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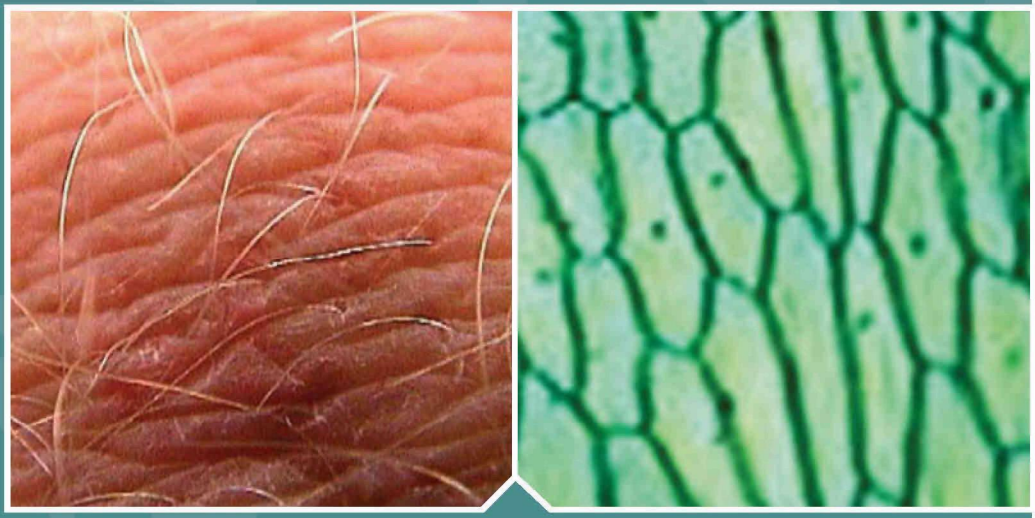
United States Environmental Protection Agency

Dermal Exposure Assessment: A Summary of EPA Approaches



National Center for Environmental Assessment
Office of Research and Development, Washington, DC 20460

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September 2007

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CONTENTS

LIST OF TABLES iv
LIST OF ABBREVIATIONS AND ACRONYMS v
PREFACE ix
AUTHORS, CONTRIBUTORS, AND REVIEWERS xii

1. INTRODUCTION 1
   1.1. PURPOSE 1
   1.2. DERMAL EXPOSURE CONSIDERATIONS 2
   1.3. DERMAL ABSORPTION CONSIDERATIONS 3
      1.3.1. In Vivo Dermal Absorption Methods 4
      1.3.2. In Vitro Dermal Absorption Methods 5
      1.3.3. In Vivo/In Vitro Dermal Absorption Method Comparisons 6

2. U.S. EPA APPROACHES TO DERMAL EXPOSURE ASSESSMENT 7
   2.1. OFFICE OF PREVENTION, PESTICIDES, AND TOXIC SUBSTANCES (OPPTS) 7
      2.1.1. Office of Pollution Prevention and Toxics (OPPT) 7
      2.1.2. Office of Pesticide Programs (OPP) 10
   2.2. OFFICE OF SOLID WASTE AND EMERGENCY RESPONSE (OSWER) 18
   2.3. OFFICE OF WATER (OW) 21
   2.4. OFFICE OF RESEARCH AND DEVELOPMENT (ORD) 22

3. DERMAL EXPOSURE ASSESSMENT COMPARISONS 24
   3.1. TARGET POPULATIONS, EXPOSURE MEDIA AND EXPOSURE PARAMETERS FOR DERMAL EXPOSURE ASSESSMENTS 24
      3.1.1. Target Populations 24
      3.1.2. Exposure Media 31
      3.1.3. Assumed and Default Parameters for Exposure Assessment 33
   3.2. METHODOLOGY COMPARISON 33
      3.2.1. Skin Loading Adherence Factors 33
      3.2.2. Selection of a Permeability Coefficient 34
      3.2.3. Selection of a Transfer Coefficient 35
   3.3. DERMAL EXPOSURE ASSESSMENT METHODOLOGY FOR VARIOUS MEDIA 35

4. DERMAL EXPOSURE ASSESSMENT TRENDS AND RESEARCH NEEDS 37
   4.1. WATER 37
   4.2. SOIL 38
   4.3. TREATED SURFACES 38

5. CONCLUSIONS 40

REFERENCES 42

LIST OF TABLES

1. Target populations and assumed characteristics for dermal exposure assessment 25

2. Exposure media considered for dermal exposure assessment 27

3. Assumed and default exposure parameters for target populations for dermal exposure assessment 28

4. Dermal exposure assessment methodology for chemical contaminants in air 32

5. Dermal exposure assessment methodology for chemical contaminants in water..... 32

6. Dermal exposure assessment methodology for chemical contaminates in soil 35

7. Dermal exposure assessment methodology for treated surfaces..... 36

8. Dermal exposure assessment methodology for occupational sources 36

LIST OF ABBREVIATIONS AND ACRONYMS

General

ai	active ingredient
CHAD	Consolidated Human Activity Database
ChemSTEER	Chemical Screening Tool for Exposures and Environmental Releases
DEA	Dermal Exposure Assessment
EAG	Exposure Assessment Group
EFAST	Exposure, Fate Assessment Screening Tool
EFH	Exposure Factors Handbook
EPA	Environmental Protection Agency
ERDEM	Exposure Reconstruction and Dose Estimation Model
HEDS	Human Exposure Database System
MCL	Maximum contaminant level
MCLG	Maximum contaminant level goal
NCEA	National Center for Environmental Assessment
NERL	National Exposure Research Laboratory
NHEERL	National Health and Environmental Effects Research Laboratory
OPP	Office of Pesticide Programs
OPPT	Office of Pollution Prevention and Toxics
OPPTS	Office of Pollution Prevention and Toxic Substances
ORD	Office of Research and Development
OSRTI	Office of Superfund Remediation and Technology Innovation
OSWER	Office of Solid Waste and Emergency Response
OW	Office of Water
PBPK	Physiologically based pharmacokinetic
PCB	Polychlorinated biphenyls
PHED	Pesticide Handlers Exposure Database
PIRAT	Pesticide Inert Risk Assessment Tool
PPS	Percutaneous Penetration Subgroup
QSAR	Quantitative structure-activity relationship
RAF	Risk Assessment Forum
RAGS	Risk Assessment Guidance for Superfund
RAGS E	Risk Assessment Guidance for Superfund, Part E
SHEDS	Stochastic Human Exposure and Dose Simulation
SOP	Standard Operating Procedure
WTC	World Trade Center

LIST OF ABBREVIATIONS AND ACRONYMS (continued)

OPPTS: ChemSTEER

ADD	Average [potential] daily dose	(mg/kg-d)
APDR	Acute potential dose rate	(mg/kg-d)
AT	Work-life averaging time	(yr)
Atc	Lifetime averaging time for chronic exposure	(yr)
BW	Body weight	(kg)
D_{exp}	Dermal potential dose rate	(mg/d)
ED	Days exposed per year	(d/site-yr)
EY	Years of occupational exposure	(yr)
FT	Event frequency	(events/site-d)
LADD	Lifetime average [potential] daily dose	(mg/kg-d)
Qu	Quantity remaining on skin [surface loading per event]	(mg/cm^2-event)
S	Skin surface area	(cm^2)
Y_{derm}	Weight fraction of chemical in liquid	

OPPTS: EFAST

ADD	Average daily potential dose	(mg/kg-d)
ADR	Acute potential dose rate	(mg/kg-d)
AT	Averaging time	(yr for ADD and LADD, d for ADR)
CEM	Consumer exposure model	
Dose	Daily potential dose	(mg/kg-d)
FQ	Frequency	(events/yr)
LADD	Lifetime average daily potential dose	(mg/kg-d)
K_p	Skin permeability coefficient	(cm/h)
K_{ow}	Octanol/water partition coefficient	
MW	Molecular weight	(g/mol)
SA/BW	Surface area/body weight	(cm^2/kg)
Q	Amount retained on the skin [surface loading per event]	(g/cm^2-event)
WF	Weight fraction of product	
Y	Years of use	(yr)

LIST OF ABBREVIATIONS AND ACRONYMS (continued)

OPP

A	Maximum area treated	(acre/d or gal/d)
ADR	Absorbed Dose Rate	
AR	Maximum application rate	(lb ai/acre, lb ai/ft^2, or lb ai/gal)
AT	Averaging time (yr)	
CF, CF#	Conversion factors, e.g., "CF1 = (0.001 mg/µg)"	
C_w	Concentration of ai in the water	(mg/L)
D	Fraction of residue that dissipates daily , OR	
D	[Potential] Dose	(mg/kg-d)
DFR_t	Dislodgeable residue on day t	(µg/cm^2)
ED	Exposure duration	(yr)
EF	Exposure frequency	(d/yr)
ET	Exposure time	(h/d)
F	Fraction of ai retained on surface	
FR	Flux rate for the product of concern	(mg/m^2/d)
ISRt	Indoor surface residue on day t	(µg/cm^2)
LADD	Lifetime average [potential] daily dose	(mg/kg-d)
ñ	Specific gravity of paint	(g/mL)
N	Number of cans applied	(cans/d)
P	Percent by weight of ai in paint	
PDR	Potential dose rate	(mg/d)
PDR_t	Potential dose rate on day t	(mg/d)
SA	[Skin] surface area	(cm^2)
t	Post-application day when exposure is assessed	
T	Fraction of residue transferred to skin	
Tc	Transfer coefficient	(cm^2/h)
UE	Unit exposure	(mg/lb ai)
V	Maximum volume treated	(gal/d)

OPPT: PIRAT

A	area treated or amount used	(ft^2/d; gal/d)
ABS	absorption value	(%)
AR	application rate	(lb/ft^2; gal/d; lb/gal; mg/d)

LIST OF ABBREVIATIONS AND ACRONYMS (continued)

BW	body weight	(kg)
PDR	potential dose rate [dose]	(mg/kg/d)
UE	PHED Dermal Unit Exposure	(mg/lb)
WF	weight fraction	

OSWER: Superfund

ABS_d	Dermal-soil absorption value	
AF	Soil adherence factor	(mg/cm^2)
AT	Averaging time	(yr or d)
BW	Body weight	(kg)
CF	Conversion factor	
C_{soil}	Concentration in soil	
C_w	Concentration in water	
DA_{event}	Absorbed dose per event	(mg/cm^2-event)
DAD	Dermal absorbed dose	(mg/kg-d)
ED	Exposure duration	(yr)
EF	Exposure frequency	(d/yr)
EV	Event frequency	(events/d)
FA	Net fraction available in *stratum corneum* for absorption after exposure has ended	
K_{ow}	Octanol-water partition coefficient	
K_p	Permeation [permeability?] coefficient	(cm/h)
RME	Reasonable maximum exposure	(mg/kg-d)
SA	[Skin] Surface area	(cm^2)
$t_{event\text{-}RME}$	Event duration	(hr)

PREFACE

Dermal exposure can be an important pathway in environmental health risk assessments. Exposure can occur from working or playing in contaminated water, soil, or sediment or from contact with treated or contaminated surfaces indoors or outdoors. Not surprisingly there are numerous activities and events where dermal exposure can occur and a number of methods and models have been developed to estimate this route of exposure.

