with a mild washing of leaf discs or the like, is linearly related to dermal exposure (Iwata, 1977; Brouwer et al., 1992; Popendorf, 1992; Kangas et al., 1993; van Hemmen et al 1995). The combined sampling of dislodgeable foliar residue and dermal exposure enables the calculation of dermal transfer coefficients for specific work activities (Krieger et al., 1992).

3.2 Biological monitoring

It is claimed that, when actual uptake is assessed, biological monitoring should be the method of choice (Krieger et al., 1992; Woollen, 1993; van Hemmen & Brouwer, 1995). Quick dermal absorption or the evaporation of chemicals, together with other methodological inconsistencies, may cause problems in interpreting the results of dermal exposure measurements (Fenske & Lu, 1994; Cherrie & Robertson, 1995). Biological monitoring gives information on the exposure of an individual worker. Because of individual variability, its use in designing a safe work environment for all workers is, however, limited (Savolainen & Kalliokoski, 2001).

A biological monitoring method of good quality has been claimed to need human pharmacokinetic studies for validation, due to the differences between animal and human metabolism. However, studies on human volunteers have been restricted or even banned in many countries (Woollen, 1993). The main advantages and disadvantages of the two approaches are listed in Table 2.

Table 2. Advantages and disadvantages of dermal exposure measurements with dosimetric methods and biological monitoring in dermal exposure assessment (taken from Fenske, 1993; Woollen, 1993; van Hemmen & Brouwer, 1995; US EPA, 1996; Savolainen & Kalliokoski, 2001).

	Advantages	**Disadvantages**
Dermal dosimetry	Routes and areas of exposure clearly defined	Dermal and respiratory absorption must be estimated
	Routine experimental design and execution	Extrapolation from patch to body area must be made
	Generic database can be created	Not all exposure scenarios are amendable
	Can be used to assess local skin effects	No dermal exposure limits available
	Useful in designing personal protective clothing and other control measures	
Biological monitoring	Actual dose can be measured	Limited methods without potential interferences or cross-specificity
	Unnecessary to adjust for value for garment or protective clothing	No information on the causes of exposure
	Integrates all routes of exposure	Routes of exposure can not be distinguished
	Useful in ascertaining the effectiveness of protective equipment	Pharmacokinetics must be known: need for human studies
		Only a few biological exposure limits available
		Potential problems when using invasive techniques for specimen collection
		Requires more intervention to collect completely
		Requires controlled dose database to interpret
		Not relevant for local skin effects

If biological monitoring is to be performed together with dermal exposure sampling, it is not possible to use any methods that would disturb normal absorption. Whole-body sampling with chemical resistant coveralls, and hand washing or skin wiping with organic solvents are such methods. If removal techniques are used, they must mimic normal hygienic procedures (Nigg & Stamper, 1985; Chester, 1995).

As it is often difficult to predict whether dermal exposure is likely to be a major route of uptake, an integrated approach to dermal exposure assessment has been recommended. In an ideal situation, surface and dermal sampling would 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 clarified (Krieger et al., 1992; van Hemmen & Brouwer, 1995). A guideline for biological monitoring in field studies of pesticides has been proposed by Woollen (1993).

4. ASSESSMENT STRATEGIES FOR DERMAL EXPOSURE

Assessment strategies for dermal exposure have not gained as much attention as those for inhalation exposure. Nevertheless, some approaches have been published that address issues such as the validity and representativeness of the sampling methods, sampling duration, the distribution of the contaminants, temporal variation, duration of the exposure, and the efficiency of protective clothes and other measures (Fenske, 1993; van Hemmen & Brouwer, 1995; OECD, 1997). Another important factor is the cooperation of the subjects in that their work should be done exactly as it generally is during a normal workday (van Hemmen & Brouwer, 1995). However, there are no standardised strategies for such studies as there are for inhalation exposure (EN 689) (CEN, 1995).

All the sampling methods described earlier have advantages and disadvantages. When a dermal exposure field study is designed, these advantages and disadvantages should be carefully considered. For example, in cases of a transfer of substances from contaminated surfaces or equipment to the skin, it is reasonable to measure only hand exposure (Brouwer et al., 1999). This assumption of a non-uniform deposition of contaminants must be ascertained a priori. A fluorescent tracer method is excellent for this purpose, when applicable (Fenske, 1993).

The commonest methods used to assess hand exposure are hand washing and the glove method. For example, the US Environmental Protection Agency (US EPA) recommends both methods for assessing the exposure of pesticide handlers (US EPA, 1996). Both are considered reasonable because the glove method may overestimate exposure, especially in cases of contact with concentrated liquids due to spills and splashes, while hand washing on the other hand only measures the amount that can be removed from the skin, and it may underestimate the exposure (Fenske et al., 1999). Both of these methods are also mentioned in the OECD guidance document for assessing pesticide exposure in agriculture (OECD, 1997).

Current initiatives presented in the scientific literature for strategies assessing dermal exposure are cited briefly in the next sections.

4.1 Strategy for assessing dermal exposure on the basis of the conceptual model and European standard EN 689

It has been suggested that the conceptual model proposed for assessing dermal exposure could act as a starting point for the development of a sampling strategy (Schneider et al., 2000; Vermeulen et al., 2000b). A proposed assessment strategy is based on a tiered approach. As the first step, potential exposure would be identified from lists prepared of all chemical substances used at the workplace, including relevant toxicological information. The second tier consists of evaluating workplace factors such as tasks, work patterns and techniques, production processes, sources of contamination (direct skin contact, spilling, splashing and emission to air) and safety precautions and procedures, including the use of protective clothing and gloves. The third step would be to use a structured

approach to assess exposure according to a conceptual model of dermal exposure. If dermal uptake of hazardous substances cannot be ruled out during this assessment, a basic survey should be made to provide quantitative information about the level of exposure and the distribution (Schneider et al., 2000).

The measurement strategy proposed by Schneider et al. (2000) follows the protocol presented in European standard EN 689 (CEN, 1995):

1. The *selection of workers* should be based on the exposed groups being similar, and stratified random sampling from each subgroup should be used. This approach is close to the basis of the air sampling strategy standard.

2. In air sampling, stationary sampling is used to monitor g*eneral concentration levels and trends*. For dermal exposure assessment, a similar approach would be the monitoring of various workplace surfaces with which the worker has frequent contact.

3. The *sampling effort* should be directed efficiently; possible approaches are as follows:

- Worst-case measurements
- Task-based approach (i.e. measurement during each individual task and the combination of the results using time weights
- Randomly taken shift-long measurements with simultaneous collection of information on tasks, processes, and the like. This approach enables exposure-affecting factors to be separated statistically.

4. *Statistical properties.* For air concentrations, there are large databases of typical values for within- and between-worker and between-group variances. For dermal exposure such data do not exist to the same extent. Repeated measurements are needed to optimise grouping schemes.

The sampling method should also be selected according to the conceptual model (see Figure 2 on page 25). If the transport rates (i.e., penetration/permeation and removal/resuspension or evaporation) are low, removal techniques can be applied. If the penetration rate is high and the removal rate low, surrogate skin methods give a realistic estimation of the exposure. In an opposite situation, surrogate skin methods overestimate the exposure. Fluorescence techniques are recommended in both cases. If both transport rates are high, only biological monitoring is considered appropriate (Schneider et al., 2000). However, even then, due to the limitations of biological monitoring (see Table 2 on page 33) dermal or surface sampling may be needed (US EPA, 1996).

4.2 DREAM

A structured, semi-quantitative dermal exposure assessment method called DREAM (DeRmal Exposure Assessment Method) has been developed for use by occupational hygienists and epidemiologists in all kinds of dermal exposure situations (van-Wendel-de-Joode et al., 2003). The aim of the method is to provide an initial dermal exposure assessment for liquids and solids, to serve as a framework for measurement strategies, and to form a basis for control measures. With the aid of the method, it is also possible to rank tasks or groups of workers, and to prioritise and to carry out direct sampling (van-Wendel-de-Joode et al., 2003). The approach is largely based on the conceptual model of dermal exposure (Schneider et al., 1999).

DREAM consists of two parts, an inventory and an evaluation. The inventory is based on a questionnaire filled out by an occupational health professional, by observing the process and interviewing the workers. Information is collected about the company, the characteristics of the substances used, the cleanliness of the environment, personal hygiene, protective clothing, and exposure duration. The investigator also has to estimate the probability and intensity of dermal exposure and the relevancy of different body parts. In the evaluation, the potential and actual dermal exposures of nine body parts are determined by 33 variables at the task level. The estimation of the exposure level is based on the product of probability and intensity of each exposure route, i.e., emission, transfer and deposition. Information about the direction and magnitude of the effect of the variables has been collected from the literature and through expert judgement (van-Wendel-de-Joode et al., 2003).

The limitations of the method include the wide use of expert judgement, as the data about dermal exposure determinants are limited. In addition, because the approach is task-based and every observer may have his or her own definition of the tasks, the comparability between different studies may also be poor. The method is also considered time consuming (van-Wendel-de-Joode et al., 2003).

Neither of the methods based on the conceptual model have yet been applied and validated by other researchers.

4.3 AIHA strategy for assessing occupational exposures

American Industrial Hygiene Association (AIHA) recently updated its strategy for assessing and managing occupational exposures at workplaces. The dermal route has been identified as an important pathway of exposure, and, therefore, logically, the strategy presented includes dermal exposure assessment. The major steps of the strategy are presented as a flowchart in Figure 3. At the start, it is recommended that a written exposure assessment programme is produced that defines the goals of the procedure and ensures that all relevant exposures are included. During the basic characterisation, all process, task, chemical, and other related information is identified and

collected. In other words, for dermal exposure, the relevant contaminants and possible sources of exposure are pointed out the work practices potentially leading to exposure are characterised, and the use of protective clothing and equipment is determined (Mulhausen & Damiano, 1998).

The actual exposure assessment is used to define the exposure profile. When dermal exposure is concerned, the delineation is to be done with biological monitoring, occupational hygiene measurements, or modelling. The recommended modelling approach is based on the EPA methods (US EPA, 1992) described in the section on EPA models (section 5.3.3). Subsequently, the defined exposures are compared with biological exposure limits or OELs. As there are no dermal OELs available, it is suggested that the daily-absorbed dermal dose (mg/day) is compared with the equivalent total body dose converted from the inhalation OEL (Mulhausen & Damiano, 1998).

At large workplaces, it is recommended that the workers should be divided into similarly exposed groups in order to save resources through priorisation and to ensure that the assessments cover every task (Mulhausen & Damiano, 1998). The concept of similarly exposed groups is a practical version of the homogenous exposure group used in the European standard (CEN, 1995). The homogeneous exposure group has a strict statistical description (Rappaport et al., 1993), which makes it inflexible, whereas the definition of similarly exposed groups places more emphasis on practical similarities (Mulhausen & Damiano, 1998).

The strategy also emphasises the importance of information gathering. Depending on the exposure profiles, the information needed includes monitoring and modelling data and toxicological and epidemiological information. All the information should lead to the development of control measures. For dermal exposures, the order of action should begin with the substitution of materials, process changes, and technical controls. Prescribing work practices or the use of personal protection is considered the last option. Personal hygiene is also important. The exposure assessment programme compiled in the first phase of the assessment process should specify the re-assessment interval (Mulhausen & Damiano, 1998).

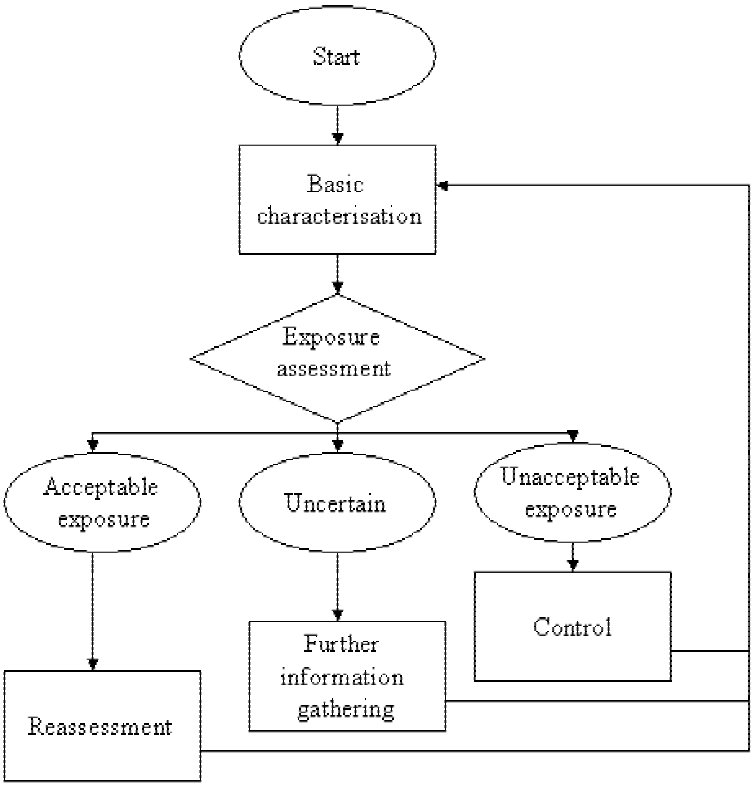

Figure 3. AIHA occupational exposure assessment strategy (from Mulhausen & Damiano, 1998).

5. DERMAL EXPOSURE MODELLING

5.1 Use of models

Models are used to assess occupational exposure particularly in cases when few or no measurements are available. An important example is regulatory exposure assessment (Marquart et al., 2003). Models can also serve as tools in epidemiological studies (Vermeulen et al., 2002). Generally, the exposure models can be divided into the following three categories: 1) mathematical mechanistic models, 2) empirical or knowledge-based models, and 3) statistical mathematical models. The models in the first category are usually based on mass balance equations. Only a few have been developed for workplace assessments. None of the dermal exposure models currently used fall into this category. Empirical models are based on field exposure measurements, and, with the model, it is possible to predict exposure in similar situations. Statistical models are a combination of empirical and mechanistic models, and they use statistical distributions to predict exposures. In the probabilistic approach, the model variables are distributions instead of point estimates. They are not yet used in European risk assessments (EC, 2002), but, in the United States, the implementation of probabilistic methods has been faster (US EPA, 2001). Dermal exposure has also been modelled probabilistically in residential settings (Zartarian et al., 2000). However, for pesticides, Europeans and North Americans are together currently developing operator exposure models using the probabilistic approach in a project coordinated by the Risk Science Institute of the International Life Sciences Institute (ILSI RSI).

As most of the currently available data about dermal exposure concern pesticides, in general, the present regulative models have been developed for the assessing the exposure of pesticide operators (van Hemmen, 1992b; van Hemmen, 1993). Some process-specific empirical models have been developed, such as a model for spray painting (Brouwer et al., 2001) and for pesticide exposure (Dosemeci et al., 2002). The algorithms of these types of models incorporate exposure factors from the literature, and are based on expert judgement. The only empirical generic model for assessing dermal (and inhalation) exposure to industrial chemicals, the EASE model, has been developed by the Health and Safety Executive in the United Kingdom (CEC, 1996). A variety of models for assessing occupational and consumer exposure to biocidal products have recently been developed (EC, 2002).

The basic quality requirements for model development include transparency in derivation and construction, wide discussion and validation with peer review, and openness to further development and validation (Marquart et al., 2003).

The available models described in this section are meant to be used by professionals, especially in regulative risk assessment. There are no simple, qualitative tools for employers and employees to use as screening assessments for dermal exposure or to aid decision-making concerning control measures (Marquart et al., 2001). One of the aims of the RISKOFDERM project is the development of a simple tool-kit especially for small and middle-size enterprises (Oppl et al., 2003).