Agency programs evaluate intentional and incidental dermal exposure for the general public and in some cases for workers based on various regulatory mandates and activities. The Office of Pesticide Programs (OPP) considers dermal exposure for pesticide application to pesticide workers and to consumers. The Office of Pollution Prevention and Toxics (OPPT) considers dermal exposure for consumer products containing high volume use chemicals and to chemical production workers for production of new chemicals. The Office of Water (OW) assesses dermal exposure to organic compounds during bathing, and the Office of Solid Waste and Emergency Response (OSWER) deals with dermal exposure to workers for hazardous waste site cleanup and to residents for incidental contact with chemically contaminated water, soil, and sediment from these sites.

The National Center for Environmental Assessment (NCEA) conducts research to improve exposure and risk assessment methods, models, and guidance. Dermal exposure projects are being conducted for identification of the chemical and physical properties of soil that affect chemical movement from soil to skin, development of mechanistic models for dermal penetration of contaminants in water and soil, and evaluation of in vitro dermal absorption test methods, in particular those for analysis of highly lipophilic compounds. This research is conducted in close cooperation with Agency program office staff to ensue it is designed to meet Agency needs and is conducted in close collaboration with other researchers throughout the world to benefit from their viewpoints and expertise.

This report was produced as a result of an internal dialogue among a group of exposure assessors from different Agency programs. When OPPT began an update of its Chemical Screening Tool for Exposures and Environmental Releases and Consumer Exposure Models in 2003, the staff looked outward for comments on their standard operating procedures, approaches, and assumptions. They convened meetings with various experts on dermal exposure assessment from around the Agency to discuss recent advances and the current state of dermal exposure assessment practice. These experts recognized there would be a benefit to describe the different approaches used to conduct dermal exposure assessment in the Agency. The result would increase awareness and understanding of alternate approaches to estimate dermal penetration and identify areas where approaches might be harmonized to exchange information and to share methods and data to improve the transparency of dermal exposure assessment in the Agency.

To achieve this, an ad hoc group of scientists formed to initiate this effort. They identified other Agency experts and offices where dermal exposure assessment is practiced. They eventually brought their effort to the attention of the Risk Assessment Forum (RAF) and suggested the effort be conducted as a RAF project because of its Agency-wide scope and value. A committee was formed to explore the merits of the issue. Their efforts resulted in the RAF commissioning a report in 2004 documenting and comparing the approaches, assumptions, and methods used across the Agency for dermal exposure assessment. This report was used in turn to prime the dialogue at a RAF sponsored cross-Agency colloquium, the Colloquium on Dermal Exposure Methods Comparison in 2005, to identify common factors and differences of dermal exposure assessment methods, to identify opportunities for harmonization among different dermal exposure assessment methods, and to determine future research needs (U.S. EPA, 2005).

Coincidentally, the RAF report and colloquium coincided with NCEA research efforts to evaluate methods used to estimate permeability coefficients (K_p) and to assess the importance of dermal exposure to chemically contaminated water, soil, and sediment. K_p is a key ingredient in dermal exposure equations but estimates are subject to great variability due to different methods in use to generate them. Moreover, because many chemicals of interest to the Agency do not have a K_p reported in the literature, evaluation of dermal absorption methods and models to obtain K_p represented a major focus of the NCEA dermal research program. Likewise, because little is known about the mechanics of dermal absorption from contact with chemically contaminated soil, NCEA initiated studies to ascertain the physical and chemical characteristics of chemicals bound to soil particles and the influence of soil particles on dermal absorption.

The Agency's interest in harmonization of dermal exposure assessment methods is to improve the efficiency and transparency of dermal risk assessment. It is intended to reduce the burden of repeated testing, information and data collection; foster information exchange across the Agency; apply current science and provide complete documentation for Agency methods; and to stimulate research in areas where it is needed. Participants discussing harmonization at the Dermal Exposure Methods Comparison Colloquium in 2005 supported greater interaction among the different program offices at EPA and encouraged collaboration with external organizations such as the Agency for Toxic Substances and Disease Registry; the National Institute for Occupational Safety and Health; the European Union; and the World Health Organization, to promote data sharing and more effective utilization of existing databases.

However, as described in this report, harmonization of dermal exposure assessment procedures is difficult for several reasons. First, regulatory mandates necessitate that Agency programs focus on specific chemicals of interest in different media. Not surprisingly the physical and chemical characteristics of pesticide compounds, hazardous wastes, and water contaminants can be substantially different. Second, exposure scenarios considered by the Agency programs are substantially different due to the nature of the exposures that occur in the environment. For example chemical exposure associated with residential pesticide usage is

substantially different from contact with chemically contaminated soil migrating from a nearby hazardous waste site or dermal exposure to organic compounds in contaminated water during showering. Third, the procedures currently used to estimate surface contact and dermal absorption require different input variables that are not interchangeable. The net result is different approaches are being used in the Agency to estimate dermal exposure.

Despite these difficulties to harmonize dermal exposure assessment procedures, the intent of this report is to focus on dermal penetration methods and the issues the Agency faces in assessing dermal exposure. Accordingly this report is anticipated to serve as a useful reference for Agency exposure assessors to

(1) describe the current scope of dermal exposure assessment methods in the Agency;
(2) identify and enable sharing of common approaches, models, methods, and databases;
(3) identify areas where harmonization might proceed to foster efficiency and transparency;
(4) and identify areas where more research is needed to improve the precision and accuracy of dermal exposure assessments.

AUTHORS, CONTRIBUTORS, AND REVIEWERS

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1. INTRODUCTION

1.1. PURPOSE

This report provides brief summaries of the approaches to dermal exposure assessment to toxic chemicals used by the various offices of the U.S. Environmental Protection Agency (EPA). These include the component offices, the Office of Pesticide Programs (OPP) and the Office of Pollution Prevention and Toxics (OPPT) in the Office of Prevention, Pesticides, and Toxic Substances (OPPTS); the Office of Superfund Remediation and Technology Innovation (OSRTI) in the Office of Solid Waste and Emergency Response (OSWER); the Office of Water (OW); and the Office of Research and Development (ORD).

The approaches that are summarized here are extracted primarily from documents and electronically available information that constitute the published guidance and support documents for dermal exposure assessment from the U.S. EPA offices listed above. Information sources include the following among others:

- Dermal Exposure Assessment: Principles and Applications, Interim Report (U.S. EPA, 1992a)
- Standard Operating Procedures (SOPs) for Residential Exposure Assessments (U.S. EPA, 1997a)
- Summary Report for the Workshop on Issues Associated with Dermal Exposure and Uptake (U.S. EPA, 2000a)
- Risk Assessment Guidance for Superfund (RAGS), Vol I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment [RAGS E]), Final (U.S. EPA, 2004a)
- Guidelines for Exposure Assessment (U.S. EPA, 1992b)
- ChemSTEER – Chemical Screening Tool for Exposures and Environmental Releases (U.S. EPA, 2004b)
- EFAST – Exposure, Fate Assessment Screening Tool (U.S. EPA, 2007a)
- U.S. EPA Exposure Research Abstracts (U.S. EPA, 2004c)
- Pesticide Handlers Exposure Database (PHED) surrogate guide
- Office of Pesticides Programs 875 Guidance Document
- U.S. EPA Exposure Research Models (U.S. EPA, 2004d)
- Example Exposure Scenarios (U.S. EPA, 2003a)
- Informal discussions with several staff in the relevant EPA offices

This document does not include recommendations regarding the appropriate approaches to use nor does it address risk estimation. Some of the information sources above do address

risk, for example the Superfund guidance (U.S. EPA, 2004a). Available toxicity and other data useful in estimating risk based on these exposure assessments can be obtained from the following references and databases among others: Integrated Risk Information System (U.S. EPA, 2007b), Registry of Toxic Effects of Chemical Substances (NIOSH, 1997), PHED (2007), Agency for Toxic Substances and Disease Registry Toxicological Profiles (ATSDR, 2007), Toxicology Data Network (TOXNET, 2007).

1.2. DERMAL EXPOSURE CONSIDERATIONS

Classically exposure is described as the amount of an agent that contacts the outer boundary of the body. However, this definition of exposure is limited because the real interest in risk assessment is the amount of an agent that breeches the outer boundary of the body (dose) and is capable of being distributed to one or more organs to exert a toxic effect (target dose). For dermal exposure to occur, an individual must have contact with the chemical in a given medium. The amount of exposure will depend on the concentration of the chemical contacting a given area of skin—the dermal loading or skin adherence, the ability of the chemical to penetrate and pass through intact skin—the dermal dose, and the duration and frequency of contact in terms of the intervals of contact and the number of intervals per day, weeks, months or even a lifetime.

Correspondingly, in dermal exposure assessment, the contaminant concentration is the amount of chemical contaminant in the media, such as water or soil available for contact. The potential dermal dose is the amount of a chemical which could be deposited on the skin during a given activity. The absorbed dermal dose is the amount of a chemical that is absorbed into the body through the skin. The target dose is the amount of absorbed chemical that exerts a toxic effect at the site of contact or is distributed throughout the body to one or more target organs to exert a toxic effect. These features are reflected in the various measurement methods and models used in the Agency to estimate dermal exposure.

Individuals may be exposed to toxic chemicals in the workplace through contact with industrial and commercial chemicals, products or intermediates. They may also be exposed in non-occupational settings—their homes, schools, play areas, etc.—as they work or play, through contact with chemicals emitted into the environment from industrial sources or hazardous waste sites or contact with chemicals in consumer products. Exposure to toxic chemicals can occur through contact in any environmental medium. Dermal exposure is most likely to occur through contact with chemically contaminated surfaces, soil, sediment, liquids, and water. Exposure may also occur through the air pathway, for example, through aerosols from use of consumer products. In the workplace, the exposure media may contain industrial products and intermediates, chemical mixtures, or neat (pure) chemicals. Outside the workplace, dermal exposures are most likely to occur through contact with treated surfaces such as turf, chemically contaminated surfaces, soil, sediment, water, and consumer product usage.

The site of dermal exposure is directly related to the activity being performed at the time of exposure. Depending on the contaminated media and anatomical site of contact, the contaminants may be absorbed differently. Several factors can influence dermal exposure (Jackson, 1999; Kissel et al., 1996). These include:

- Reduction or increases in the chemical contact with skin due to clothing;
- Protective clothing and gloves and the amount of protection they offer;
- Individual differences in dermal exposure due to differing degrees of speed, care, and dexterity in performing work;
- Variance in the amount of material available for dermal absorption due to actions such as wiping the affected area with the hand;
- Variances in the penetrability of the skin in different areas of the body;
- Individual variability of skin penetrability due to age of the individual and skin condition; and
- The matrix (liquid, solid, vapor) of the chemical contaminant.

The amount of chemical coverage on the skin surface can influence the amount of dermal absorption. Chemical coverage of the skin surface may be incomplete where only part of the surface is covered or it may be complete where the entire skin surface is covered. In both cases only the amount of chemical in contact with the skin surface is available for absorption such that the capacity of the skin to absorb the chemical may be exceeded. This is particularly true for cases of chemically contaminated solids such as soil where the material can pile up on the skin. Likewise the transfer efficiency of a chemical from a contaminated surface or a liquid solution to the skin may be highly variable due to the nature and extent of the contact, chemical composition and its affinity for skin relative to the surface or media, or the deposition of chemical residue due to evaporation of the liquid. Additionally, actual exposures can be affected by both external and personal characteristics, for example temperature, humidity, the medium containing the contaminant, the presence of other pollutants or inert ingredients in the medium, variations in the amount of thickness of the exposed skin, or the degree of hydration of the skin.

1.3. DERMAL ABSORPTION CONSIDERATIONS

The skin is a highly complex organ that effectively performs a barrier function to protect the body from a variety of environmental insults. Its structure and function has been extensively described previously (Roberts and Walters, 1998). Passive diffusion is considered to be the main processes of dermal penetration of chemicals through the stratum corneum, the outermost layer of the skin. After a chemical has absorbed into the stratum corneum it can pass through it into the viable epidermis (the next skin layer) and then into the dermis where it can be transported

systemically by the dermal blood supply. Dermal penetration can be measured by in vivo or in vitro methods.

1.3.1. In Vivo Dermal Absorption Methods

In vivo techniques can be used to measure dermal penetration either directly or indirectly (Bunge and McDougal, 1999). In direct methods a chemical is measured in the blood or excreta, on strips of tape that progressively remove stratum corneum, or estimated by biological or pharmacological responses. In indirect techniques dermal absorption is inferred from the disappearance of the chemical from the skin surface. The following list describes several in vivo methods used to estimate dermal absorption (Wester and Maibach, 1999):

- Surface recovery. The amount of chemical remaining on the surface of the skin at the end of the exposure is measured (recovered dose). The absorbed dose is assumed to be the difference between the amount of chemical applied to the skin (applied dose) and the recovered dose.
- Surface disappearance. The disappearance of a compound from the surface of the skin is measured over time using the appropriate instrumentation. This method is limited because it does not measure the amount of the chemical that is absorbed into the skin.
- Measuring the total amount of chemical appearing in the excreta. The chemical (often radiolabeled) is applied to the skin and the total amount excreted in the feces and urine is compared to the amount of excreted following a parenteral administration. When determined by radioactivity, this method does not account for dermal or systemic metabolism because the amount of radioactivity includes both parent compound and metabolites.
- Measuring the total amount of chemical in the blood. This is measured by the ratio of the areas under the plasma concentration versus time curves following dermal and intravenous administration of the chemical. When radiolabeled chemicals are used, this method does not account for dermal or systemic metabolism because the radioactivity could include both parent compound and metabolites, unless combined with methods that separate parent and metabolite.
- Biological and pharmacological response. A biological assay is substituted for a chemical assay such that absorption is estimated by observing the magnitude of the biological response. This method is limited to compounds that elicit responses that can be measured easily.
- Tape stripping. This method determines the concentration of the chemical in the stratum corneum after a specified exposure time. The technique involves sequentially application of adhesive tape strips to the exposed site, after any remaining chemical on the skin surface is removed, until all of the stratum corneum is removed from the skin.

Direct in vivo testing methods are more complicated and time consuming. However, they can provide estimates of the total absorbed amount of chemical in the blood or tissue and the amount eliminated (Zendzian, 2000). For example, the in vivo protocol specified by OPP for

testing pesticides in the rat measures the amount of chemical in excreted material during the exposure and the amount in the carcass at the end of the exposure (Zendzian, 1994, 2000). In addition, the amount of chemical remaining in the washed skin from the exposed site is measured. Provided that the wash is 100% efficient, this amount combined with the amount in the carcass and the excreted material should be the total amount dermally absorbed. Indirect in vivo techniques have been used successfully but there are some drawbacks. These techniques can be used only for chemicals that are not volatile. However, pharmacokinetic modeling can be used to estimate absorption from blood, exhaled breath, or tissue concentrations (Bunge and McDougal, 1999). The tape stripping method can be used to determine the amount of chemical in the stratum corneum. Disadvantages of tape stripping method are: the stratum corneum must be stripped completely and rapidly and chemical analysis can be difficult because the amount of chemical recovered can be small.

1.3.2. In Vitro Dermal Absorption Methods

In vitro dermal absorption methods have appeal because they lack use of live animals, are less expensive than in vivo methods, can be used with skin from a variety of animal species (most notably human), and can be used to test toxic or corrosive chemicals without concern for ethical considerations. Two different types of in vitro techniques have been used to study dermal absorption, the infinite dose and finite dose technique (OECD, 2004; Sartorelli et al., 2000; Franz, 1973). The infinite dose technique is the most frequently utilized method. It involves mounting the skin as a barrier between two chambers of fluid. A large amount of chemical, usually in water or an aqueous solution is added on one side and absorption is quantified by measuring the concentration in a receptor solution on the other side as a function of time. Measurements are continued until steady state is achieved as indicated by the cumulative mass in the receiving chamber increasing as a proportion to time. The permeability coefficient is then calculated using the slope of the linear regression of the cumulative mass versus time (Bunge and McDougal, 1999). In the finite dose technique, skin is mounted in a diffusion cell and bathed from below by a receptor solution kept at a temperature of 37°C. The donor chamber contains a known amount of the chemical and the concentration of the penetrating chemical is measured in the receiving chamber to provide a measure of the cumulative amount that has penetrated a specified area of skin in a given exposure time (usually expressed as the percent absorbed per square centimeter of skin exposed). An advantage of the finite dose technique is that it allows for any type or amount of substance to be tested in conditions that mimic those encountered in vivo (Sartorelli et al., 2000).

One of the major factors affecting in vitro dermal penetration results is the choice of receptor fluid for collecting the chemical that penetrates the skin. Generally, it should provide sink conditions without altering the skin barrier function. The current OECD guidelines require that sink conditions be insured by proving adequate solubility in the receptor fluid (OECD,

2004). The receptor fluid should be chosen to maintain skin metabolic activity when fresh skin is used and the absorbing chemicals may be metabolized.

1.3.3. In Vivo/In Vitro Dermal Absorption Method Comparisons

Efforts to compare in vivo and in vitro dermal absorption methods have generated mixed results (Franz, 1975; Zendzian and Dellarco, 2003). In vitro methods may overestimate or underestimate in vivo measurements depending on the nature of the chemical, the skin preparation used, chemical vehicle used, experimental procedures followed and the data analysis procedures used. In vivo measurements for exposure times that are not long relative to the time to penetrate through the skin (lag time) will usually overestimate the steady-state permeability coefficient because in vivo dermal absorption is initially faster than at steady state. Bunge and McDougal (1999) concluded that this is consistent with the "widely stated observation that in vivo permeability coefficients are larger than those measured in vitro." However this observation may be due to a failure to account for the lag time in data analysis rather than reflect differences between in vitro and in vivo methods (Bunge and McDougal, 1999).

The Percutaneous Penetration Subgroup (PPS) of the Dermal Exposure Network published a report that focused on standardization and validation of in vitro experiments (Sartorelli et al., 2000). The objectives of the PPS were to analyze the guidelines on dermal penetration in vitro studies presented by various organizations and suggest standardized in vitro methods while taking into account their individual research experience, literature data and existing guidelines. Key issues and data gaps reported by the subgroup included:

- How to use dermal penetration data in risk assessment;
- Factors influencing the results from dermal penetration in vitro studies (i.e., the choice of the donor phase, cell characteristics, skin membranes present, and receptor fluids);
- Agreement on and validation of existing guidelines for conducting in vitro studies;
- Use of penetration data to predict plasma levels;
- Effects of cutaneous metabolism on dermal penetration;
- The selection of appropriate reference chemicals for in vitro study;
- Use of microdialysis in in vivo studies; and
- The correlation of in vitro and in vivo study results.

2. U.S. EPA APPROACHES TO DERMAL EXPOSURE ASSESSMENT

2.1. OFFICE OF PREVENTION, PESTICIDES, AND TOXIC SUBSTANCES (OPPTS)

Two offices in the Office of Prevention, Pesticides, and Toxic Substances (OPPTS) address dermal exposure issues: the Office of Pollution Prevention and Toxics (OPPT) in their regulatory and voluntary programs for new and existing industrial chemicals and consumer products and the Office of Pesticide Programs (OPP) in their regulation of new and existing pesticides. Dermal exposure in these areas is assessed using a variety of models and tools for specific situations.

2.1.1. Office of Pollution Prevention and Toxics (OPPT)

The OPPT makes available on-line two PC-based tools: ChemSTEER and EFAST. ChemSTEER is currently available in a Beta Version, which was released in late May 2004, and EFAST is available in Beta Version 1.1, which was released in March 2000. They are accessible on-line at http://www.epa.gov/oppt/exposure/.