5.2 Predictive models for pesticide operators and re-entry workers

During the last 20 years in Europe and North America, several descriptive deterministic models have been introduced for regulative risk assessments of pesticidal active substances and commercial products. These models are used to predict pesticide operators' dermal and inhalation exposure (JMP, 1986; Lundehn et al., 1992; PHED, 1992; van Hemmen, 1992a; EUROPOEM I, 1996 and EUROPOEM II, 2003) and re-entry workers' exposure (e.g., harvesters, pickers, etc.) (Popendorf, 1992; van Hemmen et al., 1995; EUROPOEM II, 2003). However, inhalation exposure is considered much less important than dermal exposure in pesticide work, and it has, therefore, not been considered in this presentation.

Tasks in the operator models are the mixing and loading of the undiluted pesticide product and application work. With the use of the PHED (Pesticide Handlers Exposure Database), the exposure of flaggers (ground workers during aerial application) can also be modelled (van Hemmen, 1993). EUROPOEM II (European Predictive Operator Exposure Model, second version) also includes by-stander exposure (i.e., the incidental exposure of persons not involved in actual pesticide work) and re-entry exposure. In Europe, the underlying reason for such activity is the Commission directive on the placement of plant protection products on the market (EC, 1991).

The operator models are based on the assumption that the level of exposure is dependent on, for example, the type of pesticide formulation, spraying techniques and equipment, environmental conditions, and the hygienic measures taken by the worker (Table 3). The chemical or toxicological properties of the pesticide are considered to be less important. The exposure is considered external (i.e., the amount of a pesticide available for inhalation or dermal absorption under the ambient conditions is calculated). Possible oral exposure must be assessed by biological monitoring, which, however, is not included in the models (van Hemmen, 1992b). The descriptive databases are based on data sets, with which it is possible to estimate a surrogate exposure level with suitable statistics, so that it is possible to use the database for other comparable exposure situations. The validity of the measurements within the database and the amount and quality of the determinants recorded leads credence to the accuracy of the exposure estimates (van Hemmen, 1993). The main determinants of re-entry exposure are the quantity of pesticide applied, decay, and the type and duration of contact (Popendorf, 1992).

Table 3. Factors affecting the quality of underlying data in databases of predictive operator models (taken from van Hemmen, 1993)

Factors	**Work task**	
Agricultural	***Mixing and loading:*** formulation (e.g., solid vs. liquid), particle size of solid products, size and shape of the container, number of operations, amount of formulation used, loading technique	***Application:*** spraying method (tractor vs. hand-held spraying, downwards vs. upwards), equipment and technique, particle size of the aerosol, amount applied, area treated, application time
Climatic	temperature, wind speed and direction, relative humidity	
Analytical	accuracy, reproducibility, stability, field recovery	
Personal	clothes, personal protective equipment, level of personal hygiene	
Statistical	representativeness, grouping and variability of data, percentiles used as surrogates	

5.2.1 National European and North American operator models

The development of predictive operator models started in the United Kingdom (the so called UK model) (JMP, 1986), Germany (the German model) (Lundehn et al., 1992), the United States and Canada (the PHED) (PHED, 1992), and The Netherlands (the Dutch model) (van Hemmen, 1992a). The differences between the models are largely due to restricted geographical representativeness, source of data (e.g., studies done by industry vs. published research), variability in sampling methods, and choice of statistics (van Hemmen, 1993; Kangas & Sihvonen, 1996). A general description of the default values used in the aforementioned models is presented in Table 4, which emphasises some of the factors causing differences between different approaches.

Table 4. Description of different predictive models for operator exposure (van Hemmen, 1992b; van Hemmen, 1993; Kangas & Sihvonen, 1996)

Model	Terms of exposure (exposure expressed in/per which units)		Default values (area treated per day (ha), work time per day (h))	Source of data (obtained from or location of)	Statistics applied for surrogate value
	Mixing & loading	Application			
UK model	ml or mg of formulation handled (determined by container size and type)	ml of spray liquid handled	mixing/loading for 1 h application for 6 h downwards 50 ha; upwards 30 ha, hand-held 1 ha	industry or authorities/ UK	75th percentile
Dutch model	ml or mg of formulation handled	ml or mg of spray liquid or dust handled	mixing/loading for 1 h application for 6 h downwards 10 ha; upwards 5 ha; hand-held 1 ha	peer-reviewed literature/ international, some Dutch studies	90th percentile
German model[a]	per amount of active ingredient handled (mg/kg)		downwards: 20 ha upwards: 8 ha hand-held: 1 ha	industry/ Germany	geometric mean
PHED[a]	various formats to choose from		no defaults	universities, authorities, industry/ North America	chosen by the assessor

[a] In German model and PHED the terms of exposure are similar in both work tasks

The predictive modelling of pesticide exposures is related to the concept of the tiered approach of exposure assessment (Figure 4). In the first tier, the potential exposure scenario is modelled simply with no personal protection. In the second tier, more specified data are taken into account, like protective measures and more realistic data about the dermal absorption. Other parameters may also be specified. The third and final tier includes (validated) biological monitoring and possible substance-specific field studies (van Hemmen, 1998).

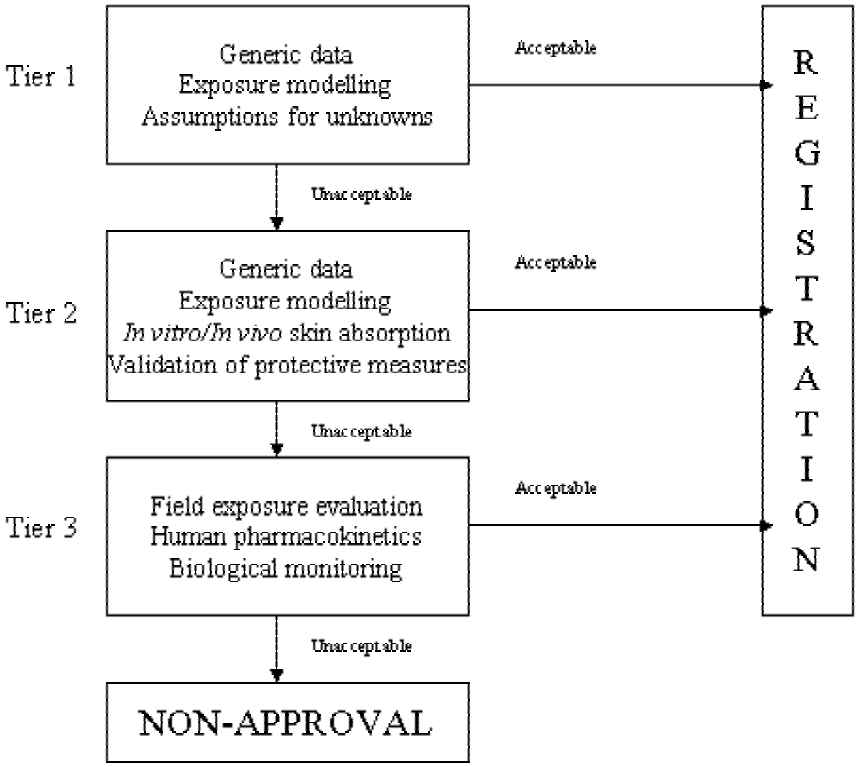

Figure 4. The tiered approach of pesticide worker exposure assessment (Henderson et al., 1993).

The models have been, and are being, used in registration procedures for pesticide products. In order to harmonise the approach not only regionally, but also methodologically in Europe, much effort has been put into developing a joint model (van Hemmen, 1998; van Hemmen, 2001).

5.2.2 Harmonised EU model, the EUROPOEM

At the request of the European Commission, a harmonised model for predicting pesticide handlers' exposure, with strict criteria for the relevancy and representativeness of the field studies in the database, was developed in 1996 (EUROPOEM I, 1996). The number of data in the first version was, however, considered small and unrepresentative for certain exposure scenarios, and, therefore, a more-validated and enlarged model was developed. In addition, the EUROPOEM I did not contain a model to predict the exposure of re-entry workers or by-standers. These features were also developed in the new version, EUROPOEM II, which is still unaccomplished (EUROPOEM II, 2003). Some critical data gaps, for example, exposure in greenhouses, were filled with a project funded by the European Commission (SMT4-CT96-2048).

The surrogate exposure levels for each scenario modelled are compared with an acceptable operator exposure value (AOEL) derived from relevant toxicological data, usually the no-observed adverse effect level of a subchronic study. When the ratio of exposure and the AOEL is below 1, the exposure in the scenario is considered acceptable. Exceeding the AOEL leads to a more-detailed assessment, according to the tiered approach (see Figure 4 on page 34) (van Hemmen, 1998).

EUROPOEM (European Predictive Operator Exposure Model) models specifically aim at having representative data in their databases. Therefore, all the field studies included are carefully selected according to criteria agreed upon a priori and described transparently, and they use justified statistical methods. The field sampling of both versions followed the protocol approved in an OECD guidance document (OECD, 1997). The accuracy of the model even 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 (van Hemmen, 1998; van Hemmen, 2001).

5.2.3 Re-entry exposure model

Post-application (re-entry) exposure takes place during maintenance activities, (e.g., harvesting and thinning), during which frequent contact with plants occurs. For some crops, a worker sometimes needs to enter the treated areas relatively soon after pesticides have been applied. This situation may lead to notable dermal exposure, while inhalation exposure is considered low (Popendorf, 1992; van Hemmen et al., 1995).

The model development for re-entry work started in the early 1980's in California (reviewed by Popendorf, 1992). The exposure of a re-entry worker depends highly on the residues on the foliage of the plants and on the type of activity of the worker. The exposure is, therefore, determined by the dislodgeable foliar residue (see section on surface sampling techniques, 3.1.3) on the plant surface and on the work scenario, the crop specific transfer coefficient, and the duration of the work. Default values for the parameters of the algorithm searched from the literature have been collected into EUROPOEM II (EUROPOEM II, 2003).

As the amount of knowledge increased about re-entry exposure, it was considered possible to publish a harmonised European re-entry model within EUROPOEM II. Even though the modelling of re-entry exposure has become more scientifically valid due to similar improvements, as for operator exposure modelling, it must be noted that there is still an urgent need for more field data. The current model estimates only worst-case exposure, as it is not capable of taking the decay of the product into account (EUROPOEM II, 2003).

5.3 Models for other chemicals

Even though various non-validated models exist, the modelling of dermal exposure to industrial chemicals is still in its early phases of development. It has been claimed that the lack of models of

good quality depends on the poor understanding of the complex processes involved in dermal exposure (Marquart et al., 2001). An inventory of potential determinants of dermal exposure for exposure modelling was collected and evaluated recently by Marquart et al. (2003). The determinants estimated to have scientific evidence of effect were divided into six categories (Table 5). This approach is going to be used in practice in the model development process included in the European RISKOFDERM programme (RISKOFDERM, 1999).

Table 5. Categorised presentation of potential dermal exposure determinants with examples or the parameters found in the literature and judged by experts (adapted from Marquart et al., 2003)

Category of determinants	Examples of the parameters
Substance and product characteristics	Physical state, viscosity, particle size, moisture, organic content (soil)
Task done by the worker	Frequency, intensity, duration, number of items handled, volumes handled, concentrations, treated area, level of contamination
Process technique and equipment	Distinguishing type of process or equipment, orientation, pressure
Exposure control measures	Gloves: use, material; clothing: use, material, skin area covered, organisation of work
Worker characteristics and habits	Accuracy of working: training, touching contaminated surfaces; skin moistness and roughness, personal hygiene: frequency of hand washing, personal manner of working
Area and situation	Type of contaminated surfaces: roughness; weather conditions: temperature, wind speed

Many of the established determinants have not shown a uniform direction of effect in the studies reviewed, and only a few parameters have been identified as independent determinants of exposure. The effect and its direction also depend on the type of exposure (i.e., whether the exposure is caused by direct contact with contamination [splashing, immersion, etc.], contact with contaminated surfaces, or deposition). For example, it has been found that using a solvent-based formulation as a wood preservative leads to higher dermal exposure than work with a water-based one. However, when surfaces treated earlier with a solvent-based formulation are touched, the exposure is lower than when surfaces treated with a water-based substance are touched, due to the difference in the evaporation rate (Roff, 1997a; Garrod et al., 1999).

5.3.1 EASE

The knowledge-based EASE model (Estimation and Assessment of Substance Exposure) was designed for assessing exposure to new and existing chemicals in the European Union (CEC, 1996). The model ranks the workplaces in broad bands of exposure, and, therefore, it always assumes homogeneous exposure within the workplace (Vermeulen et al., 2002). Even though several validation studies have been published recently (Devillers et al., 1997; Hughson & Cherrie, 2000; Bredendiek-Kämper, 2001; Llewellyn, 2001; Mäkinen et al., 2002), they have usually concentrated on the better functioning inhalation exposure part of the model. The dermal exposure part of the

model is based on a very limited set of experiments on the adherence of material to hands and forearms immersed in liquid and on expert judgement (Benford et al., 1999). The only study that has been published on the validation of the dermal part showed that it overestimated dermal exposure to zinc by one or two orders of magnitude (Hughson & Cherrie, 2001).

5.3.2 Biocide models

A European Commission working group was assigned to discuss the assessment of human exposure to biocides and to develop models for this purpose. The final report of the working group contains a list of possible models to be used in biocide exposure assessment and a large database of use patterns for biocidal products. Several database models were introduced, but, for the most part, they have only a limited number of data points (EC, 2002). British researchers have combined some of these data and published empirical models for six processes related to the use of non-agricultural pesticides, timber preservatives, and anti-fouling agents. The sampling data consist of field measurements of different kinds of biocides during spraying with different equipment, and also industrial pre-treatment of timber. Medians or other indicative surrogates of the distribution can be used to describe the exposure. The databases can also be used in a more generalised way to model other similar scenarios (Phillips & Garrod, 2001).

The new Bayesian Exposure Assessment Tool, a probabilistic task-based model, has also been introduced, even though it is still under development. The basic idea behind the approach is to compare the process information given by the assessor with the data in the database. The more similar the scenarios, the closer their geometric means and standard deviations should be. The "similarity score" calculated by the model consists of information about the physical state of the substance used, tasks done in the scenario, and time spent in each task. The similarity of the tasks is evaluated with modifiers of exposure, such as extent and frequency of contact, the contamination of objects, and the application rate. At the end, the achieved similarity score can be used to estimate the probability (%) of the geometric mean being within a certain factor (EC, 2002).

5.3.3 EPA models

The models developed by the US EPA primarily focus on assessing lifetime residential exposure to contaminants in water and soil. However, after modifications, they can be used in occupational exposure assessment. An adaptation of the EPA models has been used in the AIHA strategy for screening level assessments of dermal exposure (Mulhausen & Damiano, 1998).

The US EPA has large databases containing default values to be used in mathematical models, including skin surface areas, adapted from the *Exposure Factors Handbook*, (US EPA, 1989), typical and worst-case contact times, frequencies and durations of exposure, and dermal adherences. The databases of skin surface areas have been used in many occupational exposure models, such as the EUROPOEM. The approach uses the concept of "event" (expressed as mg/cm^2/event). "Event" is determined by the absorption, surface area, exposure duration, frequency (events/year), and body

weight. Total dermal exposure and absorption are calculated by summing the events occurring during a period of time. Furthermore, a stepwise process scheme is used for assessing dermal exposure in situations quantifying the dermal absorption of contaminants from water or soil (US EPA, 1992). The model can be applied using either measured data or defaults from the literature.