ChemSTEER allows screening-level estimation of chemical releases from industrial and commercial sources and operations, and estimation of worker exposures through inhalation and dermal contact. These estimates are derived from user input parameters and default parameters based on industry data collected by EPA. The beta version includes 34 models, each with a set of default settings and values. Among the models for dermal exposures are one-hand liquid, two-hand liquid, and mass-balance dermal exposure models, as well as degree of "immersion" or contact. All models assume that no protective equipment is used. Four scenarios that address multiple sources and activities for specific industries are currently incorporated in ChemSTEER: exposure during adhesives formulation, during new and refinishing automobile spray-coating, and water additives in recirculating water-cooling towers.

The dermal models require selection of an operation: manufacturing, processing, or use; and an activity, such as loading containers. The specific model is chosen based on the activity. One can view the model equation, the input parameters, the source of the model, the mechanism of exposure, and the chemical state (for example liquid) of the subject chemical. Two daily potential dose rate estimates, such as for typical and high-end (worst-case) exposures, can be calculated and viewed simultaneously.

User input parameters can include chemical name, chemical category, trade name, Chemical Abstracts number, vapor pressure (torr), molecular weight (g/mol), density (g/cm^3), water solubility (g/L), production and use volumes, weight fractions and physical states. In addition, inputs can include numbers of sites, working days, and workers; release sources and worker activities; workplace concentrations and release amounts and media; and types and sizes of containers used to transport the chemical or mixture. Default parameters are incorporated in the program for use if input data are not available. Some parameters cannot be changed. For

example, in the two-hand liquid loading model, the skin surface area S is set at 840 cm^2, and the quantity Qu remaining on the skin is set at either 0.7 or 2.1 mg/cm^2. Other parameters such as body weight, weight fraction of active ingredient, exposure duration can be changed. Similarly, for the two-hand solid loading model or for direct contact with solids, the quantity S times Qu is set at 3,100 mg/event, although other parameters in the model can be changed. The model assumes that the quantity remaining on the skin or surface loading per event is not affected by wiping off the excess, nor do additional contacts increase the quantity significantly.

An example of ChemSTEER estimates for the operation "adhesives formulation" and the activity "loading liquid into drums" is: default weight-fraction of active ingredient (ai) is 0.33, work-life averaging time is 40 yr (lifetime is 70 yr), skin surface area is 840 cm^2 (for the two-hand model), and the body weight is 70 kg. In this example, the surface loading selected is 2.1 mg/cm^2, a high end estimate which is based on industrial data for this operation involving liquid handling. These parameters give a potential dose rate of 581 mg/d and an acute potential dose of 8.32 mg/kg-d.

In the ChemSTEER user-defined input model, dermal exposures for liquid or soil contact are calculated as the following:[1]

$$D_{exp} = S * Qu * Y_{derm} * FT$$

$$LADD = (D_{exp} * ED * EY) / (BW * Atc * 365)$$

$$ADD = (D_{exp} * ED * EY) / (BW * AT * 365)$$

$$APDR = (D_{exp} / BW) \quad (1)$$

where:

D_{exp}	=	dermal potential dose rate	(mg/d)
LADD	=	lifetime average [potential] daily dose	(mg/kg-d)
ADD	=	average [potential] daily dose	(mg/kg-d)
APDR	=	acute potential dose rate	(mg/kg-d)
S	=	skin surface area	(cm^2)
Qu	=	quantity remaining on skin [surface loading per event]	(mg/cm^2-event)
Y_{derm}	=	weight fraction of chemical	
FT	=	event frequency	(events/site-d)

[1] An asterisk (*) denotes multiplication throughout this document.

ED	=	days exposed per year	(d/site-yr)
EY	=	years of occupational exposure	(yr)
BW	=	body weight	(kg)
Atc	=	lifetime averaging time for chronic exposure	(yr)
AT	=	averaging time	(yr)

EFAST allows screening-level estimation of consumer exposures through inhalation and dermal contact, as well as estimation of industrial releases to air, landfills, and water. The outputs cover site-specific general population exposures to chemicals through ingestion of drinking water and fish, and estimates of ecosystem risks through contamination of surface waters. Human dermal exposures are estimated through selection from three pre-set consumer product-related scenarios: application of products to hard surfaces, such as paint during application; contact with chemicals added to water, such as detergents; and direct contact with products, such as motor oil. Consumer product scenarios include use of a general purpose cleaner, use of liquid laundry detergent, use of bar soap, and changing motor oil. User scenarios can also be entered in the program.

The EFAST Consumer Exposure Model (CEM) allows conservative estimates of potential and absorbed dermal dose to chemicals in some consumer products, as well as screening-level estimates of acute potential dose rates, and average and lifetime daily potential dose rates. A film-thickness approach is used, which assumes a thin film of product on a defined skin area to determine exposure, but the uncertainty is great, as there are few supporting data on film thicknesses on skin. Film thickness values in the CEM are derived from experimental data (Versar, 1992). For exposure to chemicals in water, such as washing clothes by hand, the film thickness is based on the initial film thickness of water on the hands after immersion in water; for washing the body and/or hands with bar soap, it is based on the initial film thickness of a bath oil/water mixture on the hands; and for changing motor oil, it is based on the thickness of a mineral oil film on the hands after immersion.

User inputs can include release information from the product to the environment, based on activity, site, media, amount, and frequency; physical and chemical properties of the pollutants of interest; and fate and transport properties. Users can also create their own scenarios if a product does not fit into one of the pre-defined scenarios. The default parameters are generally those provided in the EPA Exposure Factors Handbook (EFH; U.S. EPA, 1997b). For example, 50th percentile body weights are 71.8, 26.9, and 10.2 kg for an adult, a child, and an infant, respectively. Averaging times (AT) for non-carcinogenic chemical exposures are 30 yr for ambient and 57 yr for consumer product exposures of adults; for acute exposures of adults, children, and infants, the AT is one day. The averaging time for carcinogenic chemical exposures is 75 yr for all individuals. Because there is a direct relationship between an individual's weight and skin surface area, the EFAST dermal exposure model uses the surface

area/body weight ratio (SA/BW). Use of SA/BW may reduce bias that could occur if surface area distributions were combined with unrelated body weight, for example if one were to combine upper-percentile SA with lower-percentile BW. Distributions of SA/BW can be obtained from the EFH (U.S. EPA, 1997b, Table 6-9).

Three different dermal exposure calculations can be performed: a lifetime average daily potential dose (LADD), an average daily potential dose (ADD), and an acute potential dose rate (ADR). The form of the general equation used to calculate potential dose is:

$$\text{Dose} = (Q * SA/BW * FQ * Y * WF * 1000\ mg/g) / (AT * 365) \quad (2)$$

where:

Dose	=	daily potential dose	(mg/kg-d)
Q	=	amount retained on the skin [surface loading per event]	(g/cm^2-event)
SA/BW	=	surface area/body weight	(cm^2/kg)
FQ	=	frequency	(events/yr)
Y	=	years of use	(yr)
WF	=	weight fraction of product	
AT	=	averaging time	(yr)

Absorbed dermal dose rates can be calculated in user-defined scenarios, using a skin permeability coefficient K_p specific to the given chemical, which may be chosen from a list of common chemicals in the program, entered directly by the user, or calculated by the program from the octanol/water partition coefficient (K_{ow}). In the program, K_p is calculated from the following equation (U.S. EPA, 1992a):

$$\log K_p = 0.71 * \log K_{ow} - 0.0061 * MW - 2.72 \quad (3)$$

where:

K_p	=	permeability coefficient	(cm/h)
K_{ow}	=	octanol/water partition coefficient	
MW	=	molecular weight	(g/mol)

2.1.2. Office of Pesticide Programs (OPP)

The Office of Pesticide Programs uses several SOPs to estimate dermal exposures (U.S. EPA, 1997a). These SOPs cover both commercial and residential pesticide applications. Exposures resulting from direct contact with pesticides during application and contact with treated surfaces after application can be estimated for adults and children. Updates to the SOPs,

including information on exposure frequency, are being developed by OPP. The underlying assumptions and definitions are available on line (U.S. EPA, 2000b, c, 1997a, Appendix A). Occupational dermal exposure issues are addressed by the PHED surrogate table and guidance document policy 12. An evaluation of exposure assessment methods for agricultural pesticide workers was recently presented to the Scientific Advisory Panel (U.S. EPA, 2007c).

The residential SOPs rely on high-end scenarios that are assumed to represent the upper end of the distribution of exposures that could occur in residential settings. They have the flexibility to be used as a screening tool but can be refined based on the availability of chemical and scenario data and the interest of the user. They rely on one or more upper-percentile assumptions such as the 90th percentile skin surface area values or exposure durations. Each SOP includes a description of the exposure scenario, recommended methods for quantifying dose, example calculations, the limitations and uncertainties associated with the use of the SOP, and relevant references. Pesticide handler and post-application SOPs are provided for pesticide applications in several residential scenarios. Each provides methods for estimating short-term or acute daily doses for a single route of exposure (inhalation, ingestion, dermal absorption). Those that include dermal methods are scenarios for exposure during application and post-application contact to pesticides applied to lawns, gardens, trees, swimming pools, and pets; to paint and wood preservatives; and to rodenticides. Other SOPs address dermal exposures to pesticides during and after crack-and-crevice and broadcast applications; to pesticides in detergents and hand soap; and to pesticides in impregnated materials. Use of products according to label directions is assumed. Several SOPs rely on field monitoring data from the PHED, the Outdoor Residential Exposure Task Force, or other studies that are available, including studies in the scientific literature, to estimate handler exposures.

In all cases, the dermal potential dose rate is normalized to body weight by dividing the potential dose rate (PDR) by the body weight BW in kg to give the potential dose, with the body weight chosen to fit the specific population of individuals:

$$\text{Dose} = \text{PDR} / \text{BW} \qquad (\text{mg/kg-d}) \tag{4}$$

<u>Pesticide handler</u>: Daily potential dose rates are calculated using equations of the following form:

$$\text{PDR} = \text{UE} * \text{AR} * \text{A} \tag{5}$$

where:

UE	=	unit exposure	(mg/lb ai)
AR	=	maximum application rate	(lb ai/acre or lb ai/gal)
A	=	maximum area treated	(acre/d or gal/d)

This calculation gives the maximum potential dose rate.

Transfer of residues from treated surfaces: Dermal potential dose rates on post-application days are calculated as follows:

$$PDR_t = DFR_t * CF1 * Tc * ET \quad (6)$$

where:

PDR_t	=	potential dose rate on day t	(mg/d)
DFR_t	=	dislodgeable (transferable) residue on day t	($\mu g/cm^2$)
CF1	=	conversion factor	(0.001 mg/µg)
Tc	=	transfer coefficient	(cm^2/h)
ET	=	exposure time	(h/d)

and

$$DFR_t = AR * F * (1-D)^t * CF2 * CF3) \quad (7)$$

where:

AR	=	application rate (of active ingredient)	(lb ai/ft^2 or lb ai/acre)
F	=	fraction of ai retained on surface	
D	=	fraction of residue that dissipates daily	
t	=	post-application day	
CF2	=	conversion factor[2]	(4.58E8 µg/lb)
CF3	=	conversion factor	(1.08E-3 ft^2/cm^2 or 24.7E-9 acre/cm^2)

An appropriate dermal absorption factor can be used, if available, to estimate absorbed dose. Most of the SOPs (U.S. EPA, 1997a) assume that 50% of the application to treated surfaces is available initially as transferable residues on the day of application. It is important to note that in some cases such as turf, DFR is replaced by transferable residue which is determined

[2]The abbreviation E followed by a numeral denotes a power of 10, e.g., 4.58E8 is equivalent to 4.58 times 10^8.

from the Turf Transferable Residue method based on roller methods, foliar washes and other techniques (U.S. EPA, 1999).

Lifetime average daily dose: For exposures over a lifetime, which are relevant to cancer and other health effects that may result from chronic exposure, the lifetime average potential daily dose is calculated as follows:

$$LADD = (D * EF * ED) / (AT * CF) \quad (8)$$

where:

D	=	dose [potential daily dose][3]	(mg/kg-d)
EF	=	exposure frequency	(d/yr)
ED	=	exposure duration	(yr)
AT	=	averaging time	(yr)
CF	=	conversion factor	(365 d/yr)

Handler exposure to chemicals in treated water in swimming pools: The potential dose rate is calculated as:

$$PDR = UE * AR * V \quad (9)$$

where:

UE	=	unit exposure	(mg/lb ai)
AR	=	maximum application rate	(lb ai/gal)
V	=	maximum volume treated	(gal/d)

Swimming post-application of pesticides: The dermal absorbed dose rate from swimming in areas treated with pesticides post-application is calculated as:

$$ADR = C_w * SA * ET * K_p * CF1 \quad (10)$$

where:

ADR	=	absorbed dose rate	(mg/d)
C_w	=	concentration of ai in the water	(mg/L)
SA	=	skin surface area exposed	(cm^2)
ET	=	exposure time	(h/d)

[3]The symbol D in the residential SOP document (U.S. EPA, 1997a) is used both for the daily fractional dissipation of surface residue in estimating exposure to pesticides on surfaces and for the daily dose in estimating lifetime average daily dose.

K_p	=	skin permeability coefficient	(cm/h)
CF1	=	conversion factor	(L/1000 cm^3)

Applications of paint or stain in residential settings: Handler dermal potential doses from painting or staining in residential settings assume a single daily event and do not include exposure duration. Therefore these doses are based on the amount of active ingredient handled per day. Unit exposure values from PHED can be used. The calculation is of the form:

$$PDR = UE * AR * N \tag{11}$$

where:

UE	=	unit exposure	(mg/lb ai applied)
N	=	number of cans applied	(cans/d)

and

$$AR = V * ñ * (P/100) * CF1 \tag{12}$$

where:

AR	=	active ingredient applied per can	(lb ai/can)
V	=	paint volume per can	(mL/can)
ñ	=	specific gravity of paint	(g/mL)
P	=	percent by weight of ai in paint	
CF1	=	conversion factor	(2.2E-3 lb/g)

Crack-and-crevice or broadcast applications: Estimates of potential doses of pesticides during crack-and-crevice or broadcast applications rely on surrogate PHED data, and are calculated similarly to those for the paint/stain scenario. Post-application dermal doses of pesticides on carpets are estimated assuming: an average of 50% of the application is available as dislodgeable residue, chemical-specific daily dissipation rates, exposure duration 8 h/d, and dermal transfer coefficients of 43,000, 8,700, and 6,000 cm^2/h for adults, toddlers, and infants, respectively. Post-application dermal potential dose rates are calculated as follows:

$$PDR_t = ISR_t * CF1_t * Tc * ET \tag{13}$$

where:

PDR_t	=	potential dose rate on day t	(mg/d)
ISR_t	=	indoor surface residue on day t	(μg/cm^2)

CF1	=	conversion factor	(0.001 mg/μg)
Tc	=	transfer coefficient	(cm^2/h)
ET	=	exposure time	(h/d)

and

$$ISR_t = AR * F * (1-D)^t * CF2 * CF3 \quad (14)$$

where:

AR	=	application rate	(lb ai/ft^2)
F	=	fraction of ai retained on surface	
D	=	fraction of residue dissipated daily	
t	=	post-application day	
CF2	=	conversion factor	(4.54E8 μg/lb)
CF3	=	conversion factor	(1.08E-3 ft^2/cm^2)

For exposure to residues on hard surfaces, such as hard floors or counter tops, the same equations are used, but the exposure duration is assumed to be 4 h/d, rather than 8 h/d.

Applications of pesticides to pets: Dermal doses to individuals who treat pets with pesticides for vermin control are based on the amount of active ingredient handled per day and a single treatment per day, as for paint and stain applications. The default fraction of the active ingredient (F) available for exposure is 10%, except for flea collars, which it is 1%. Thus the potential dose rate is:

$$PDR = AR * F \quad (15)$$

where:

AR	=	application rate	(mg/d)
F	=	fraction of active ingredient available	(0.1 or 0.01)

Spray applications of pesticides to pets: The amount handled per treatment is assumed to be the maximum available on the label, or ½ can. Unit exposure values from PHED for typical aerosol applications of pesticides are used. The potential dose rate is calculated as:

$$PDR = UE * AR * N \quad (16)$$

where:

UE	=	unit exposure	(mg/lb ai)

N	=	number of cans used	(cans/d)

and

$$AR = V * ñ * P/100 * CF1 \quad (17)$$

where:

AR	=	active ingredient per can	(lb ai/can)
V	=	liquid volume of spray per can	(mL/can)
ñ	=	specific gravity of spray solution	(g/mL)
P	=	percent by weight of active ingredient	
CF1	=	conversion factor	(2.2E-3 lb/g)

Pesticide residues on pets: It is assumed that 20% of the application is retained on the pet as dislodgeable residue, 10% of the residue is transferred during contact with a treated animal, one animal is contacted per day, and that there is no dissipation of the residues on subsequent days. The dermal potential dose rate for liquid applications is

$$PDR = AR * F * T \quad (18)$$

where:

AR	=	active ingredient applied	(mg ai/d)
F	=	fraction of ai available	
T	=	fraction of residue transferred to skin	

Note that these SOPs provide a standard method for estimating potential doses that homeowners may receive during pet treatment from inhalation and dermal contact when chemical specific data are unavailable. This scenario assumes that pesticide exposure occurs while applying the pesticide to pets using aerosol spray products. The method to determine handler inhalation and dermal dose from pesticides while treating pets relies on using surrogate PHED data and does not apply to livestock. Thus, these methods are used when actual field data are not available or as a supplement to estimates based on field data.

Pesticides in soaps, detergents, and other consumer products: Handler and post-application exposure can be estimated with a screening model, DERMAL (U.S. EPA, 1995), which covers 16 types of consumer products, and can accommodate user inputs for other products. The model is said to calculate dermal exposure using the weight fraction of the chemical in the product, assumed film thicknesses on the skin, and assumed exposed skin area. Default values are used for the event frequency, exposure duration, and body weight. The EFAST Consumer Exposure Model, mentioned above, includes DERMAL.

Materials impregnated with pesticides: Exposures from contact with materials impregnated with pesticides, including paint and stain post-application on surfaces, are estimated based on the flux rate through the material of interest and the skin area that is likely to be contacted. An EPA guidance document allows estimation of the flux rate (U.S. EPA, 1992c). The skin surface area depends on the product, for example, 1 m^2 and 0.35 m^2 for plastic mattress contact of adults and toddlers, respectively. The duration of exposure is likewise dependent on the specific activity and material. The potential dose rate is calculated as:

$$PDR = FR * SA * ET * CF1 \quad (19)$$

where:

FR	=	flux rate for the product of concern	($mg/m^2/d$)
SA	=	skin surface area	(m^2)
ET	=	exposure time	(h/d)
CF1	=	conversion factor	(d/24 h)

An additional SOP covers the pesticide exposures of individuals in the post-application scenario of "pick-your-own" strawberries. It is assumed that 20% of the application is available, exposure time is 2 h, and dermal transfer coefficients are 10,000 cm^2/h for adults and 5,000 cm^2/h for youth ages 10 to 12. Potential dose rates are calculated similarly to those for contact with other treated surfaces.

The OPP has developed a tool that deals with the risk from the inert ingredients in pesticide products. A test version (V 1.0) of this screening tool, Pesticide Inert Risk Assessment Tool (PIRAT), is available on-line (U.S. EPA, 2007d). In PIRAT, one selects handler or post-application exposures, dermal or inhalation, formulation, duration, and carrier. One also selects the product use category and the application method. The weight fraction of product (inert ingredient) depends on the formulation selected. PHED unit exposure values are incorporated. Toxicity and absorption values can be entered if known. Post-application dermal exposures can be estimated for adults and toddlers (age 3 yr), assuming the fraction of skin area exposed is 0.05, the transfer coefficients are 14,500 cm^2/h for adults and 5,200 cm^2/h for toddlers, and the body weights are 70 kg for adults and 15 kg for toddlers. PIRAT provides screening-level estimates of exposure and risk associated with the use of pesticides in residential settings, both indoors and outdoors. Acute and chronic risk assessments for adults and children are to be provided separately.