The dermal absorbed dose rate (DA) expressed as mg/day can be estimated with the following equation (Equation 2):

Equation 2.	DA = S x Q x FQ x ABS x WF

where:

S = surface area of the skin available for contact with contamination, cm^2
Q = quantity of the contaminant deposited on the skin per event, mg/cm^2/event
FQ = number of events per day
ABS = fraction absorbed through the skin (during the event)
WF = weight fraction of the substance in the mixture, unitless

6. AIMS OF THE PRESENT STUDY

Occupational hygiene should take all major routes of exposure into consideration. In addition to the respiratory route, skin is an important pathway through which chemicals can both enter the body and cause local effects. However, techniques used for dermal exposure assessment are not yet as standardised or validated and biologically relevant as the methods developed for assessing respiratory exposure. The aims of this study were to enhance the knowledge of dermal exposure through sampling with different methods and, especially, to evaluate results concerning the viewpoint of modelling.

The detailed objectives of this study were:

1. To test current measurement methods for estimating dermal exposure and effectiveness of personal protection at various types of workplaces (**I**-**V**)

2. To characterise the existing dermal exposure modelling approach for pesticides (**IV**)

3. To evaluate a database of dermal exposure measurements from the perspective of modelling dermal exposure to industrial chemicals (**II**-**III**)

4. To make a preliminary assessment of the ability of the European standard EN 689 to incorporate dermal exposure (**V**)

7. MATERIALS AND METHODS

7.1 Field studies

7.1.1 Subjects and workplaces

Occupational hygiene measurements were done in a plywood factory (studies **I** and **V**), a paint factory (**V**), six electroplating or chromating shops (**II**), four companies producing stainless or acid-proof steel articles (**III**), and four greenhouses cultivating cut roses (**IV**). Respiratory exposure was also measured in all the studies using breathing-zone or stationary samples.

Unpublished summary data from the European RISKOFDERM study are also presented in the results and discussion (RISKOFDERM, 1999; Rajan-Sithamparanadarajah et al., 2003; RISKOFDERM, 2003). The results presented in original publications **II** and **III** derive from the RISKOFDERM study (RISKOFDERM, 1999).

The Ethics Committee of the Finnish Institute of Occupational Health approved the study protocols of all the projects done in Finland. The workers participating in the studies gave their informed consents. The analytical procedures adhered to the laboratory quality manual.

7.1.1.1 Plywood factory (**I**, **V**)

The occupational hygiene survey was accomplished in the plywood factory during the period 1996-1997. Dermal exposure to phenol was measured during assembling and gluing of veneers. Four female workers were measured four times during the same week for approximately four hours at the beginning of the morning shift (one worker only three times). Therefore, the total number of measurements was 15.

7.1.1.2 Paint factory (**V**)

Dermal exposure to solvents was measured in the paint factory in 1997. Fifteen workers (both men and women) from the manual and process manufacturing lines, and filling department participated in the dermal exposure study. The total number of measurements was 20. The measurements took place over a period of three days and lasted for about 2-3 hours.

7.1.1.3 Electroplating (**II**, **IV**)

Electroplating was studied in five chromium- and nickel-plating factories. Hard chromating was done in one of the factories. The total number of workers participating in the study was 16 (all men) and the number of measurements was 29. Consequently, the exposure of most of the workers was measured twice. The average sampling time was 267 (range 81-483) minutes.

7.1.1.4 Grinding (**III**, **IV**)

The four companies in which grinding work was studied produced stainless steel kitchen furniture, or cookware, acid-proof steel pipes and pipe parts, or boiling kiers for pulp production. The total number of manual grinding workers participating in the study was 15 (all men), and the number of measurements was 29. Most of the workers were measured twice. The average sampling time was 138 minutes, and it varied between 47 and 214 minutes.

7.1.1.5 RISKOFDERM studies

Dermal exposure data were gathered in 88 workplaces (industrial and other types) situated in five countries in Europe. The number of individual workers measured was 254. The exercise resulted in 567 body measurements and 758 measurements on hands. A summary of the details of the survey is presented in Table 6.

Table 6. Summary of the RISKOFDERM survey. Industrial sectors and chemicals studied, sampling methods used, responsible institutes, and number and type of samples collected. Adapted from the draft final report of the Work Part II of RISKOFDERM, 2003 (RISKOFDERM, 2003).

Industrial sector	Substance	Institute	Body	Hands	
			Potential samples	Potential samples	Actual samples
Wood working	Wood - Resin Acids	NIWL	59 (P)	59 (P)	
Motor vehicle repair	Paint - Aluminium	INSHT	90 (P)	90 (G)	90 (G)
Health care	Cyclophosphamide	UU	90 (P+w)	90 (G+W)	
Surface coating manufacture	Paint - DEGBE	TNO	18 (P)	58 (G)	
Ship repairing	Antifouling paint - Copper oxide	IOM	49 (S)	33 (G)	
Health care	Biocide - Potassium	IOM	46 (S)	46 (G)	
Construction	Paint - DEGBE	KRIOH	12 (P)	30 (W)	30 (W)
Boat building	GRP - Styrene	NIWL	45 (P)	30 (P)	
Construction	Paint -DEGBE	TNO	12 (P)	36 (G)	
Powder coating	Powder coating - Triglyceryl iso-cyanurate, Titanium and Barium	HSL	22 (S)	23 (G)	23 (G)
Electroplating	Plating solution - Chromium	KRIOH	29 (P)	29 (W)	29 (W)
Electroplating	Plating solution - Chromium, Nickel	HSL	27 (S)		26 (G)
Engineering	Metal working fluid - Boron	IOM	8 (S)		
Engineering	Metal working fluid - Boron	HSL	31 (S)		7 (G)
Engineering	Grinding- Chromium	KRIOH	29 (P)		29 (W)
		TOTAL	**567**	**524**	**234**

P = patches; S = whole-body suits; G = gloves; W = hand washing; w = wipes
NIWL = National Institute of Working Life; INSHT = National Institute for Occupational Safety and Hygiene, Spain; UU = University of Utrecht, The Netherlands; TNO = TNO Nutrition and Food Research, The Netherlands; IOM = Institute of Occupational Medicine, United Kingdom; KRIOH = Kuopio Regional Institute of Occupational Health; HSL = Health and Safety Laboratory, United Kingdom.

7.1.1.6 Pesticide application in greenhouses (**V**)

Nine certified pesticide operators (seven men, two women) using hand-held lances to spray pesticides were studied in four greenhouses. The mixing and loading period varied from 6 to 12 minutes, and the application lasted from 58 to 68 minutes. The work phases were measured separately.

7.1.2 Sampling methods

The sampling methods used for assessing dermal exposure are described next in more detail, whereas information concerning the air sampling methods can be found in the original articles.

7.1.2.1 Plywood factory (**I**, **V**)

The whole-body method, combined with glove sampling, was used to assess dermal exposure to phenol during the assembling and gluing of veneers in the plywood factory. The workers wore unused, clean Tyvek® coveralls (Tyvek Practik, Apparel SL100MP, elastic hooded coveralls) to monitor the potential skin exposure of the body and pre-washed, clean cotton gloves (Famon Ltd., Finland) under their protective gloves to monitor actual hand exposure.

The coveralls were cut into 20 pieces for the analysis, and the gloves were analysed separately. All the samples were analysed within 2-3 hours, as free phenol polymerises rapidly. The amount of phenol was calculated as micrograms per area of the piece of the coverall representing the part of the body in question. The coveralls were loose fitting on the female workers, and, therefore, the area of the coveralls was estimated to be approximately 30% larger than the area of the skin. This difference was taken into account in the calculations.

7.1.2.2 Paint factory (**V**)

Dermal exposure to solvents in the paint factory was assessed with 5 x 5 cm active charcoal patches cut from protective suit fabric, used, for example, by the military. The patches were attached with safety pins to the workers' clothing (both forearms, back, chest, and right thigh). For monitoring hand exposure, the patches were stitched onto the cotton gloves (palm and back of the hand). The patches on the clothing were always placed on top of the clothes, while the cotton gloves were worn under the protective gloves, if used.

The method was not properly validated to give quantitative results, as we could not separate the exposure to liquid or vaporised solvents. Nevertheless, the results can be considered indicative. Exposure to the xylene mixture was quantified, as it was the predominant compound found in all the samples.

7.1.2.3 Electroplating (**II**) and grinding (**III**)

Potential dermal exposure of the body was measured during both the electroplating and grinding tasks with 10 x 10 cm alpha-cellulose patches taped onto polyethylene plastic and attached with safety pins to the top of the clothes of the workers. The patches were attached to the chest, back, left and right forearms, left and right upper arms, left and right upper legs, and left and right lower legs. Actual exposure and the possible transfer through the protective clothing were assessed with one patch attached to the chest under the work clothing.

Hand exposure was studied by hand washing. The washing procedure followed the EN 1499 standard. A washing solution (200 ml) containing deionised water and hypoallergenic liquid soap (1.0 ml/l) as a detergent was poured onto workers' hands for 30 seconds above a large, plastic beaker. The workers rubbed their hands according to the instructions presented in the standard (CEN, 1996).

The exposure of the different body parts was calculated according the procedure presented in the OECD guidance document (OECD, 1997) using the default areas found in the EPA *Exposure Factors Handbook* (US EPA, 1989). No area adjustment was needed for the hand exposure, as the hand-wash method covers the whole area of the hands.

7.1.2.4 Sampling in the RISKOFDERM study

The sampling methods used by the different institutes in different scenarios are shown in Table 6. The OECD guidance document (OECD, 1997) formed the basis of the method development. The sampling methods used in Finnish sub-studies are described in section 7.1.2.3.

7.1.2.5 Pesticide application in greenhouses (**IV**)

Potential dermal exposure to malathion, iprodione, and deltamethrin pesticides was measured with alpha-cellulose patches attached to clean Tyvek® coveralls to avoid contamination from workclothes. Patches were also attached on the operators' hood (front and back). Mixing and loading and application tasks were measured separately.

Potential hand exposure was studied with cotton gloves worn over clean, pre-washed nitrile rubber gloves. The left and right gloves were analysed separately.

The exposure of the different body parts was calculated according the procedure presented in the OECD guidance document (OECD, 1997).

7.1.3 Information on determinants

In the earlier studies (**I** and **V**), no structured data collection was used for additional information or the determinants of exposure. In the RISKOFDERM studies (**II** and **III** and the unpublished data presented), a questionnaire was used for observing the tasks and collecting information concerning the workplace (e.g., ventilation), workers (personal protective clothing, habits of personal hygiene), process parameters, accidental contaminations, and characteristics of the chemicals used (Hebisch & Auffarth, 2001). In the greenhouse study, data about the working and sampling conditions, like the equipment used, characteristics of the crop cultivated, and the amount of spray liquid used, were collected according to the instructions of the EUROPOEM I model, which follows the OECD guidance document for pesticide field studies (EUROPOEM I, 1996; OECD, 1997).

7.2 Modelling

7.2.1 EUROPOEM

The model described in this thesis (original publication **IV**) is the EUROPOEM I (EUROPOEM, 1996). Exposure during the mixing and loading and application tasks in greenhouses is discussed. The basic structure and function of the model and the databases have been presented in the literature review (see section 5.2.2).

In EUROPOEM I, only a very limited number of data were available for greenhouse exposure assessment. In that phase of the model development, it could not be independently used to assess the exposure of the operators working in greenhouse environments. One important aim of the published study (**IV**) was to increase and enlarge the applicability and validity of the model. The study was part of a joint 5th framework project ("The Assessment of Operator, Bystander and Environmental Exposure to Plant Protection Products", EU-project SMT CT96-2048), in which also many other greenhouse scenarios were studied by the European institutes.

Different statistics can be used in applying the models, depending on the size and validity of the database and the aims of the assessor. Therefore, geometric means, different percentiles, and maximum values are presented.

7.2.2 Task-based approach for modelling dermal exposure to industrial chemicals

In the RISKOFDERM project, the industrial processes leading to dermal exposure were divided into dermal exposure operation (DEO) units to optimise the data collection and to develop a representative picture of dermal exposure. Expert judgement and existing literature were used for this grouping. The DEO units and the scenarios formed and measured within the RISKOFDERM project are presented in Table 7. The aim of this approach was to combine work tasks so that, in a later phase of the project, the results of the measurements could be used for modelling dermal exposure to chemical compounds according to the requirements of European directives on chemical safety. The collection of the determinants affecting dermal exposure was also important for the model development (Rajan-Sithamparanadarajah et al., 2003).

Table 7. DEO units developed in the RISKOFDERM project and the scenarios measured (*in italics*) within the project to be used as a basis for modelling (Rajan-Sithamparanadarajah et al., 2003)

DEO unit	Scenarios studied
Handling objects	Transferring/transporting, Unloading/storing, Collecting, Sorting/grading, Coupling/uncoupling transfer lines, *Maintenance and servicing,* Assembling, Loading (liquids), Dumping (solids), *Filling,* Drawing from small containers, Sampling, Weighing, *Mixing/diluting*
Manual dispersion	Washing, *Wiping,* Manual strewing
Manual dispersion with hand-held tool	*Pouring, Spreading,* Trawling, *Rolling,* Brushing, Gluing, Strewing, Scooping, Sweeping, Mopping, Scrubbing, Lustering/polishing
Spray dispersion	Spray cleaning, *Spray painting*
Dip coating	*Electroplating,* Impregnating, Manual dipping/bathing, Automated dipping/bathing
Mechanical treatment of solid objects	Cutting, *Machining,* Boring/drilling, Sawing, Edging, *Grinding,* Abrading

The results of the measurements done for the model development have been presented as geometric means, which is a statistical value commonly used to describe log-normally distributed data. In risk assessment, the worst-case scenario is usually described with the 95th percentile.

7.3 Sampling strategy

7.3.1 Exposure assessment strategy (EN 689)

As discussed in the literature review, there are no standardised strategies for assessing dermal exposure at workplaces (see section 4 on dermal exposure assessment strategies). For inhalation exposure assessment, a European standard (EN-689) has been published (CEN, 1995). The applicability of the approach of using homogeneous exposure groups as a starting point for exposure assessment and the planning of the sampling procedures presented in the standard was the focus of the field studies (original publication **V**).

Homogeneous exposure groups are formed with an analysis of variance (ANOVA). In testing the group with an analysis of variance, the within-population component of variance is the temporal variance of the measurements done for the workers, and the between component is due to different exposure between workers (Snedecor & Cochran 1976; Rappaport 1991; Bolej et al., 1995). The ANOVA table used in this study is shown in Table 8. The homogeneity of the groups is defined by the ratio of the 97.5th and 2.5th percentiles of the log-normally estimated mean exposures of a group of workers ($_BR_{0.95}$). The exposure group is considered homogeneous if $_BR_{0.95} = \exp(3.92 \times {}_BS_Y) \leq 4$ (Rappaport, 1991). The components of variance related to the total variance were calculated as percentages.

Table 8. ANOVA table (modified from Bolej et al. 1995). SS = sum of squares, k = number of populations (workers), N = total number of observations (measurements), ${}_{W}S_{Y}^{2}$ = variance component due to days (temporal variance), ${}_{B}S_{Y}^{2}$ = variance component due to workers (spatial variance), n = mean number of samples per worker.

Sum of the squares	Degrees of freedom	Mean sum of the squares	Expected values
SS_B	k-1	$SS_B(k-1)$	$= {}_{W}S_{Y}^{2} + n \times {}_{B}S_{Y}^{2}$
SS_W	N-k	$SS_W/(N-k)$	$= {}_{B}S_{Y}^{2}$

The standard provides instructions on the sampling frequency for groups with different exposure levels. The closer the exposure of the group to the OEL, the more often the group should be monitored.

7.4 Statistical methods

SAS, version 8.02 (SAS Institute, Cary, North Carolina, USA), and SPSS-PC, version 10.0.7 (SPSS Inc., Chicago, Illinois, USA) statistical software and MS-EXCEL versions 95-2000 (Microsoft Corp., Redmont, Washington, USA) spreadsheet programs were used to analyse the results.

8. RESULTS

8.1 Field studies

The results of the dermal exposure measurements have been presented separately for body and hands. The distributions of the contamination per body part have also been included. This thesis concentrates on dermal exposure. Therefore, the results of the inhalation exposure have not been included but can be found in the original publications. The validation data of the sampling and analytical methods have also been presented in the respective articles.

8.1.1 Exposure to industrial chemicals

The overall results of the patch and whole-body measurements are presented in Table 9. The concentrations found on the workers' clothing were adjusted by the default total area of skin, 18 720 cm^2 (excluding hands) (US EPA, 1989), and by the sampling time.

Table 9. Potential dermal exposure of the body (mg/h) in four different industrial processes

Process	Contaminant measured	N	n	Median	AM	SD	Range
Plywood manufacturing	Phenol	15	4	0.68	1.02	0.74	0.26-2.63
Paint manufacturing	Xylene mixture	15	15	4.95	6.98	6.77	1.43-28.6
Electroplating	Chromium	29	16	0.78	1.42	1.93	0.02-7.19
Grinding	Chromium	29	15	32.6	61.7	114	1.03-613

N = number of measurements
n = number of workers
AM = arithmetic mean
SD = standard deviation

In Table 10, the actual hand exposure measurements are presented. The results were adjusted by the sampling time. For plywood manufacturing, the glove method was used as the sampling method. In paint manufacturing, patches sewed to the gloves were used. Hand washing was used in the electroplating and grinding studies.

Table 10. Actual dermal exposure of hands (mg/h) in four different industrial processes

Process	Contaminant measured	N	n	Median	AM	SD	Range
Plywood manufacturing	Phenol	15	4	0.02	0.04	0.04	<0.01-0.13
Paint manufacturing	Xylene mixture	10	9	0.95	2.63	4.88	0.01-16.1
Electroplating	Chromium	29	16	0.07	0.12	0.13	0.01-0.48
Grinding	Chromium	29	15	1.38	2.74	3.45	0.13-14.3

N = number of measurements
n = number of workers
AM = arithmetic mean
SD = standard deviation

The median exposures per square centimetre of the sampler attached or representing the respective body part, are presented in Table 11. The concentrations normalised to represent the default body areas are presented in Table 12. In the paint manufacturing study, not all body parts were covered, and, therefore, the patches attached to the lower arms represent the whole upper extremities. Lower extremities were sampled with only one patch attached to the right thigh.

Table 11. Dermal exposure distribution per body part, expressed as μg/(cm^2·h)

Body part	Plywood manufacturing	Paint manufacturing	Electroplating	Grinding
Hands	0.050	2.021	0.965	6.261
Chest + forehead	0.112	0.119	0.222	4.753
Back + back of head	0.012	0.119	0.038	2.242
Forearms	0.271	0.631	0.222	4.746
Upper arms	0.018		0.185	6.324
Thighs	0.016	0.522	0.606	6.930
Lower legs	0.024		0.471	2.153

Table 12. Dermal exposure distribution per body part (mg/h) adjusted by the default areas

Body part	Plywood manufacturing	Paint manufacturing	Electroplating	Grinding
Hands	0.04	1.66	0.79	5.13
Chest + forehead	0.40	0.65	0.79	16.9
Back + back of head	0.04	0.42	0.13	7.96
Forearms	0.33	2.60	0.27	5.74
Upper arms	0.05		0.54	18.4
Thighs	0.06	3.23	2.32	26.5
Lower legs	0.06		1.12	5.12

8.2 Exposure to pesticides

The results for the pesticide exposure are presented in Table 13 as the mass per used amount of active ingredient of the respective pesticide. This format was used in the predictive models for pesticides. The exposure distributions between the different body parts during the mixing and loading and application phases are presented as the mean exposures of all three active ingredients in Table 14.

Table 13. Potential dermal exposure (mg/kg of active ingredient) during mixing and loading and the application of the pesticides malathion, deltamethrin and iprodione in greenhouses. The arithmetic means of three measurements (two are given for deltamethrin mixer-loader).

	Mixing and loading			Application		
Body part	**Malathion**	**Deltamethrin**	**Iprodione**	**Malathion**	**Deltamethrin**	**Iprodione**
Body	0.3	5.1	2.5	665	134	1400
Hands	201	930	68	6100*/234	212	46
Left	101	754	33	159	110	27
Right	100	176	36	5900*/75	102	19
Total dermal exposure	201	935	71	6700*/900	346	1500

* A case of an excessive, accidental contamination of the right hand taken into account when calculating the mean.

Table 14. Dermal exposure distribution between body parts as in different work phases, expressed as μg/(cm^2·h)

Body part	Mixing and loading	Application
Hands	113	38.9
Head	0.016	38.4
Chest	0.030	71.2
Back	0.0008	354
Upper limbs	0.026	2350
Thighs	0.018	2370
Lower legs	0.089	1340

8.3 Sampling for database enlargement of EUROPOEM

The dermal exposure data obtained in this study (**IV**) are summarised in Table 15 together with the existing indoor application data of the EUROPOEM I database. The measurement data were summarised together disregarding the type of active ingredient used, as it was not relevant for the modelling. For enabling the comparison with the existing database, the mixing and loading and application data have been combined.

Table 15. Comparison between exposure estimates (mg/kg of active ingredient) in the EUROPOEM I database and in the field study of original publication **IV**. Accidental, strong hand contamination in one study has not been included.

Study	N	GM	75th percentile	90th percentile	Maximum
EUROPOEM					
Hands	16	30	56	200	1300
Body	17	15	28	42	130
Field study					
Hands	7	230	620	1200	1900
Body	7	502	1600	2400	2900

N = number of measurements

GM = geometric mean

8.4 Sampling for the development of the task-based dermal exposure model for industrial chemicals

The measurements in original articles **II** – **III** and the unpublished RISKOFDERM data presented were grouped so that the results could serve as a basis for task-based model construction. The applicability of the dermal exposure operation units a priori set was tested with field studies in several branches of industry in five different European countries. The results of the RISKOFDERM study showed that the variation is large (Tables 16 and 17). The results were converted into the concentration of the formulation used in order to obtain comparable results from different studies. The electroplating (dip coating) and grinding (mechanical treatment of solids) results obtained in the Finnish part of RISKOFDERM are presented in more detail earlier in Tables 9 and 10. The hand exposure measurement methods used in the grinding study did not measure potential exposure, but actual, and, therefore, the results are not included in Table 17.

Table 16. Potential dermal exposure levels of the body in different DEO units, expressed as µg/(cm^2·h) (Rajan-Sithamparanadarajah et al., 2003)

DEO-unit	N	Median	GM	GSD	Range	95 %ile
Handling objects	117	23	7	27	0.0007-1700	490
Manual dispersion	30	340	280	6.9	6.9-5800	4500
Manual dispersion with hand-held tools	61	430	190	8.1	0.15-2200	1200
Spray dispersion	87	78	80	4.2	1.3-1200	840
Dip coating	55	1.4	2.2	26	0.034-340	150
Mechanical treatment of solids	68	18	25	8	0.27-1200	450

N = number of measurements

GM = geometric mean

GSD = geometric standard deviation

95 %ile = 95th percentile

Table 17. Potential dermal exposure levels of the hands in different dermal exposure operation – units (DEO-units). Exposure expressed as µg/(cm^2·h) (Rajan-Sithamparanadarajah et al., 2003).

DEO-unit	N	Median	GM	GSD	Range	95 %ile
Handling objects	151	750	590	20.8	0.0005-250000	63000
Manual dispersion	30	130000	58000	10.2	3.4-300000	290000
Manual dispersion with hand held tools	88	180	140	11.7	0.055-5400	3600
Spray dispersion	77	430	660	6.5	24-52000	17000
Dip coating	29	0.43	0.46	3.7	0.052-7.8	7.1

N = number of measurements
GM = geometric mean
GSD = geometric standard deviation
95 %ile = 95th percentile

8.5 Utility of the EN 689 at workplaces

In plywood manufacturing, monitoring the work indicated that the assembly workers were similarly dermally exposed. All the workers of the group were handling freshly glued veneers with relatively similar machinery. However, as the results show in Table 18, this group was not homogeneous according to standard EN 689. Both components of variance were equally important.

Table 18. Homogeneity of the dermal exposure and the percentages of the between-worker and within-worker components of variance in the assembly of veneers ($p < 0.01$)

Task group	N/n	${}_{B}R_{0.95}$	Between	Within
Assembling, body + hands	15/4	7.0	49	51

N = number of measurements
n = number of workers
AM = arithmetic mean

European standard EN 689 was originally developed as guidance for exposure assessment via the respiratory route. The plywood factory workers were divided also into four exposure groups by both their breathing-zone exposures and the area concentrations, as most of the workers had permanent work areas. Only one of these groups appeared to be homogeneous according to the standard.

9. DISCUSSION

9.1 Dermal exposure assessment

9.1.1 Industrial chemicals

The results have been presented both as mass per square centimetre and as mass per total area of a respective bodypart of a standard human (US EPA, 1989), adjusted in both cases for the sampling time. Concentration per cm^2 describes the contamination load found on the clothing or on the skin. This measure can serve as a tool when risk of the skin diseases is assessed. The actual amount of the contaminant is in this case the most important factor. For occupational hygiene purposes, (i.e., when designing technical control measures or personal protection) the contamination level of a whole bodypart is a more useful measure.

The body exposure was measured on top of the clothing, and hand exposure by cotton gloves worn under protective gloves or washing hands covered with protective gloves. It must be noted that they are not fully comparable measures as discussed in the section 3.1.

9.1.1.1 Phenol exposure in plywood manufacturing

Some contamination could be found on all the coveralls monitored for phenol exposure in plywood manufacturing, whereas some of the glove samples were under the detection limit. The glove use habits affected hand exposure, as some workers took off their gloves while working. It may be concluded, that the rubber impregnated cotton gloves used were effective in decreasing the exposure when used properly.

The main contaminated body parts were the forearms and chest, which was expected in this kind of work. Most workers used only short-sleeved T-shirts, whereas the chest area was, of course, covered with clothing. In the cases when the gloves were not properly used the upper limbs, together with hands, are therefore the most important areas of exposure when uptake is considered. In Figure 5, the distribution of exposure is presented graphically as percentages.

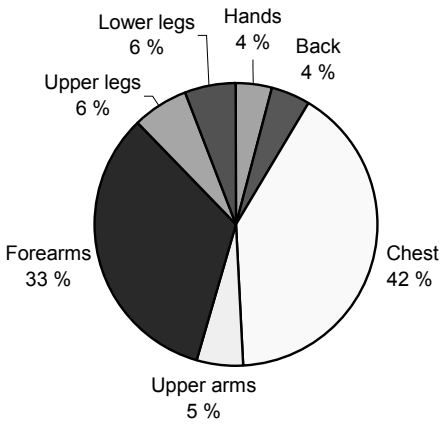

Figure 5. Distribution of contamination during plywood manufacturing.

In order to decrease exposure during gluing of veneers in plywood industry, it is recommended to use long sleeved clothes. In addition, it is important to use gloves all the time. Nitrile or natural rubber impregnated cotton gloves are suitable for this kind of work. Totally impermeable gloves should be used in situations of process malfunction, when it is possible to get massively exposed to the glue.

9.1.1.2 Solvent exposure in paint manufacturing

For the workers exposed to solvent mixtures (xylenes analysed), it was difficult to conclude which parts of the body would contribute most to the exposure, as it was not possible to separate exposure to liquid and vaporous solvents. The distribution obtained in this study is presented in Figure 6. The body exposure correlated well with the breathing zone results (see the section on correlations between dermal measurements and air sampling, 9.1.3). This correlation is due to the fact that exposure to vapourised solvents dominated the exposure. Patches sample the surrounding air not exclusively the portion having a direct contact with the skin. However, the hand exposure results indicated that work habits influenced the level of exposure. For example, the hands of workers who used gloves properly were less exposed. One especially careful worker in the filling department of the factory, who used double gloves and had also otherwise well internalised the meaning of safety at work, was only exposed to a concentration level of 7 µg/h, whereas the maximum hand exposure measured in the same work task was 16 100 µg/h. This illustrates the importance of good personal hygiene and conscientious working habits.

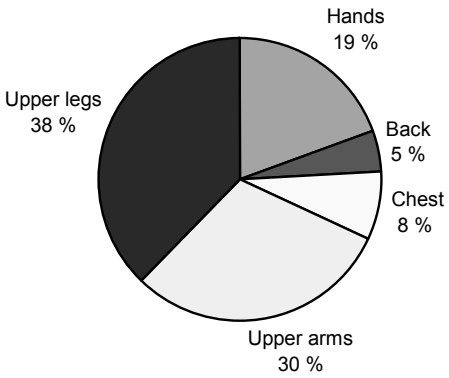

Figure 6. Distribution of contamination during paint manufacturing.

9.1.1.3 Chromium exposure in electroplating

The hands and legs were the most contaminated body parts during electroplating (Figure 7). Hand exposure was relatively high, even though it was measured under the protective gloves. The workers' glove using habits varied. Only part of the workers used impermeable gloves, which are considered necessary when handling irritating plating solutions. However, the type of the gloves did not affect the level of exposure (see the section on determinants of dermal exposure, 9.3). The workers relied on the impermeable gloves, and tended to be more careless when using them, by, for example, putting their hands straight into the solution. Exposure of the upper legs was expected, as the workers often leant over the contaminated, wet basins.

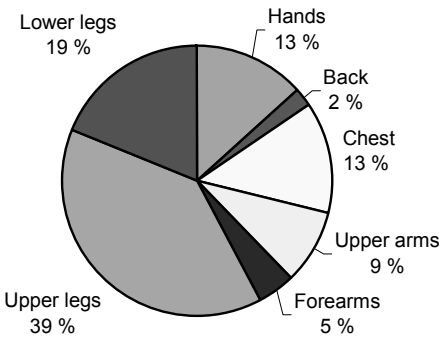

Figure 7. Distribution of contamination during electroplating.

The exposure can be decreased by using intact impermeable gloves. It is also essential to change the gloves often enough. A rubber apron will efficiently cover the thighs.

9.1.1.4 Chromium exposure in grinding

In grinding, the exposure was relatively evenly distributed over different parts of the body (Figure 8). This was expected, as the contamination was mainly due to airborne dust. Almost 10% of the exposure could even be found from the back. Good personal hygiene is essential in decreasing the exposure. Small metal particles are easily redistributed from contaminated clothes to, for example, rest rooms or even home. Therefore, it is important to change work clothes regularly.

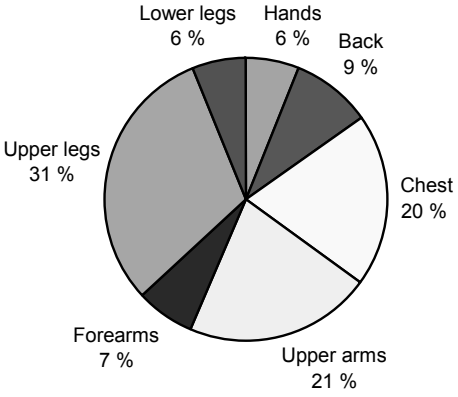

Figure 8. Distribution of contamination during grinding.

In Figure 9, the relative distributions in different work tasks are shown together for the comparison.