The form of the equation for the potential dose rate[4] for handler exposure in PIRAT is given as

$$PDR = (UE * AR * WF * A * ABS) / BW \quad (20)$$

where:

PDR	=	potential dose rate	(mg/kg/d)
UE	=	PHED Dermal Unit Exposure	(mg/lb)
AR	=	application rate	(lb/ft^2; gal/d; lb/gal; mg/d)
WF	=	weight fraction	
A	=	area treated or amount used	(ft^2/d; gal/d)
ABS	=	percent absorption value	(%)
BW	=	body weight	(kg)

2.2. OFFICE OF SOLID WASTE AND EMERGENCY RESPONSE (OSWER)

Within OSWER, the Office of Superfund Remediation and Technology Innovation (OSRTI) has developed guidance to address dermal exposures to toxic chemicals that result from contact with either contaminated water or contaminated soil for both adults and children from hazardous waste sites (U.S. EPA, 2004a). It incorporates the ingredients of the Agency guidance document, Dermal Exposure Assessment: Principles and Applications (U.S. EPA, 1992a) and includes several dermal exposure equations, tables of screening values for exposure to contaminated water, absorption values for contaminants from soil, soil adherence factors, and parameters that are consistent with the U.S. EPA Exposure Factors Handbook (U.S. EPA, 1997b).

Recommended default exposure values are presented in RAGS E for the dermal-water and dermal-soil pathways. In general, to estimate exposure to an average individual, the 95% upper confidence limit on the arithmetic mean is chosen for the exposure point concentration, and central estimates, such as arithmetic mean, 50th percentile, etc., are chosen for all other exposure parameters. The reasonable maximum exposure (RME) values are the highest exposures that might reasonably be expected at a given site. Central tendency values can also be calculated.

For dermal exposure to contaminated water, only those chemicals that contribute more than 10% of the dose that may occur from water ingestion are considered sufficiently important to carry through a risk assessment (U.S. EPA, 2004a, Chapter 6). Predicted values of the skin permeability coefficient K_p (cm/h) are given for 19 metals and more than 200 organic pollutants.

[4]In PIRAT, PDR is defined as the potential dose rate. This differs from the definition of PDR in the equations discussed in other sections of this document, as it includes the body weight BW and therefore refers to the potential dose.

The K_p values are updated from those given in the DEA, but are limited to only those in vitro studies using human skin. K_p is estimated with an empirical correlation, which is a function of the octanol-water partition coefficient K_{ow} and molecular weight for about 90 chemicals, obtained from an experimental database on absorption of chemicals from water through human skin in vitro. These K_p values are then used in default scenarios to estimate exposures from contact with contaminated water. Dermal absorbed dose (DAD) values for several hundred chemicals through the water pathway, based on the default exposure scenarios, are provided.

The skin surface area used in calculating dermal-water exposures is based on EFH values and assumed to be the entire skin surface for swimming and bathing. In calculating dermal-soil exposures, the default skin surface area for adults in non-occupational (residential) settings includes the head, hands, forearms, and lower legs; in occupational settings it includes the head, hands, and forearms. For children, ages 0 to 6, the default skin surface area includes the head, hands, forearms, lower legs, and feet.

The dermal absorbed dose that results from contact with organics in contaminated water is calculated as:

$$DAD = (DA_{event} * EV * ED * EF * SA) / BW * AT \qquad (21)$$

where:

DAD	=	dermal absorbed dose	(mg/kg-d)
DA_{event}	=	absorbed dose per event	(mg/cm^2-event)
SA	=	skin surface area available for contact	(cm^2)
EV	=	event frequency	(events/d)
EF	=	exposure frequency	(d/yr)
ED	=	exposure duration	(yr)
BW	=	body weight	(kg)
AT	=	averaging time	(d)

The parameter DA_{event} is a function of several chemical-specific and site-specific parameters: the dermal permeability coefficient K_p, the concentration in the water C_w, the lag time per event t_{event}, the event duration, the time to reach steady state, and the ratio of the permeability coefficient through the stratum corneum to the permeability coefficient across the viable epidermis. The model assumes that absorption continues after exposure, depending on the specific chemical. DA_{event} is estimated to be the total dose dissolved in the skin when steady state is reached. For highly lipophilic chemicals or for chemicals that are not highly lipophilic, but for which t_{event} is long, an additional parameter, fraction absorbed (FA), the net fraction available for absorption after exposure has ended, is included in DA_{event} to account for losses of the chemical due to desquamation. For normal desquamation, the stratum corneum is completely

replaced in approximately 14 days. Therefore FA is considered to be important only for those chemicals with log K_{ow} >3.5 or for t_{event} >10h. Default values for several of these parameters are given in RAGS E (U.S. EPA, 2004a). The screening procedures include updated values for K_p and FA, for use when the dermal dose is likely to provide more than 10% of the dose from ingestion.

For contact with inorganics or highly ionized organics in water,

$$DA_{event} = K_p * C_w * t_{event} \tag{22}$$

where:

K_p	=	dermal permeability coefficient	(cm/h)
C_w	=	concentration in water	(mg/cm^3)
t_{event}	=	event duration	(h/event)

The value of K_p for inorganics ranges from 6E-4 to 2E-3 cm/h for metals, except mercury vapor, for which K_p is 0.24 cm/h. For all other inorganics, the K_p is given as 1E-3 cm/h. Screening procedures are included in RAGS E (U.S. EPA, 2004a) to drop estimation of dermal absorption of inorganics which do not exceed 10% of the ingested dose, when the fraction absorbed from the gastrointestinal tract has been estimated or quantified.

Few dermal absorption values for specific chemicals are available for estimating dermal exposures from contact with contaminated soil. The guidance document provides dermal-soil absorption values (ABS_d) for ten pollutants: As, Cd, and a few chlorinated organic compounds. Recommended experimental mean values of ABS_d, taken from published studies, range from 0.001 to 0.25, with a default value of 0.1 for semivolatile organic compounds. No screening values for inorganic compounds are provided. Dermal exposure to soils is considered to be more significant than direct ingestion only for those chemicals that have a soil absorption fraction exceeding 10% (U.S. EPA, 2004a, Chapter 6).

Soil to skin adherence factors (AF) are provided for a variety of exposure scenarios. For adult RME in residential settings, a high-end soil contact activity such as gardening leads to the default AF = 0.07 mg/cm^2. For child residential exposures, average exposures while playing both in dry and wet soil lead to the default AF = 0.2 mg/cm^2. For adult occupational exposures, the central tendency and high contact assumption lead to the default AF = 0.2 mg/cm^2. Activity-specific AF values are given for children and adults in several residential and commercial settings, such as indoor and outdoor play, sports, construction work, and farming.

The dermal absorbed dose that results from contact with chemicals in contaminated soil is calculated using the same equation as the one for dermal absorbed dose for organics in contaminated water. For exposure to chemically contaminated soil however, the parameter

DA_{event} is a function of chemical and site-specific parameters: the concentration in the soil, an adherence factor of soil to skin, and the dermal absorption fraction ABS_d.

$$DA_{event} = C_{soil} * CF * AF * ABS_d \quad (23)$$

where:

DA_{event}	=	absorbed dose per event	(mg/cm^2-event)
C_{soil}	=	chemical concentration in soil	(mg/kg)
CF	=	conversion factor (10-E6 kg/mg)	
AF	=	adherence factor of soil to skin	(mg/cm^2-event)
ABS_d	=	dermal absorption fraction	

Dermal exposures to chemicals present in air are considered unlikely, in most cases, to provide more than 10% of aggregate exposure. Therefore methods for assessing dermal exposure to chemicals in the vapor phase are not presented in the RAGS E document, and it is assumed that inhalation is the major route of exposure for vapor-phase chemicals (U.S. EPA, 2004a, Chapter 6). Exposure parameters for contaminated sediment and dermal toxicity to the skin at the site of contact are not addressed in RAGS E.

2.3. OFFICE OF WATER (OW)

The Safe Drinking Water Act, as amended in 1986, requires U.S. EPA to publish a non-enforceable health-based "Maximum Contaminant Level Goal" (MCLG) and an enforceable "Maximum Contaminant Level" (MCL), to establish the safe level of each regulated contaminant in drinking water. The MCLs for various contaminants, published in the National Primary Drinking Water Regulations, were developed taking effects on health, treatment technologies, and economic impact into consideration. The MCLs apply to public water systems. Under the Clean Water Act, OW also publishes Human Health Ambient Water Quality Criteria for Protection of Human Health from exposure to ambient water including fish and water consumption. The media of OW's interest are therefore drinking water and ambient water.

Currently OW calculates risk from contaminants associated with drinking water exposure by assuming a 2 L/d drinking water ingestion rate, which is roughly at the 86th percentile of the water ingestion rate of the U.S. population (U.S. EPA, 2004e). The contribution from exposure to drinking water relative to exposures from other media (e.g., food, air, soil) is then factored with a Relative Source Contribution factor in the final MCLG derivation. OW is in the process of evaluating different methodologies to estimate the extent of dermal and inhalation exposures from various activities involving drinking and ambient water use, such as showering, bathing, or dishwashing.

2.4. OFFICE OF RESEARCH AND DEVELOPMENT (ORD)

Various exposure research studies are conducted by the National Center for Environmental Assessment (NCEA), the National Exposure Research Laboratory (NERL), and the National Health and Environmental Effects Research Laboratory (NHEERL). Some of these studies investigate dermal exposure methods and models (Geer et al., 2004; Morgan et al., 2004; Wilson et al., 2004; Zendzian and Dellarco, 2003). Results of these investigations are published in the scientific literature and incorporated into Agency guidance. The Human Exposure Database System (HEDS) contains human exposure study information and the Consolidated Human Activity Database (CHAD) contains activity data useful in estimating exposures (U.S. EPA, 2007e; McCurdy et al., 2000). Both can be accessed through U.S. EPA's Environmental Information Management System (http://www.epa.gov/eims/).

Additionally, the Stochastic Human Exposure and Dose Simulation (SHEDS) model (Zartarian, 2003) and the Exposure Reconstruction and Dose Estimation Model (ERDEM) are under development in NERL. Both can deal with transfer coefficient and loading data with chemical-specific permeability coefficient inputs.

SHEDS uses a probabilistic approach to predict the distribution of exposures and dose for specified routes in a specific population. The model is designed to estimate this distribution by simulating the time series of exposure and dose for individuals that demographically represent the population of interest. U.S. census data are used to build the simulation population, and human-activity-pattern data are assigned to each simulated individual to account for the way people interact with their environment. Pollutant concentrations in the microenvironments where people spend their time (e.g., home, car, office, school, restaurant) are calculated based on concentrations obtained from measurement study data or simulation. Each individual's exposure and dose profile is estimated from the time spent in each location, the concentration in that location and the activity-specific inhalation rate while in that location. Daily-averaged exposure and dose for each individual are calculated and combined to provide a distribution of exposure and dose for the population. Statistical methods for incorporating both variability and uncertainty in the model input parameters are utilized to obtain the predicted population distribution and the uncertainty associated with the predicted distribution. The model framework has been developed for air toxics and for pesticides.

There are two types of dermal exposure modeled in ERDEM, one for a chemical in an aqueous vehicle, most often a water based diluent, and a chemical as a dried residue or adsorbed onto particles as a dry source. Skin surface exposure due to a chemical in an aqueous vehicle may be input as a time history of time, the surface area of the skin (square centimeters) that becomes exposed to the chemical, and the concentration (mass per unit volume) of the chemical in the vehicle. This concentration and area of the skin are used to compute the rate of change of the amount of chemical absorbed. Linear interpolation is used to obtain intermediate values. A chemical residue existing on a surface is represented as a mass per unit area. It is transferred to

the skin of a subject represented by a transfer coefficient. A short exposure period would represent a bolus that can accommodate loss due to evaporation and penetration through the skin. The target populations modeled to date are primarily consumers; adults and children in residential settings.

3. DERMAL EXPOSURE ASSESSMENT COMPARISONS

The results of this study show that Agency program offices focus their efforts to characterize and assess dermal exposure to media and scenarios according to their regulatory mandates and responsibilities. Consequently each office relies on different assumptions about body weight, exposed skin area, length of exposure time and frequency of exposure events to meet their specific needs. These differences are reflected in the methods they use to estimate dermal penetration and in the specific guidance documents and tools and techniques they use to conduct dermal exposure assessments. All program offices define dermal transfer as mass/duration/area or volume or weight (e.g., $\mu g/hr/cm^2$ or cm^3 or kg) to indicate the amount of chemical (mass) transferred from one medium to the receptor over unit time (hr or day) and area or volume or weight (cm^2 or cm^3 or kg). Key differences reside in the description of the dermal transport process itself in terms of infinite or finite source of media, steady state versus unsteady state, K_p estimated from in vitro dermal absorption tests or estimates of an absorption fraction from in vivo studies and consideration for applied or absorbed dose with 100% absorption assumption sometimes applied to dose calculation. These similarities and differences among these procedures are described below and represent potential areas for harmonization to improve the consistency and transparency of dermal exposure assessments used in the Agency.

3.1. TARGET POPULATIONS, EXPOSURE MEDIA, AND EXPOSURE PARAMETERS FOR DERMAL EXPOSURE ASSESSMENTS

The target populations, exposure media, and exposure parameters currently used by the EPA offices for dermal exposure assessments are summarized in Tables 1-3. These tables can be used to identify major pathways and the data input needs to assess dermal exposure. It shows the complexity associated with the characterization and assessment of this route of exposure.

3.1.1. Target Populations

As summarized in Table 1 target populations for dermal exposure assessment comprise both workers and consumers. Consideration is given to gender differences, to age groups for consumer exposures, and to exposure associated with bathing and swimming. Parameters for both age groups and skin area exposed are different among U.S. EPA Offices. Exposure to workers addresses whole body exposure and exposure to particular body parts such as one or two hands. Generally body weight for workers is assumed to be 70 kg though OPP uses a mean of 71.8 kg for male and female occupational and residential pesticide handlers. Consideration is given to gender differences for total exposed skin area though inconsistently so. In some cases total exposed skin area estimates are provided for males and females as in the OPPT PIRAT (19,400 cm^2 males and 16,900 cm^2 females). In other cases total surface area estimates are

Table 1. Target populations and assumed characteristics for dermal exposure assessment

EPA Office	Target population	Assumed characteristics		
		Age and sex	Body weight	Skin area/exposed skin area
OPPTS: Chem-STEER	Workers	Adults	70 kg (154 lb)	Total 18,150 cm^2 (average of males and females); One hand, 420 cm^2; two hands, 840 cm^2
OPPTS: EFAST	Consumers	Adults 18-75 yr	71.8 kg, mean for males and females (EFH)	Total 19,400 cm^2 (males), 16,900 cm^2 (females); Surface area/body weight (SA/BW) 286 cm^2/kg; Two hands 840 cm^2 (EFH 50th percentile values)
		Children 2-17 yr	26.9 kg (EFH)	SA/BW 422 cm^2/kg, age 2-17 yr (EFH)
		Infants 0-2 yr	10.2 kg (EFH)	Total <5,790 cm^2 age <2 yr; SA/BW 617 cm^2/kg, ages 0-1 yr (EFH)
OPPT: PIRAT	Handlers and Consumers	Adults	70 kg	Total 19,400 cm^2 (males), 16,900 cm^2 (females); Fraction exposed 0.05
		Toddlers 3 yr	15 kg	Total 6,640 cm^2 (males), 6,490 cm^2 (females); Fraction exposed 0.05
OPP	Occupational and residential pesticide handlers	Adults, 18 yr and older	71.8 kg, mean for males and females	Total 19,400 cm^2 (males), 16,900 cm^2 (females); Default areas for bathing/swimming 20,000 cm^2; outdoor soil contact 5,000 cm^2
	Consumers; general population	Infants, 0.5-1.5 yr	10 kg	Total <6,030 cm^2 (males), <5,790 cm^2 (females) (EFH)
		Toddlers, 3 yr	15 kg	Total 6,640 cm^2 (males), 6,490 cm^2 (females), hand 350 cm^2

Table 1. Target populations and assumed characteristics for dermal exposure assessment (continued)

EPA Office	Target population	Assumed characteristics		
		Age and sex	Body weight	Skin area/exposed skin area
OPP (continued)	Consumers; general population (continued)	Children, 6 yr	22 kg	Total 8,660 cm^2 (males), 8,430 cm^2 (females); Default area for swimming/bathing 9,000 cm^2
		Youth, 10-12 yr	39.1 kg	Total 12,000 cm^2 (males), 12,400 cm^2 (females)
		Females 13-54 yr	60 kg (when considering reproductive effects)	Total 14,800 to 16,300 cm^2
		Adults 18 yr and older	71.8 kg	Total 19,400 cm^2 (males), 16,900 cm^2 (females); Default area for swimming/bathing 20,900 cm^2
OSWER: Superfund	Workers	Adults >18 yr	70 kg	3,600 cm^2; head, hands and forearms exposed
	Consumers; residential settings	Adults >18	70 kg	Swimming or bathing: 6,600 cm^2; Other: 2,800 cm^2; Head, hands, forearms, lower legs, feet exposed
		Children 1-6 yr	15 kg	Swimming or bathing: 6,600 cm^2; Other: 2,800 cm^2; Head, hands, forearms, lower legs, feet exposed
OW	Individuals in non-occupational settings	Adults and children	70 kg 10 kg	Showering, bathing, dishwashing (drinking water); Swimming (ambient water)
ORD	Individuals in non-occupational settings	Adults and children	EFH values; individual measurements	EFH values and individual measurements

Table 2. Exposure media considered for dermal exposure assessment

EPA Office	Exposure media	Comments
OPPTS: ChemSTEER	Liquid industrial and commercial products and intermediates	Workplace release and exposure estimation for new chemicals; several models or four comprehensive industry-specific scenarios; release estimates can be used as inputs to EFAST
OPPTS: EFAST	Liquid or solid consumer products applied to hard surfaces, added to or used in water, or contacting skin directly	Screening estimates of consumer dermal exposures; three default scenarios
OPPT: PIRAT	Water, soil, treated surfaces (turf, foliage, pets); liquid and solid formulations	Screening estimates of handler and post-application dermal exposures. Incorporates PHED data
OPP	Liquid and solid (granular, powder) formulations; treated surfaces; paint/stain; impregnated materials	Standard operating procedures cover handler and post-application exposures
OSWER: Superfund	Soil, water, sediment	Worker and consumer exposures to soil and water at Superfund sites
OW	Water	Primary interest in general population dermal exposure from water uses
ORD	All environmental media, including indoor and outdoor air, water, soil, house dust, and surface residues; some consumer products	Research emphasis on aggregate (all routes and pathways) and cumulative (all chemicals with similar modes of action) exposures

Table 3. Assumed and default exposure parameters for target populations for dermal exposure assessment

EPA Office	Characteristics	Skin areas	Skin loading, adherence factor	Dermal absorption	Transfer coefficients
OPPTS: Chem-STEER	~34 models with 4 specific occupational scenarios; AT 40 yr work-life; Atc 70 yr lifetime; ED 22 da/site-yr; EY 40 yr; FT = 1 event/site-da; Default weight fraction ai 0.33. For direct solids contact, S*Qu is constant at 3100 mg/event; for contact with solids containers, S*Qu is 1100 mg/event. Parameters based on industrial data supplied to U.S. EPA.	One hand 420, two hands 840 cm^2	Constant at 0.7 (low) or 2.1 (high) mg/cm^2-event for liquids	100% absorption of substance available to skin	Not used
OPPTS: EFAST	Three specific consumer product exposure scenarios. AT 30 yr for ambient exposures; Adult AT 57 yr for non-carcinogenic consumer products; AT 1 d for acute exposures; AT 75 yr for carcinogenic products. SA/BW assumes both hands exposed (hand-washing clothes), palms only (changing motor oil); whole body and/or hands (bar soap use). Parameters based on industrial data supplied to U.S. EPA.	Surface area/body wt ratio SA/BW (cm^2/kg)	Amount retained on skin Q (g/cm^2-event); based on experimental film thickness data	Permeability coefficient K_p (cm/h) values listed for specific chemicals	Not used
OPPT: PIRAT	Screening estimates for handler and post-application exposure to inert ingredients, residues on turf, foliage, pets. Formulation, application method, carrier selected. Toxicity values can be entered. PHED data incorporated.	See Table 1	Not used	User can enter absorption coefficient	14,500 (adults), 5,200 (toddlers) cm^2/h
OPP	Handler exposures generally based on amount of ai applied, e.g., residential turf handler exposure on application day assumes one event/d, 20,000 ft^2 treated, 5 gal spot treatment with specified ai; gardener handler 10,000 ft^2 treated, 5 gal spray.	Not used	Not used	Not used	Not used

Table 3. Assumed and default exposure parameters for target populations for dermal exposure assessment (continued)

EPA Office	Characteristics	Skin areas	Skin loading, adherence factor	Dermal absorption	Transfer coefficients
	Contact with residues on treated surfaces assumes 20% of application is available as transferable (dislodgeable) residues on day of application; duration 0.33 h/d (toddlers), 0.67 h/d (adults). A rate of dissipation from surfaces is included, except for pet applications, which are assumed to be steady state.	Exposed skin areas see Table 1	Not used	Not used	43,000 (adults high end), 10,000 (adults typical), 5,000 (youth 10-12 yr), toddlers (high end) 8,700 cm^2/h
	Indoor transferable residues post-application: high end from carpet 50% of application, duration 8 h/d; from hard surfaces 50%, exposure duration 4 h/d. A rate of dissipation is included.	Exposed skin areas see Table 1	Not used	Not used	High end see above. Central 6,000 (toddlers), 16,700 (adults) cm^2/h.