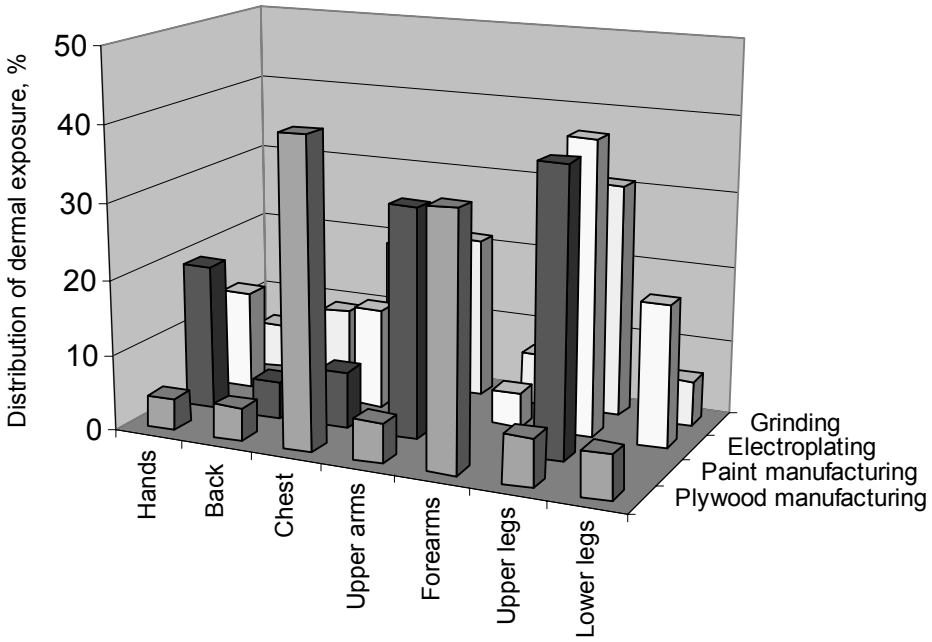

Figure 9. Dermal exposure distribution between body parts during grinding (chromium), paint manufacturing (xylenes), plywood manufacturing (phenol), and electroplating (chromium).

Distribution of the dermal contamination is highly dependent on the task and the type of the exposure. For example, in electroplating, grinding, and paint manufacturing, the legs (especially upper legs) are relatively highly contaminated, whereas in plywood manufacturing the forearms and chest are the most exposed. These differences should be taken into account when personal protection is designed and work tasks are organised. In addition, the variation of the exposure between workers is large, as can be noted from the ranges and standard deviations (e.g., range of the body exposure to chromium was 0.02-7.19 mg/h in electroplating). It was seen in all studies, that the personal work habits and the way of using protective gloves can affect the level of exposure by orders of magnitude. This should be taken into account when designing exposure control measures. It seems that the most important, even though often difficult, way of decreasing dermal exposure at workplaces is to affect the attitudes of the workers. It should also be kept in mind that it is often impossible to notice only by observing the workers, which body parts get most exposed. Illustrating the risks of dermal exposure with small-scale dermal or surface sampling studies could enhance the efficiency of the education of workers and help focusing resources when technical control measures are designed.

9.1.2 Pesticides

Dermal exposure to iprodione and malathion was higher during pesticide application, whereas deltamethrin exposure occurred especially during the mixing and loading of the product. During mixing and loading, over 99% of the dermal exposure was obtained via the hands. During application tasks, the contamination was distributed more evenly to all body parts. The lower limbs were the most contaminated. The graphic presentation in Figure 10 illustrates the distribution of the contamination during application as the percentage of the total dermal exposure.

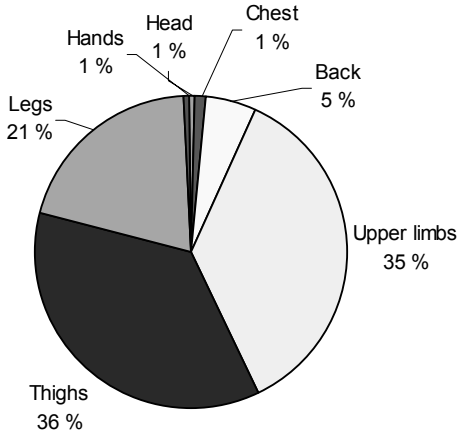

Figure 10. Distribution of contamination during the application of pesticides in greenhouses.

A leak of the spraying apparatus caused a high accidental contamination of a hand of one worker. The glove method probably overestimates the exposure in these kinds of cases, and, therefore, the results in Table 13 have been presented with and without the outlier. Accidental exposures are, however, common in pesticide work, and they must be taken into account when the exposure of individual operators is assessed. For example, in this accidental case, the exposure of the hand was almost 80-fold that of the average exposure level, even though it happened during application, during which strongly diluted products are used.

9.1.3 Correlations between the dermal measurements and air sampling

In the xylene and chromium field studies, respiratory exposure to the same chemical sampled from the body surface was measured simultaneously in the breathing zones. The scattergrams in Figures 11 to 13 present the correlation between the dermal and respiratory exposure. Only the body exposure was taken into account for three reasons. Firstly, not many xylene measurements were available for which both the body and hands had been sampled simultaneously, and some of the samples measurer actual instead of potential exposure. Secondly, the hand exposure to chromium

was measured from underneath the protective gloves. Thirdly, it is probable that most of the hand exposure was due to the touching of contaminated surfaces, tools, and the like, and not to deposition from the air.

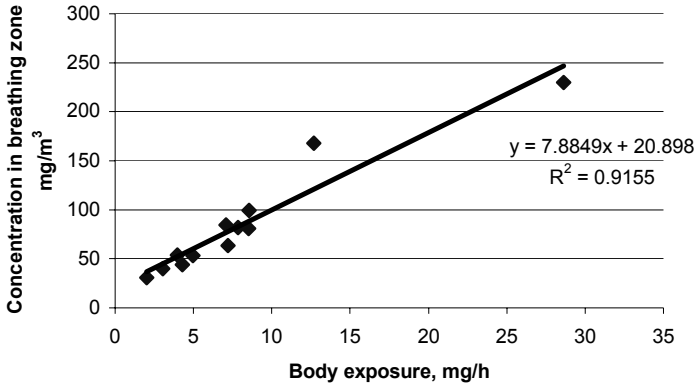

Figure 11. Correlation between body and breathing-zone exposure to xylene vapours, aerosols, and liquid splashes during paint manufacturing.

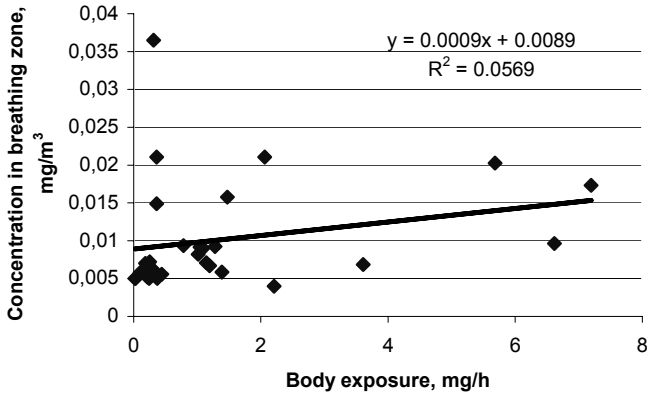

Figure 12. Correlation between body and breathing-zone exposure to dissolved chromium in plating solution during electroplating.

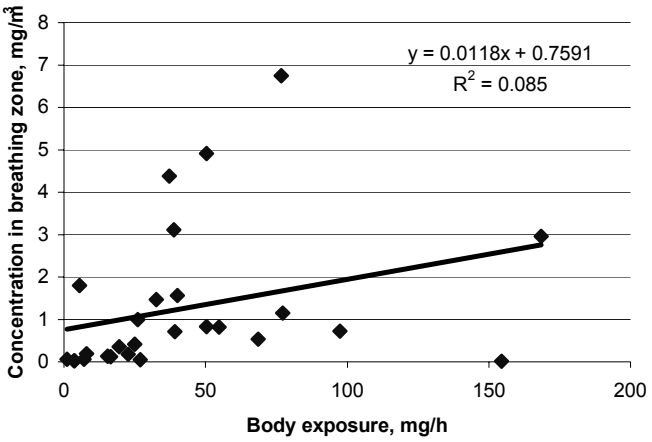

Figure 13. Correlation between body and breathing-zone exposure to chromium dust during the grinding of stainless and acid-proof steel.

It could be seen from the correlations between the respiratory and dermal exposures to chromium (liquid and solid substances) that it is not possible to predict dermal exposure by measuring air concentrations. For the solvent exposure, the correlation was good, but, in this case, the health effects of vaporised chemical via the dermal route are probably not significant. The correlation would probably have been worse if the dermal sampling method would have been able to separate the exposure to liquid and vapourised solvents.

There is not much literature available about the correlations between inhalation and dermal exposures. Vermeulen et al. (2000b) have, however, found moderate-to-good correlations between concentrations of cyclohexane-soluble matter in air and on skin surfaces, and they have claimed that it could even be a more general phenomenon. According to the results of this study, this conclusion does not, however, seem feasible. If the exposure is mainly due to touching of contaminated surfaces or other factors related to the worker and the task itself, this claim is incorrect. For example, during grinding in one of the field studies (**III**) of this dissertation, the contaminant measured was airborne dust, but even then the respiratory exposure did not correlate with the dermal exposure. The reduction of emissions in this type of exposure would probably decrease the exposure at workplace level, but it is not possible to predict the exposure of an individual worker.

9.2 Performance and comparison of sampling methods

In the plywood manufacturing study (**I**), the phenol sampling was conducted with the whole-body method. The method proved to be practical and easy in field conditions, as there was no need to attach the patches one by one. It is also advantageous that, with this method, there is no need for

area correction, as is the case with patch use. However, the area of protective coveralls was not the same as the skin. Therefore, when realistic results are the objective, some adjustment must be made. In this case, the size difference was roughly estimated to be 30%. Using more close-fitting, stretching suits could solve this problem. The large amount of extraction agent needed for whole-body methods may notably increase the costs of the analyses. The use of the method did also include analytical problems, as free phenol polymerises rapidly. The samples, even though extracted to methanol, had to be analysed within hours after sampling in order to get reliable results. Therefore, this method is not feasible in locations situated far from analytical facilities.

The active charcoal patches used in the paint factory (**V**) gave only indicative results, as the method did not take the form of the substance into account. The method has been validated by Cohen & Popendorf (1989), but they could not solve all the problems of interpretation of the results because of confounding factors, for example, evaporation.

In the case of chromium, the analytical method used created some limitations when the sampling matrix was selected. Heavier material would not have been able to burn into ash in one piece, or the size of the individual samplers would have to be decreased. Such adjustment would have led to higher costs, or it would have increased the uncertainty related to the area correction needed.

The alpha-cellulose patch methods used in studies **II**, **III** and **IV**, had been validated in the laboratory before the field studies began. However, it is not known whether this material behaves similarly with skin and the protective clothing used by workers. The uncertainty is especially large when solid substances are sampled. For pesticides, the alpha-cellulose was a good choice, as it has been used extensively for pesticide studies in the past. Therefore, it is easy to compare the results with earlier ones. The sampling performance of alpha-cellulose for pesticides was also compared with patches cut from Tyvek® material. The results correlated well, and it was shown that Tyvek® could also serve as an efficient material (Tuomainen et al., 2000). The advantage of Tyvek® would be that it is more resistant to tension than paper-like alpha-cellulose is, especially when wet.

The hand washing method measures actual exposure if the worker is using protective gloves. It would also have been advantageous to be able to measure potential hand exposure, as the body exposure was measured that way. However, some ethical and practical problems occurred. It is considered unappropriate to ask the workers not to use protection that they normally use. Cotton gloves could not have been worn over the sturdy leather gloves used by the grinders, as they would have increased the risk of injury. In electroplating, the cotton gloves would have overestimated the exposure uncontrollably since they would have become easily soaked with the plating solution. One possible solution for overcoming this difficulty could be the washing of protective gloves themselves. This has been tested with pesticides and nitrile rubber gloves. It was, however, observed that it was difficult to extract all the pesticide off the glove material, even with three repetitive rinsings (Tuomainen et al., 2000).

Careful observation of work tasks and processes before and during sampling is essential when the distributional issues must be estimated and the relevant determinants of exposure must be clarified. Whether under- or overestimation of exposure is likely, (e.g., due to transport processes) must also

be evaluated. In addition, in the RISKOFDERM study, it was clearly seen that using one standardised method and sampling material for all purposes is not a realistic goal; instead the chemical being studied and the work processes affect the selection of methods. For example, a weight limit for an individual sample in the analytical procedure used in this study (ashing) with an atomic absorption spectrometer restricted the selection of sampling matrices.

All dermal exposure measurement methods used in this study (i.e., whole body and patch methods for body exposure assessment and hand-washing and glove methods for hand exposure assessment), have both advantages and disadvantages. The major characteristics and an evaluation of different sampling methods used in this study are presented for comparison in Table 19. All the methods measure the mass of contaminant deposited on skin or retained on the skin at the end of the exposure period and not the concentration of the substance, which has been claimed to be biologically more relevant when dermal uptake is concerned (Cherrie & Robertson, 1995). So far, only one attempt to produce a sampling method for the purpose has been published (HSE, 2003). However, the results of the methods measuring mass per area can be used to estimate exposure for regulative or epidemiological modelling purposes. It is also crucial for designing control methods, for example, protective clothing, to know the distribution of contamination.

The aim of dermal exposure measurements should also affect the selection of the methods. When potential exposure is investigated, the results are more comparable as there is no need to extrapolate the effect of protective clothing. This approach is valuable when models needed for regulatory purposes are developed. If the aim is to estimate the uptake, other methods must be applied and developed further. Combining potential exposure measurements with well-validated biological monitoring would provide both information about individual exposures and tools with which to develop technical control measures or choose protective garments.

Table 19. Characteristics and performance of the sampling methods used in this study. The advantages and disadvantages observed. (BM = biological monitoring).

Method	Method description	Advantages observed	Disadvantages observed	Overall remarks
Patch method, alpha-cellulose	Potential body exposure	Ease of use Large amount of existing pesticide data available for comparisons Simultaneous BM possible	Assumes uniform distribution Poor durability	Helpful in designing PPE Methods measure the mass of the contaminant deposited or retained on the skin at the end of the exposure period Not clear whether any of the methods behave similarly as the skin Biological relevance not known Potential measures more applicable for modelling, but impossible for hands in this study Assessment of internal dose not possible without more knowledge of dermal absorption
Patch method, active charcoal	Potential body/hand exposure	Ease of use Would be specific for solvents, if properly validated Simultaneous BM possible	Assumes uniform distribution Difficult to validate, does not separate vapour and liquid	
Whole body method, Tyvek®	Potential body exposure	No need for area corrections Durable material Easy to handle in the field BM not possible	Area differed form skin area Cumbersome and costly analysis	
Handwashing, soap solution	Actual hand exposure	Whole area covered Did not preclude BM (as normal hygienic procedures were mimiced)	Measures the loading available on the time of sampling Actual measures not easily applicable in modelling	
Cotton gloves underneath the protective gloves	Actual hand exposure	Whole area covered Measures all mass deposited during sampling time BM not possible	Actual measures not easily applicable in modelling	

9.3 Determinants of dermal exposure

Typical determinants in industrial settings, which would be the most useful in modelling, include process parameters (e.g., the amount of chemical used or product rate). In all cases, these kinds of

determinants cannot be found, or recording them is difficult. This was also the case in the electroplating and grinding studies. It was not possible to calculate the amount of plating liquid actually used by an individual worker or the amount of dust emitted during the grinding of an article.

In the electroplating study (**II**), it was reasoned a priori that the level of automation may be a possible determining factor, but the assumption proved false. The exposure did not clearly decrease with increasing automatisation of the process. The highest median exposure was, expectedly, observed in processes classified as manual (13.6 mg/h). However, the exposure was not the lowest in automatic processes; instead semi-automatic ones proved to involve the least exposure (median exposures 4.9 mg/h and 2.2 mg/h, respectively). This result was mainly due to the fact that, even when using computer-controlled processes, workers had to adjust the process manually, and they visited the basin area frequently. In addition, the use of protective gloves did not determine the amount of hand exposure. The exposure of the workers' using gloves made of polyvinyl chloride was twice as high as the ones using cotton or rubber-coated cotton gloves. This finding was not statistically significant, however. Using impermeable gloves may even increase risky behaviour (e.g., touching contaminated surfaces or immersing hands in plating solution), which leads, in some cases, to more contamination of hands than working without gloves or with permeable ones. In addition, as thick PVC gloves are quite durable, they are not changed as often as they should be. It is presumable that the inside of the gloves gets contaminated and the exposure is increased.

In grinding (**III**), the type of the tool was considered a determinant. This conclusion proved to be correct. The band grinders were less exposed to chromium dust by an order of magnitude than the workers using hand-held grinding tools. This result was clearly due to the fact that it is easier to use local exhaust equipment efficiently when the tool and the piece ground are not moving. Another determinant tested was the existence and performance of ventilation. Classification between "adequate" and "inadequate" local ventilation was made by using smoke detector tubes. The results were controversial. The highest average exposure levels were found in workplaces having only general ventilation (282 mg/h) or general ventilation with adequate local ventilation (307 mg/h), whereas, in workplaces classified as having an inadequate local exhaust system, the exposure was the lowest (116 mg/h). The reason for this finding, in addition to the ventilation efficiency, was that the exposure depended on the in-plant emission rates of the contaminants. The local exhaust systems were better designed and more efficient in the workplaces, in which the amount of dust emitted was high. Leather gloves provided twice as good protection than leather-cotton gloves. This result was expected since small particles can get through cotton fabric.

Many of the determinants selected did not turn out to have as much of an effect as estimated a priori. This emphasises the finding of this study that personal work habits highly influence the dermal exposure levels. In some cases the direction of the effect of a determinant was opposite the predicted one. However, it was generally possible to conclude the reasons for the differences. In a recent review of dermal exposure determinants, this problem has been also recognised (Marquart et al., 2003). More studies and statistical testing should be done in order to delineate the determining factors useful for modelling.

9.4 Measurements for task-based model construction

The dermal exposure operation units that were established before the study did not prove useful in predicting exposure to all the included scenarios, for example, in the electroplating studies carried out in the United Kingdom and Finland, even though the scenario was the same. The median body exposure level measured in the Finnish electroplating shops was 0.23 μg/(cm^2·h), whereas the corresponding figure obtained in the United Kingdom was 29 μg/(cm^2·h). Inevitably, the differences in sampling and analytical methods, and probably also the variations in work practices in different countries caused differences even within these highly similar scenarios. Results obtained in the mechanical treatment of objects (DEO unit 6) varied remarkably, as two different scenarios (machining and grinding) were included in the same DEO unit. The database of DEO unit 6 now contains measurements of liquid metalworking fluids and solid chromium dust. These exposure scenarios did not prove to be similar enough; the median body exposure to metalworking fluids was ten times higher than the exposure to solid chromium.

Another extreme example of a misleading DEO unit was the mixing scenarios (in DEO unit 1) undertaken in the ship-repairing industry (mixing large amounts of antifouling agents to paint) and drug preparation (mixing components of an anti-neoplastic drug in a fume hood). The enormous variability was in this case, clearly due to the vast differences in the scales of the processes, work practices, and control measures used.

It can be concluded from the examples mentioned, and from some other cases of the RISKOFDERM project, that the range of exposure within the DEO units is usually large. A need for further refinement of the DEO units is pointed out. These results show that the averaged results for DEO units are not applicable to the prediction of dermal exposure in all scenarios within the DEO unit if the factors causing variability are not taken into account properly. If used as such, they may vastly over- or underestimate the exposure, depending on the scenario. In addition, it is of utmost importance to subdivide the liquid and solid substances into their own databases. However, it must be emphasised that there were also successful groupings. For example the measurements done in the "spray dispersion" unit showed highly similar results (means and deviations) in different sub-studies and as reported earlier in the literature. Also in this case, the exposure ranges varied, as expected, between studies.

It was mentioned earlier in the section on the performance and comparison of sampling methods, 9.2, that it is probably impossible to find a sampling method for dermal exposure assessments that would cover all tasks, processes, chemicals, and the like. However, in a multi-centred study like RISKOFDERM, in which data were collected in several countries, at least for the same scenarios with the same compounds, a common procedure should be developed. If methods vary from one institute to another, as was unfortunately the case in the RISKOFDERM study, it is impossible to determine the most important causes of variability. As emphasised earlier, the lack of standardised sampling methods has been a major difficulty in the area of dermal exposure research. This inconsistency of sampling methods of dermal exposure is due to the novelty of the area of research. These kinds of problems in international research cooperation have been overcome in the field of

respiratory exposure studies, which is proved by, for example, the EXPOLIS study (EXPOLIS, 1999). In the future, it will be easier to find uniform sampling methods and procedures also for dermal exposure studies since RISKOFDERM project produced several new sampling methods.

9.5 Characteristics of the sampling data produced for EUROPOEM

When the number of data is low, it is necessary to use high percentile values in the database to ensure the safety of workers (van Hemmen, 1993). In the case of indoor applications, a maximum value has been recommended to ascertain the safety of operators. Even after the data obtained in the field study (**IV**) are added, maximum values should probably still be used for exposure assessments, as the number of data points and different exposure scenarios still remain low. The European project (the Assessment of Operator, Bystander and Environmental Exposure to Plant Protection Products) has, however, later produced data from other indoor scenarios, and it is possible that after all newly available measurements are added, lower percentiles (e.g., 75^{th}), may be usable.

In the case of hand exposure, the additional data from the greenhouse study will not significantly change the outcome of the modelling, as the exposure ranges were on the same level. The body exposure, however, was drastically higher in the field study due to differences in the crops cultivated in different studies. The existing data in EUROPOEM derive from the spraying of chrysanthemums growing in pots on tables, and such a situation differs greatly from spraying tall and densely grown roses, as in this study. Differences in the measurement methods may, also in this case, have caused variation between the results.

The results highlight the need of the user of the model to become carefully acquainted with the sampled data within the database before applying it in exposure assessment. When the model is used to assess exposure in a certain scenario, it must be known whether the type of plants grown, the agricultural conditions, the growing season, the equipment used, and the like are comparable with the ones in the studies already included in the database. If the database is considered not to represent the scenario well enough, it is necessary to use a high percentile of the database in the exposure assessment in order to ascertain the safety of workers.

When dermal exposure is modelled in the agricultural use of pesticides, the differences between the workplaces, the amounts and properties of the chemicals handled, the variability of personal work habits and the tools used are considered small compared with the corresponding factors in industrial settings. If the existing differences and variation are taken properly into account and the databases are large enough, it is possible to assess pesticide operator exposure for regulative purposes. These models are not capable of, or even aimed at, estimating the exposure of an individual worker; instead they are meant to provide insight into the overall exposure level in different kinds of scenarios. Probabilistic methods will probably improve these models further in the future.

9.5 Applicability of the EN 689 approach to assessments of dermal exposure

The strategy based on homogenous exposure groups did not seem to function either for inhalation exposure assessment or for dermal exposure assessment when it was applied as strictly as described in the EN 689. For the dermal exposure, the study was only a preliminary one, as there was only one group of workers tested for their homogeneity. The variability of dermal exposure is at least as large as the variability of inhalation exposure. Even in the case of the assemblers, who had highly similar tasks in a static, process-type of production, the requirements of the standard were not met.

The homogeneity of the groups of electroplaters and grinders in this study can be considered similar, even though they were not all at the same worksite. The group of electroplaters was not homogeneous ($_{B}R_{0.95}$ was 5.4 for the body, and 11 for the hands). The grinders, even though working in different companies, formed a homogeneous group ($_{B}R_{0.95}$ was 3.6 for the body and 2.3 for the hands). This information could be used when the exposure of stainless steel grinders is estimated as a group in general.

The approach is, however, not practical in general for assessing dermal exposure, as the statistical handling of the data required such a large number of measurements, which is not possible in practice as sampling becomes too expensive and time consuming. The appropriateness of extensive sampling is also questionnable since there are no dermal exposure limits available. Therefore, it is difficult to interpret the results. With current knowledge, it is especially difficult to determine the relationship between the results and possible health effects.

The approach using homogeneous exposure groups has been criticised by the AIHA (Mulhausen & Damiano, 1998). In order to keep the exposure assessment as simple as possible, it would, however, be valuable to be able to use the same procedures in the assessment strategies for both respiratory and dermal exposure. It could be fruitful if the practical exposure assessment protocol proposed by AIHA were applied to dermal exposure situations. The applicability of the AIHA approach of similarly exposed groups should be studied in the future for dermal exposure.

Some proposals, described in detail in the literature review, have been presented recently (Schneider et al., 2000; van-Wendel-de-Joode et al., 2003). Their applicability and validity should be tested. The results of the occupational hygienic measurements and the knowledge obtained about factors determining dermal exposure in the RISKOFDERM study should be carefully taken into account when strategies are developed.

10. CONCLUSIONS

The whole body method is preferred if it seems that the contamination during the respective work task is non-uniform. Usually, the patch method is, however, more applicable in practice, as it is less laborious and time-consuming in field and in the laboratory. Hand-washing method measures the removable residue, whereas glove collects more or less the total amount contaminating the hand. This difference must be remembered when interpreting the results. In many cases of this study, the desirable measure would have been the total contamination, but the glove method was not, unfortunately, practical. The results of the measurements done in this study have been presented as mass per square centimetre and as mass per total area of a respective body part. The measure mentioned first describes the exact contaminant load on the skin and it can be utilised in assessing the risk of skin disease. The latter measure serves better in developing of protective garments, and, most importantly, to see which areas of the skin need protection. It is important to explain the need for recommended protection, as workers are often reluctant to use the protective garments or equipment. Personal protective garments are incontrovertibly necessary for decreasing dermal exposure, but it was shown that the manner using them affects the exposure. In general, the dermal exposure sampling results may be used in screening level exposure estimations and modelling purposes if the causes of the variability are carefully taken into account.

The feasibility of the indoor applications dataset of the EUROPOEM I model increased when more data covering more broadly the greenhouse scenario were produced in this study. The results of this dissertation (along with many others) have now been included in the model, and the reliability of the model has improved. The database for indoor applications can be used for regulatory risk assessment, at least for scenarios resembling those included in the database. The EUROPOEM model allows the user to use higher percentiles if there is much uncertainty. In order to obtain less conservative predictions, the models should be enlarged and developed further. Probabilistic methods using distributions of modelling parameters instead of point estimates may improve the situation in the future. Like deterministic models as EUROPOEM, the probabilistic models need diverse data from different agricultural and geographical conditions. Most importantly, expert judgement is always essential for the successful application of the model.

It proved difficult to find relevant exposure determinants for industrial chemicals that could serve as a basis for exposure assessments or models. The tasks vary largely both spatially, temporally, and between individuals causing large variability. For exposure reduction, it is important to recognise that personal properties, skills, working habits and ways of using personal protective equipment have a great influence on the dermal exposure. When the whole European study in considered, the differences between the currently used sampling methods in different countries further increased the variability. If task-based models are to be published for exposure assessment of industrial chemicals, only well-defined tasks should be chosen to ensure the validity of the model, and the variability must efficiently be taken into account. The approach was proven promising, and it has potential to be applied in the future, if new methods for grouping of the tasks and processes, and finding useful exposure determinants are found.

The usefulness of the EN 689 strategy, using homogeneous exposure groups with strict statistical definitions, has not only been questioned in this study, but also elsewhere in the literature. In order to carry out the task of dermal exposure assessment efficiently and extensively, valid and practical exposure assessment strategies are needed. The strategies cannot be based on large amount of sampling, as it is laborious and expensive. The lack of standardisation of the sampling methods is slowing the development of dermal exposure assessment. There is, however, urgent need for well-defined assessment strategies of dermal exposure. In order to be truly able to apply the concept of total exposure assessment, these strategies should follow and be combined appropriately with strategies already introduced and settled to respiratory exposure assessment. New approaches are being developed, for example, by the RISKOFDERM group.

The currently used sampling methods are applicable for screening level purposes, e.g., finding tasks and processes causing dermal exposure or for designing technical control measures and assessing pesticide risks in regulative processes, but it is clear that the methods should be developed further and that the sampling procedures and assessment strategies should be standardised. However, dermal exposure measurements with the current, available methods hardly ever become a part of routine workplace exposure assessment. This is especially due to the fact that there are no dermal exposure limit values available, and that current knowledge of dermal uptake of many chemicals is still poor. The measurements are needed in specific cases, when it is not otherwise possible to find out the level of exposure, or the distribution. When highly dermatotoxic substances, or agents causing severe skin diseases are considered, it may be necessary to ascertain the assumptions. In addition, illustrative dermal or surface sampling can serve as a tool in the education of the workers, even though there are no dermal exposure limits available.

Dermal exposure is a significant route of exposure for several chemical substances, and a large part of occupational diseases are caused by dermal exposure. It is necessary to further develop dermal exposure measurement and modelling methodology to more biologically relevant and practical direction. This would also work in the favour of developing scientifically sound exposure assessment strategies. At the workplaces, it is very important to pay attention to the level of cleanliness, the personal hygiene and the appropriateness of the personal protection. It is the task of the scientific community to find out the valid ways of assessing dermal exposure in different workplace scenarios and to produce methods to be used as a part of workplace risk assessments. In addition, the dermal route must be taken into account in risk assessment of chemical substances.

11. REFERENCES

ACGIH (2000) *Threshold Limit Values for chemical substances and physical agent & Biological Exposure Indices*, American Conference of Governmental Industrial Hygienists, Cincinnati, Ohio.

Ammattitaudit 2001. Työperäisten sairauksien rekisteriin ilmoitetut uudet tapaukset (2001). Karjalainen et al. (eds.) Finnish Institute of Occupational Health, Helsinki (in Finnish with English summary).

Archibald, B.A., Solomon, K.R. and Stephenson, G.R. (1994a) Estimating pirimicarb exposure to greenhouse workers using video imaging. *Archives of Environmental Contamination and Toxicology*. 27:126-129.

Archibald, B.A., Solomon, K.R. and Stephenson, G.R. (1994b) A new procedure for calibrating the video imaging technique for assessing dermal exposure to pesticides. *Archives of Environmental Contamination and Toxicology*. 26: 398-402.

Archibald, B.A., Solomon, K.R. and Stephenson, G.R. (1994c) Fluorescent tracer and pesticide penetration through selected protective clothing. *Bulletin of Environmental Contamination and Toxicology*. 53:479-485.

Archibald, B.A., Solomon, K.R. and Stephenson, G.R. (1995) Estimation of pesticide exposure to greenhouse applicators using video imaging and other assessment techniques. *American Industrial Hygiene Association Journal.* 56:226-235.

Basketter, D., Gerberick, F., Kimber, I. and Willis, C. (1999) *Toxicology of contact dermatitis*. *Allergy, irritancy and urticaria* Chapter 1, *Clinical perspectives in contact dermatitis*. John Wiley et Sons Ltd, Chichester, p. 1-10.

Basketter, D., Horev, L., Slodonik, D., Merimes, S., Trattner, A. and Ingber, A. (2001) Investigation of the threshold for allergic reactivity to chromium. *Contact Dermatitis*. 44:70-74.

Benford, D.J., Cocker, J., Sartorelli, P., Schneider, T., van Hemmen, J.J. and Firth J.G. (1999) Dermal route in systemic exposure. *Scandinavian Journal on Work Environment and Health*. 25:511-520.

Bierman E.P.B., Brouwer, D.H. and van Hemmen, J.J. (1998) Implementation and evaluation of the fluorescent tracer technique in greenhouse exposure studies. *Annals of Occupational Hygiene*. 42:467-475.

Black, K.G. and Fenske, R.A. (1996) Dislodgeability of chlorpyrifos and fluorescent tracer techniques on turf: Comparison of wipe and foliar wash sampling techniques. *Archives of Environmental Contamination and Toxicology*. 31:563-570.

Bolej, J.S.M., Buringh, E., Heederik, D. and Kromhout, H. (1995) Exposure modelling. In: *Occupational hygiene of chemical and biological agents*. Elsevier, Amsterdam. pp 97-136.

Bos, P.M.J., Brouwer, D.H., Stevenson, H., Boogaard, P.J., de Kort, W.L.A.M, and van Hemmen, J.J. (1998) Proposal for the assessment of quantitative dermal exposure limits in occupational environments: Part 1. Development of a concept to derive a quantitative dermal occupational exposure limit. *Occupational and Environmental Medicine*. 55:795-804.

Bredendiek-Kämper, S. (2001) Do EASE scenarios fit workplace reality? A validation study of the EASE model. *Applied Occupational and Environmental Hygiene*. 16:182-187.

Brooke, I., Cocker, J., Delic, J.I., Payne, M., Jones, K., Gregg, N.C. and Dyne, D. (1998) Dermal uptake of solvents from the vapour phase: an experimental study in humans. *Annals of Occupational Hygiene*. 42:531-540.

Brouwer, D.H., Boeniger, M.F. and van Hemmen, J.J. (2000a) Hand wash and manual skin wipes. *Annals of Occupational Hygiene.* 44:501-510.

Brouwer, D.H., Hoogendoorn, L., Bos, P.M.J., Boogaard, P.J. and van Hemmen, J.J. (1998) Proposal for the assessment of quantitative dermal exposure limits in occupational environments: Part 2. Feasibility study for application in an exposure scenario for MDA by two different dermal exposure sampling methods. *Occupational and Environmental Medicine*. 55:805-811.

Brouwer, D.H., Kroese, R. and van Hemmen, J.J. (1999) Transfer of contaminants from surface to hands: Experimental assessment of linearity of the exposure process, adherence to the skin, and area exposed during fixed pressure and repeated contact with surfaces contaminated with powder. *Applied Occupational and Environmental Hygiene.* 14:231-239.

Brouwer, D.H., Lansink, C.M., Cherrie, J.W. and van Hemmen, J.J. (2000b) Assessment of dermal exposure during airless spray painting using a quantitative visualisation technique. *Annals of Occupational Hygiene.* 44:543-549.

Brouwer, D.H., Semple, S., Marquart, J. and Cherrie, J.W. (2001) A dermal model for spray painters, part I: Subjective exposure modelling of spray paint deposition. *Annals of Occupational Hygiene*. 45:15-23.

Brouwer, R., Brouwer, D.H., Tijssen, S.C.H.A. and van Hemmen, J.J. (1992) Pesticides in cultivation of carnations in greenhouses: Part II – Relationship between foliar residues and exposures. *American Industrial Hygiene Association Journal*. 53:582-587.

CEC (1996) *Technical guidance documents in support of the commission directive 93/67/EEC on risk assessment for new and notified substances and the commission regulation (EC) 1488/84 on risk assessment for existing substances.* European Chemicals Bureau, Ispra.

CEN (1995) EN 689, *Workplace atmospheres - Guidance for the assessment of exposure by inhalation to chemical agents for comparison with limit values and measurement strategy.* European Committee for standardization (CEN), Brussels.

CEN (1996) *Chemical disinfectants and antiseptics. Hygienic handwash. Test method and requirements* (Phase 2/step 2). Final draft prEN 1499. European Committee for Standardization (CEN), Brussels.

Cherrie, J.W. and Robertson, A. (1995) Biologically relevant assessment of dermal exposure. *Annals of Occupational Hygiene.* 39: 387-392.

Cherrie, J.W., Brouwer, D.H., Roff, M., Vermeulen, R. and Kromhout, H. (2000) Use of qualitative and quantitative fluorescence techniques to assess dermal exposure. *The Annals of Occupational Hygiene.* 44:519-522.

Chester, G. (1995) Revised guidance document for the conduct of field studies of exposure to pesticides in use. In: Curry, P.B., Iyengar, S., Maloney, P.A. and Maroni, M. (eds.) *Methods of pesticide exposure assessment*. pp. 179-215. Plenum Press, London.

de Cock, J., Heederik, D., Kromhout, H. and Bolej, J.S.M. (1996) Strategy for assigning a "skin notation": A comment. *Annals of Occupational Hygiene.* 40:611-614.

de Cock, J., Heederik, D., Kromhout, H., Bolej, J.S.M., Hoek, F., Wegh, H. and Ny, E.T. (1998) Exposure to captan in fruit growing. *American Industrial Hygiene Association Journal*. 59:158-165.

Cohen, B.-S. and Popendorf, W. (1989) A method for monitoring dermal exposure to volatile chemicals. *American Industrial Hygiene Association Journal.* 50:216-223.

Cullander, C., Jeske, S., Imbert, D., Grant, P.G. and Bench, G. (2000) A quantitative minimally invasive assay for the detection of metals in the stratum corneum. *Journal of Pharmaceutical and Biomedical Analysis*. 22:265-279.

Davis, J.E. (1980) Minimizing occupational exposure to pesticides: Personnel monitoring. *Residue Reviews*. 75:33-50.

Davis, J.E., Stevens, E.R. and Staiff, D.C. (1983) Potential exposure of apple thinners to azinphosmethyl and comparison of two methods for assessment of hand exposure. *Bulletin of Environmental Contamination and Toxicology*. 31:631-638.

Devillers, J., Domine, D., Bintein, S. and Karcher, W. (1997) Occupational exposure modelling with EASE. *SAR and QSAR in Environmental Research*. 6:121-134.

Diepgen, T.L. and Coenraads, P.J. (1999) The epidemiology of occupational contact dermatitis. *International Archives of Occupational and Environmental Health.* 72:496-506.

Dosemeci, M., Alavanja, M.C., Rowland, A.S., Mage D., Hoar Sham, S., Rothman, N., Lubin, J.H., Hoppin, J.A., Sandler, D.P. and Blair, A. (2002) A quantitative approach for estimating exposure to pesticides in the Agricultural Health Study. *Annals of Occupational Hygiene*. 46:245-260.

Dost, A.A. (1995) A European meeting held to discuss dermal exposure monitoring and related issues, Brussels, Belgium, 21-23 June 1994. *Annals of Occupational Hygiene.* 39:241-255.

EC (1967) *Commission Directive 93/67/EEC on risk assessment for new notified substances.* European Commission, Brussels.

EC (1991) *European Community Council Directive 91/414/EEC concerning the placing of plant protection products on the market*. European Commission, Brussels.

EC (1994) *Commission Regulation (EC) No 1488/94 on risk assessment for existing substances.* European Commission, Brussels.

EC (1998a) *Council Directive 98/24/EC on the protection of the health and safety of workers exposed to chemical agents at work*. European Commission, Brussels.

EC (1998b) *Directive 98/8/EC of the European Parliament and the Council concerning the placing of biocidal products on the market*. European Commission, Brussels.

EC (2002) *Human exposure to biocidal products – Guidance on exposure estimation. Technical notes for guidance*. B4-3040/2000/291079/MAR/E2, European Commission, DG Environment, Brussels.

EUROPOEM I (1996) *The development, maintenance and dissemination of a European Predictive Operator Exposure Model (EUROPOEM) database*. *A EUROPOEM I database and harmonised model.* AIR3 CT93-1370, TNO-BIBRA International, Carshalton.

EUROPOEM II (2003) *The development, maintenance and dissemination of a European Predictive Operator Exposure Model (EUROPOEM II) database.* A EUROPOEM II Database and Harmonised Model, FAIR3-CT96-1406, TNO-BIBRA International, Carshalton.

EXPOLIS (1999) *Air Pollution Exposure Distributions of Adult Urban Populations*. ENV4-CT96-0202 and ERB IC20-CT96-0061, Final Report. Publications of the National Public Health Institute, B16, Kuopio, 127 p. + app.

Fenske, R.A. (1988a) Correlation of fluorescent tracer measurements of dermal exposure and urinary metabolite excretion during occupational exposure to malathion. *American Industrial Hygiene Association Journal*. 49:438-444.

Fenske, R.A. (1988b) Comparative assessment of protective clothing performance by measurement of dermal exposure during pesticide applications. *Applied Industrial Hygiene*. 3:207-213.

Fenske, R.A. (1990) Nonuniform dermal deposition patterns during occupational exposure to pesticides. *Archives of Environmental Contamination and Toxicology*. 19:332-337.

Fenske, R.A. (1993) Dermal exposure assessment techniques. *Annals of Occupational Hygiene.* 37:687-706.

Fenske, R.A. (2000) Dermal exposure: a decade of real progress. *Annals of Occupational Hygiene.* 44:489-491.

Fenske, R.A. and Birnbaum, S.G. (1997) Second generation video imaging technique for assessing dermal exposure (VITAE System). *American Industrial Hygiene Association Journal.* 58:636-645.

Fenske, R.A., Birnbaum, S.G., Methner, M.M., Lu, C. and Nigg, H.N. (2002) Fluorescent tracer evaluation of chemical protective clothing during pesticide applications in Central Florida citrus groves. *Journal of Agricultural Safety and Health*. 8:319-331.

Fenske, R.A., Birnbaum, S.G., Methner, M.M. and Soto, R. (1989) Methods for assessing fieldworker hand exposure to pesticides during peach harvesting. *Bulletin of Environmental Contamination and Toxicology*. 43:805-815.

Fenske, R.A., Horstman, S.W. and Bentley, R.K. (1987) Assessment of dermal exposure to chlorophenols in timber mills. *Applied Industrial Hygiene*. 2:143-147.

Fenske, R.A., Leffingwell, J.T. and Spear, R.C. (1986a) A video imaging technique for assessing dermal exposure I. Instrument design and testing. *American Industrial Hygiene Association Journal.* 47:764-770.

Fenske, R.A. and Lu, C. (1994) Determination of handwash removal efficiency: Incomplete removal of the pesticide chlorpyrifos from skin by standard handwash techniques. *American Industrial Hygiene Association Journal.* 55:425-432.

Fenske, R.A., Simcox, N.J., Camp, J.E. and Hines, C.J. (1999) Comparison of three methods for assessment of hand exposure to azinphos-methyl (Guthion) during apple thinning. *Applied Occupational and Environmental Hygiene.* 14:618-623.

Fenske, R.A., Wong, S.M., Leffingwell, J.T. and Spear, R.C. (1986b) A video imaging technique for assessing dermal exposure II. Fluorescent tracer testing. *American Industrial Hygiene Association Journal.* 47:771-775.

Fiserova-Bergerova, V. (1993) Relevance of occupational skin exposure. *Annals of Occupational Hygiene.* 37:673-685.

Fiserova-Bergerova, V., Pierce, J.T. and Droz P.O. (1990) Dermal absorption potential of industrial chemicals: Criteria for skin notation. *American Journal of Industrial Medicine.* 17:617-635.

Gaborek, B.J., Mullikin, J.M., Pitrat, T., Cummings, L. and May, L.M. (2001) Pentagon surface wipe sampling health risk assessment. *Toxicology and Industrial Health*. 17:254-261.

Garrod, A.N.I., Martinex, M., Pearson, J., Proud, A. and Rimmer, D.A. (1999) Exposure to preservatives used in the industrial pre-treatment of timber. *Annals of Occupational Hygiene.* 43:543-555.

Geno, P.W., Camann, D.E., Harding, H.J., Villalobos, K. and Lewis, R.G. (1996) Handwipe sampling and analysis procedure for the measurement of dermal contact with pesticides. *Archives of Environmental Contamination and Toxicology*. 30:132-138.

Grandjean, P. (1990) *Skin penetration – Hazardous chemicals at work*. Taylor and Francis, pp. 4-6, London.

Hebisch, R. and Auffarth, J. (2001) Dermal exposure: How to get information? *Applied Occupational and Environmental Hygiene*. 16:169-173.

van Hemmen, J.J. (1992a) Agricultural pesticide exposure data-bases for risk assessment. *Reviews of Environmental Contamination and Toxicology*. 126:1-85.

van Hemmen, J.J. (1992b) Estimating worker exposure for pesticide registration. *Reviews of Environmental Contamination and Toxicology*. 128:43-54.

van Hemmen, J.J. (1993) Predictive exposure modelling for pesticide registration purposes. *Annals of Occupational Hygiene*. 37:541-564.

van Hemmen, J.J. (1998) Pesticide worker exposure assessment for registration purposes. *Occupational Hygiene*. 4:243-257.

van Hemmen, J.J. (2001) EUROPOEM, a predictive occupational exposure database for registration purposes of pesticides. *Applied Occupational and Environmental Hygiene*. 16:246-250.

van Hemmen, J.J. and Brouwer, D.H. (1995) Assessment of dermal exposure to chemicals. *Science of Total Environment*. 168:131-141.

van Hemmen, J.J., van Goldstein Brouwers, Y.G.C. and Brouwer, D.H. (1995) Pesticide exposure and re-entry in agriculture. In: Curry et al. (Eds) *Methods of Pesticide Exposure Assessment*. Plenum Press, New York. pp. 9-19.

HSE (2003) *Development of a method to assess biologically relevant dermal exposure*. Research report 117 prepared by the Institute of Occupational Medicine for the Health and Safety Executive. Health and Safety Executive, Sudbury, Suffolk, 51 p.

Hughson, G.W. and Cherrie, J.W. (2000) *External validation test of EASE for Windows version 2.* Contract research report 3846/R51.172. Institute of Occupational Medicine, Edinburgh, 32 p.

Hughson, G.W. and Cherrie, J.W. (2001) Validation of the EASE expert system for dermal exposure to zinc. X2001 - Exposure assessment in epidemiology and practice, Gothenburg, June 10-13, 2001, *Arbete och Hälsa*.10:17-19.

Iwata, Y., Spear, R.C., Knaak, J.B. and Forster, R.J. (1977) Worker re-entry into pesticide treated crops. I. Procedure for the determination of dislodgeable pesticide residues on foliage. *Bulletin of Environmental Contamination and Toxicology*. 18:648-655.

JMP (1986) *Estimation of exposure and absorption of pesticides by spray operators*, SC 8001. Joint Medical Panel of the scientific subcommittee on pesticides (MAFF) and British Agrochemicals Association, Ministry of Agriculture, Fisheries and Food, Harpenden.

Jolanki, R., Savela, A., Estlander, T. and Kanerva, L. (1998) Ammatti-ihotautien aiheuttajat Suomessa vuosina 1990-96. *Suomen Lääkärilehti*. 53:409-415. (in Finnish).

Jones, K., Cocker, J., Dodd, L.J. and Fraser, I. (2003) Factors affecting the extent of dermal absorption of solvent vapours: A human volunteer study. *Annals of Occupational Hygiene*. 47:145-150.

Kallunki, H., Mäkinen, M., Ojanen, K., Laitinen, S. and Kangas. J. (2003) Chemical and biological exposure in forestry harvesting. *Scandinavian Journal of Forestry Research*. (in press).

Kangas, J., Laitinen, S., Jauhiainen, A. and Savolainen, K. (1993) Exposure to sprayers and plant handlers to mevinphos in Finnish greenhouses. *American Industrial Hygiene Association Journal*. 54:150-157.

Kangas, J. and Sihvonen, S. (1996) *Comparison of predictive models for pesticide operator exposure*. TemaNord 560. Nordic Council of Ministers, Copenhagen, 48 p.

Kimber, I., Gerberick, G.F. and Basketter, D. (1999) Thresholds in contact sensitization: Theoretical and practical considerations. *Food and Chemical Toxicology*. 37:553-560.

Krieger, R.I., Ross, J.H. and Thongsinthusak, T. (1992) Assessing human exposure to pesticides. *Reviews of Environmental Contamination and Toxicology*. 128:1-15.

Kromhout, H., Hoek, F., Uitterhoeve, R., Huijbers, R., Overmars, R.F., Anzion, R. and Vermeulen, R. (2000) Postulating a dermal pathway for exposure to antineoplastic drugs among hospital workers. Applying the conceptual model to the results of three workplace surveys. *Annals of Occupational Hygiene.* 44:551-560.

Kromhout, H. and Vermeulen, R. (2001) Temporal, personal and spatial variability in dermal exposure. *Annals of Occupational Hygiene.* 45:257-273.

Leung, H.-W. and Paustenbach, D.J. (1994) Techniques for estimating the percutaneous absorption of chemicals due to occupational and environmental exposure. *Applied Occupational and Environmental Hygiene*. 9:187-197.

Limasset, J.C., Simon, P., Poirot, P., Subra, I. and Grzebyk, M. (1999) Estimation of the percutaneous absorption of styrene in an industrial situation. *International Archives of Occupational and Environmental Health*. 72:46-51.

Llewellyn, D.M. (2001) Exposure modelling – The EASE approach. X2001 - Exposure assessment in epidemiology and practice, Gothenburg, June 10-13, 2001, *Arbete och Hälsa*.10:466.

Lumens, M.E.G.L., Ulenbelt, P., Géron, H.M.A. and Herber, R.F.M. (1993) Hygienic behaviour in chromium plating industries. *International Archives of Occupational and Environmental Health*. 64:509-514.

Lundehn, J.-R., Westphal, D., Kieczka, H., Krebs, B., Löcher-Bolz, S., Maasfeld, W. and Pick, E.D. (1992) *Uniform principles for safeguarding the health of applicators of plant protection products*. Mitteillungen aus der Biologischen Bundesanstalt für Land- und Forstwirtschaft, Heft 127, Berlin.

Lushniak, B.D. (2003) The importance of occupational skin diseases in the United States. *International Archives of Occupational and Environmental Health*. 76:325-330.

Machera, K., Goumenou, M., Kapetanakis, E., Kalamarakis, A., and Glass, C.R. (2003) Determination of potential dermal and inhalational operator exposure to malathion in greenhouses with the whole body dosimetry method. *Annals of Occupational Hygiene*. 47:61-70.

Maidment, S.C. (1998) Occupational hygiene considerations in the development of a structured approach to select chemical control strategies. *The Annals of Occupational Hygiene*. 42:391-400.

Mäkinen, M., Hämäläinen, M., Forsman, K. and Liesivuori, J. (2002) Chemical exposure and risk assessment at workplaces – Modelling approach. *Applied Occupational and Environmental Hygiene*. 17:744-749.

Marquart, H., Maidment, S., McClaflin, J.L. and Fehrenbacher, M.C. (2001) Harmonization of future needs for dermal exposure assessment and modelling: A workshop report. *Applied Occupational and Environmental Hygiene.* 16:218-227.

Marquart, H., Brouwer, D.H. and van Hemmen, J.J. (2002) Removing pesticides from hands with simple washing procedure using soap and water. *Journal of Occupational and Environmental Medicine*. 44:1075-1082.

Marquart, J., Brouwer, D.H., Gijsbers, J.H.J., Links, I.H.M., Warren, N. and van Hemmen, J.J. (2003) Determinants of dermal exposure relevant for exposure modelling in regulatory risk assessment. *Annals of Occupational Hygiene*. (in press).

McArthur, B. (1992) Dermal measurement and wipe sampling methods: A review. *Applied Occupational and Environmental Hygiene.* 7:599-606.

McDougal, J.N. and Boeniger, M.F. (2002) Methods for assessing risks of dermal exposures in the workplace. *Critical Reviews in Toxicology*. 32:291-327.

Mulhausen, J.R. and Damiano, J. (1998) *A strategy for assessing and managing occupational exposures*. 2nd ed. American Industrial Hygiene Association, Exposure Assessment Strategies Committee, AIHA Press, Fairfax, 349 p.

Ness, S.A. (1994) *Surface and dermal monitoring for toxic exposures.* Van Nostrand Reinhold, New York.

Nethercott, J.R., Finley, B., Horowitz, S. and Paustenbach, D. (1994) Safe concentrations for dermal allergens in the environment. *New Jersey Medicine*. 91:694-697.

Nigg, H.N. and Stamper, J.H. (1985) Field studies: Methods overview. In: Honeycutt, R.C., Zweig, G. and Ragsdale, N.N. (eds.), *Dermal exposure related to pesticide use.* American Chemical Society, ACS Symposium Series 273, Washington D.C., pp. 95-108.

Nylander-French, L.A. (2000) A tape-stripping method for measuring dermal exposure to multifunctional acrylates. *Annals of Occupational Hygiene.* 44:645-651.

OECD (1997) *Guidance document for the conduct of occupational exposure to pesticides during agricultural application.* In OECD Environmental and safety publications. Series on testing and assessment no. 9 OECD/GD (97) 148. OECE, Paris.

Ojanen K., Vanne A., Mäkinen M. and Karjalainen P. (2001): A new sophisticated method to evaluate liquid contamination by using fluorescence tracer. X2001 - Exposure assessment in epidemiology and practice, Gothenburg, June 10-13, 2001, *Arbete och Hälsa*.10:25-26.

Oppl, R., Kalberlah, F., Evans, P. and van Hemmen, J.J. (2003) A toolkit for dermal risk assessment and management: an overview. *Annals of Occupational Hygiene*. (in press).

Packham, C. (2003) Letter to the editor. Comment to an article Dermal exposure assessment in occupational medicine by Sartorelli. *Occupational Medicine.* 53:69-71.

PHED (1992) *Pesticide Handlers Exposure Database*. version 1.1., U.S.EPA, Health and Welfare Canada, National Agricultural Chemicals Association, Versar Inc., Springfield.

Phillips, A.M. and Garrod, A.N.I. (2001) Assessment of dermal exposure - Empirical models and indicative distributions. *Applied Occupational and Environmental Hygiene*. 16:323-328.

Popendorf, W. (1992) Reentry field data and conclusions. *Reviews of Environmental Contamination and Toxicology*. 128:71-117.

Rajan-Sithamparanadarajah, R., Roff, M., Cobos, P.D., Eriksson, K., Fransman, W., Gjisbers, J.H.J, Hughson, G., Mäkinen, M. and van Hemmen J.J. (2003) The extent and patterns of dermal exposure to hazardous substances in the European Community workplaces. *Annals of Occupational Hygiene*. (accepted).

Rappaport, S.M. (1991) Assessment of long-term exposures to toxic substances in air. *Annals of Occupational Hygiene*. 35:61-121.

Rappaport, S.M., Kromhout, H. and Symanski, E. (1993) Variation of exposure between workers in homogeneous exposuere groups. *American Industrial Hygiene Association Journal*. 54:654-662.

RISKOFDERM (1999) *Risk assessment for occupational dermal exposure to chemicals.* Contract number QLK4-CT-1999-01107. 5th framework programme of the European Community, European Commission, Luxemburg.

RISKOFDERM (2003) *The extent and patterns of dermal exposure to hazardous substances in the European Community workplaces.* Deliverable 35, main study, draft final report of work part 2, version 2, 29 July. 42 p.

van Rooij, J.G.M., Maassen, L.M., Bodelier-Bade, M.M. and Jongeneelen, F.J. (1994). Determination of skin contamination with exposure pads among workers exposed to polycyclic aromatic hydrocarbons. *Applied Occupational and Environmental Hygiene.* 9:693-699.

Roff, M.W. (1994) A novel lighting system for the measurement of dermal exposure using a fluorescent dye and and image processor. *Annals of Occupational Hygiene.* 38:903-919.

Roff, M.W. (1997a) Dermal exposure of amateur or non-occupational users to wood-preservative fluids applied by brushing outdoors. *Annals of Occupational Hygiene*. 41:297-311.

Roff, M.W. (1997b) Accuracy and reproducibility of calibrations on the skin using the fives fluorescence monitor. *Annals of Occupational Hygiene.* 41:313-324.

Roff, M.W., Wheeler, J. and Baldwin, P. (2001) Comparison of fluorescence and rinsing methods for assessing dermal exposure. *Applied Occupational and Environmental Hygiene*. 16:319-322.

Ross, J.H., Driver, J.H., Cochran, R.C., Thongsinthusak, T. and Krieger, R. (2001) Could pesticide toxicology studies be more relevant to occupational risk assessment? *Annals of Occupational Hygiene*. 45:S5-S17.

Sartorelli, P. (2002) Dermal exposure assessment in occupational medicine. *Occupational Medicine*. 52:151-156.

Savolainen, K.M. and Kalliokoski, P. (2001) Physiological and toxicological considerations: Toxicity and risks indicated by occupational exposure to chemical compounds. In: Goodfellow, H. and Tähti, E. (Eds.) *Industrial Ventilation Design Guidebook.* Academic Press, San Diego. pp. 239-344.

Schneider, T., Cherrie, J.W., Vermeulen, R. and Kromhout, H. (2000) Dermal exposure assessment. *Annals of Occupational Hygiene.* 44:493-499.

Schneider, T., Vermeulen, R., Brouwer, D.H., Cherrie, J.W., Kromhout, H. and Fogh, C.L. (1999) Conceptual model for assessment of dermal exposure. *Occupational and Environmental Medicine*. 56:765-773.

Snedecor, G.W. and Cochran, W.G. (1976) One-way classifications. Analysis of variance. Structure of model II illustrated by sampling. In: *Statistical methods* (6th ed.) The Iowa State University Press, Ames, Iowa. pp. 282-284.

Soutar, A., Semple, S., Aitken, R.J. and Robertson, A. (2000) Use of patches and whole body sampling for the assessment of dermal exposure. *Annals of Occupational Hygiene.* 44:511-518.

STM (2002) *HTP-arvot 2002*. Ministry of Social Affairs and Health, Department for Occupational Safety and Health and Advisory Board of Occupational Safety of Chemicals, Tampere. (in Finnish).

Surakka, J., Johnsson, S., Rosén, G., Lindh, T. and Fischer, T. (1999) A method for measuring dermal exposure to multifunctional acrylates. *Journal of Environmental Monitoring.* 1:533-540.

Surakka, J., Lindh, T., Rosén, G. and Fischer, T. (2000) Workers' dermal exposure to UV-curable acrylates in the furniture and parquet industry. *Annals of Occupational Hygiene.* 44:635-644.

Tucker, S.P., Reynolds, J.M., Wickman, D.C., Hines, C.J. and Perkins, J.B. (2001) Development of sampling and analytical methods for concerted determination of commonly used chloroacetanilide, chlorotriazine, and 2,4-D herbicides in hand-wash, dermal-patch, and air samples. *Applied Occupational and Environmental Hygiene*. 16:698-707.

Tuomainen, A., Kangas, J. and Mäkinen, M. (2000) *Kasvihuonetyöntekijän ja ympäristön altistuminen torjunta-aineille*. Raportti Työsuojelurahastolle ja sosiaali- ja terveysministeriön työsuojeluosastolle. Kuopion aluetyöterveyslaitos, Kuopio. 21 p. + app. (In Finnish).

U.S.EPA (1989) *Exposure factors handbook*. Office of Health and Environmental Assessments, Exposure Assessment Group, U.S. Environmental Protection Agency (EPA 600/8-89-043), Washington, D.C.

U.S.EPA (1992) *Dermal exposure assessment: Principles and applications.* Office of Research and Development, U.S. Environmental Protection Agency (EPA/6000/8-91/011B), Washington D.C.

U.S.EPA (1996) *Occupational and residential exposure test guidelines – Background for application exposure monitoring test guidelines*. Office of Prevention, Pesticides and Toxic Substances, U.S. Environmental Protection Agency, OPPTS 875.1000 (EPA 712-C-96-261), Washington D.C.

U.S.EPA (2001) *Risk assessment guidance for Superfund: Vol. III – Part A, Process for conducting probabilistic risk assessment.* Office of Emergency and Remedial Response, U.S. Environmental Protection Agency (EPA/540-R-02-002), Washington D.C.

Vermeulen, R., de Hartog, J., Swuste, P. and Kromhout, H. (2000a) Trends in exposure to inhalable particulate and dermal contamination in the rubber manufacturing industry: Effectiveness of control measures implemented over a nine-year period. *Annals of Occupational Hygiene.* 44:343-354.

Vermeulen, R., Heideman, J., Bos, R.P. and Kromhout, H. (2000b) Identification of dermal exposure pathways in the rubber manufacturing industry. *Annals of Occupational Hygiene.* 44:533-541.

Vermeulen, R., Stewart, P. and Kromhout, H. (2002) Dermal exposure assessment in occupational epidemiologic research. *Scandinavian Journal of Work Environment and Health*. 28:371-385.

de Vreede, J.A.F, Brouwer, D.H., Stevenson, H. and van Hemmen, J.J. (1998) Exposure and risk estimation for pesticides in high-volume spraying. *Annals of Occupational Hygiene*. 42:151-157.

Vo-Dinh, T. (1987) Evaluation of an improved fiberoptics luminescence skin monitor with background corrections. *American Industrial Hygiene Association Journal.* 48:594-598.

Waldron, H.A. (1983) A brief history of scrotal cancer. *British Journal of Industrial Medicine.* 40:390-401.

Wass, U. and Wahlberg, J.E. (1991) Chromated steel and contact allergy. Recommendation concerning a "threshold limit value" for the release of hexavalent chromium. *Contact Dermatitis*. 24:114-118.

van-Wendel-de-Joode, B., Brouwer, D.H., Vermeulen, R., van Hemmen, J.J., Heederik, D. and Kromhout, H. (2003) DREAM: A method for semi-quantitative dermal exposure assessment. *Annals of Occupational Hygiene*. 47:71-87.

Wheeler, J.P. and Stancliffe, J.D. (1998) Comparison of methods for monitoring solid particulate surface contamination in the workplace. *Annals of Occupational Hygiene.* 42:477-488.

Wheeler, J.P. and Warren, N.D. (2002) A dirilecht tessellation-based sampling scheme for measuring whole-body exposure. *Annals of Occupational Hygiene*. 46:209-217.

WHO (1986) 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.* 33:223-235.

Woollen, B.H. (1993) Biological monitoring for pesticide absorption. *Annals of Occupational Hygiene*. 37:525-540.

Worksafe Australia (1995) *The assessment of respiratory and dermal exposure to pesticides: A review of current practice*. Prepared by Findlay, A. Australian Government Publishing Service, Canberra.

Zartarian, V.G., Özkaynak, H., Burke, J.M., Zufall, M.J., Rigas, M.L. and Furtaw Jr., E.J. (2000) A modeling framework for estimating children's residential exposure and dose to chlorpyrifos via dermal residue contact and nondietary ingestion. *Environmental Health Perspectives*. 108:505-514.

Zweig, G., Leffingwell, J.T. and Popendorf, W.J. (1985) The relationship between dermal pesticide exposure by fruit harvesters and dislodgeable foliar residues. *Journal of Environmental Science and Health*. Part B. 20:27-59.