Table 3. Assumed and default exposure parameters for target populations for dermal exposure assessment (continued)

EPA Office	Characteristics	Skin areas	Skin loading, adherence factor	Dermal absorption	Transfer coefficients
OSWER: Superfund	Default values for dermal-water and dermal-soil pathways. Dermal absorbed dose values for several hundred chemicals from water, based on exposure scenarios. Reasonable maximum exposure (RME) values and central tendency values are calculated. Water contact: showering/bathing – events/d, 1; event duration 0.58 h (adult), 1.0 h (child); frequency 350 d/yr; exposure duration 30 yr (adult), 6 yr (child); Swimming – site-specific. Soil contact: events/d, 1; event duration 24 h (based on experimental ABS_d measurement time); frequency 350 d/yr (residential), 250 d/yr (industrial); exposure duration 6 yr (child), 30 yr (adult residential), 25 yr (adult industrial).	Exposed skin areas See Table 1	Soil adherence factor, AF (mg/cm^2), e.g., adult residential high-end 0.07; child 0.2; child indoors 0.01	Permeability coefficients K_p (cm/h) for water; net fraction absorbed FA for high-molecular weight chemicals in water; Soil absorption factors ABS_d	Not used
OW	Under evaluation	Under evaluation	Not applicable	Under evaluation	Under evaluation
ORD	Research studies include dermal methods development, inclusion of dermal exposure in models under development, e.g., SHEDS. Research study databases, e.g., HEDS. Activity pattern studies and databases, e.g., CHAD.	EFH values, See Table 1	Dermal loading (mg/cm^2)	Current research area[a]	Current research area[b]

[a] See for example, Griffin et al. (1999), Fenske and Elkner (1990).
[b] See for example, Rodes et al. (2001).

averaged between males and females to yield a single value, for example 18,150 cm^2 in the OPPTS ChemSTEER. OSRTI worker exposure is based on the assumption that head hands and forearms are exposed such that the total exposed skin area is 3,600 cm^2. Consumers are subdivided as adults or children. OPPTS uses an adult body weight of 71.8 kg except in PIRAT which uses 70 kg. Both OSRTI and OW use an adult body weight of 70 kg. There is a wide range of body weight assignments for children depending on the number of age group subdivisions. Age grouping within divisions are different too such that infants are categorized as 0-2 years old (10.2 kg) in OPPTS EFAST but as children ranging in age from 1-6 years old (15 kg) in OSRTI. OPP has provisions for several age group ranges (infants, toddlers, and youth) with corresponding levels of skin area exposed parameters.

3.1.2. Exposure Media

Not surprisingly dermal exposure assessment interests in the Agency span a wide range of media according to the mission and purview of each office. Consequently it includes exposure to industrial chemicals and intermediates during production, exposure associated with the use of consumer products, including pesticides, and exposure to chemically contaminated water, soil and sediment, and contact with chemically treated or contaminated surfaces. Dermal exposure from deposition of airborne chemicals can be estimated for certain industrial operations using OPPTS ChemSTEER and for specific consumer product uses such as painting with OPPTS EFAST and with OPP specific standard operating procedures such as spray applications (Table 4). This does not apply to exposure to aerial spray drift or to fumigation which are evaluated with specific aerosol models. Dermal exposure via air is not considered by OSRTI. Virtually all of the offices address dermal exposure in chemically contaminated water, with particular attention to swimming, showering and bathing (Table 5). Dermal exposure to soil is explicitly addressed in OSRTI with methods to estimate soil adherence to skin and to estimate dermal absorption. It is not specifically addressed in OPPTS or OW. Dermal exposure from treated surfaces is addressed in OPPTS but not OW. OPPTS ChemSTEER and OPPTS EFAST rely on defined exposure scenarios, OPP utilizes standard operating procedures. In OPPTS the focus is on worker exposures to industrial chemicals and intermediates and to consumer exposures from liquids or solid consumer products used in water that are applied to hard surfaces such as paints and cleaners. In both cases several default scenarios are provided that can be used to estimate exposure to the chemical of interest. In OPP the focus is on commercial and residential exposures associated with pesticide use. The many standard operating procedures address application of liquid or solid pesticide formulations as well as contact with treated surfaces or impregnated materials. OSRTI considers dermal exposure to both workers and the public from chemically contaminated water and soil. Contamination may arise from migration of hazardous wastes in the environment due to run off or erosion and to infiltration of hazardous waste chemicals into residences in proximity to hazardous waste sites.

Table 4. Dermal exposure assessment methodology for chemical contaminants in air

EPA Office	Methodology
OPPTS: ChemSTEER	Scenarios include estimates of dermal exposures to airborne contaminants deposited on skin from industrial operations, such as spray-coating of automobiles.
OPPTS: EFAST	Consumer product-related scenarios include estimates of dermal exposures to airborne contaminants during application of products to hard surfaces, such as painting.
OPP	Residential SOPs include spray applications of paints/stains and pet pesticides. Spray drift and fumigant exposure are considered, based on specific aerosol models.
OSWER: Superfund	Not covered.
OW	Under evaluation. OW would also like to address dermal exposure via vapors and aerosols.
ORD	Research methods, e.g., breath analysis to estimate dermal absorption.[a]

[a] See, for example, Giardino et al. (1999), Corley et al. (1997).

Table 5. Dermal exposure assessment methodology for chemical contaminants in water

EPA Office	Comments
OPPTS: ChemSTEER	Pre-set scenarios for worker exposure during four industrial operations. Includes exposure to additives from recirculating water-cooling towers. One-hand liquid, two-hand liquid, and mass balance models.
OPPTS: EFAST	Pre-set scenarios for consumer exposure include use of products that are added to water. Site-specific general population exposure estimates for chemical releases that enter surface waters. Models provide estimates of concentrations and dermal dose rates.
OPP	Standard Operating Procedures include scenarios for swimming and showering.
OSWER: Superfund	Methods for evaluating dermal-water exposure; for swimming and bathing, entire skin surface assumed. Assumed significant only if dermal absorption is likely to be >10% of the direct ingestion dose.
OW	Under evaluation, with primary interest in general population dermal exposure from water uses. Shower model under development.
ORD	Current research methods, e.g., methods to estimate dermal absorption from water.[a]

[a] See, for example, Gordon et al. (1998).

The OW is primarily interested in dermal exposure to chemically contaminated water associated with uses such as swimming and bathing.

3.1.3. Assumed and Default Parameters for Exposure Assessment

Assumed and default characteristics vary widely across the Agency according to the chemical and the nature of the exposure event under consideration. The orientation is largely for chronic exposures though provisions are made for acute exposures. For example the averaging time (AT) for occupational exposure is 40 years for occupational exposure in OPPTS ChemSTEER but ranges from 30 years to 75 years depending on the nature of the scenario and product considered in OPPTS EFAST. Skin area exposed may be based on general assumptions such as one or two hands or on industry supplied data about the exposure event (see OPPTS ChemSTEER and OPPTS EFAST). Skin loading may be estimated by use of a film thickness estimate or by an adherence factor or by estimating dermal absorption. Dermal absorption can be based on a percentage of the amount available on the skin or estimated by a permeability coefficient. Transfer coefficients used to estimate the amount of a chemical residue that can be dislodged from a treated surface and transferred to the skin range from 10,000 cm^2/hr to 43,000 cm^2/hr in adults depending on the exposure scenario.

3.2. METHODOLOGY COMPARISON

Comparative analysis among dermal exposure methodology is difficult because of the focus on specific media in different program offices, unique attributes assigned to exposure scenarios, and assignment of upper percentile assumptions for parameters such as skin surface area or exposure duration as discussed previously. Moreover, the differences in these parameters reflect user preferences to estimate exposure to the chemical of concern and situation circumstances being evaluated. Selection of the skin loading adherence factor, permeability coefficient, K_p, and transfer coefficient represent key sources of variability among dermal exposure methods.

3.2.1. Skin Loading Adherence Factors

Different approaches for skin loading adherence factors are recommended for dermal exposure models. In the OPPTS ChemSTEER model, the two-hand liquid loading on the skin surface area S is set at 840 cm^2, and the quantity Qu remaining on the skin is set at either 0.7 or 2.1 mg/cm^2. Similarly, for the two-hand solid loading model or for direct contact with solids, the quantity S times Qu is set at 3,100 mg/event. The model assumes that the quantity remaining on the skin or surface loading per event is not affected by wiping off the excess, nor do additional contacts increase the quantity significantly. In the EFAST CEM a film-thickness approach is used, which assumes a thin film of product on a defined skin area. However, there are little

supporting data on film thicknesses on skin and there are questions about the uniformity of such films associated with product usage.

To estimate dermal exposure from chemically contaminated soil, OSRTI employs a series of default values for AF for a variety of exposure scenarios. For adult RME in residential settings, the AF for a high-end soil contact activity such as gardening is 0.07 mg/cm^2. Residential average exposures for children while playing both in dry and wet soil uses a default AF of 0.2 mg/cm^2. For adult occupational exposures, the default AF is 0.2 mg/cm^2. Activity-specific AF values are given for children and adults in several residential and commercial settings, such as indoor and outdoor play, sports, construction work, and farming.

3.2.2. Selection of a Permeability Coefficient

All of these approaches permit the user to select a permeability coefficient, K_p, for the chemical being evaluated. Measured K_p values can be found in the literature for many chemicals or can be estimated by using the procedures in the Agency's Dermal Exposure Assessment: Principles and Applications (DEA) guidance document (U.S. EPA, 1992a) or the RAGS E (U.S. EPA, 2004a). In the DEA guidance document K_p is provided for 90 chemicals and in RAGS E the list has been updated to included more than 200 chemicals. In RAGS E for chemicals not listed, K_p can be estimated using a function of the octanol/water coefficient, K_{ow}, and molecular weight:

$$\log K_p = -2.80 + 0.66 \log K_{ow} - 0.0056\ MW \qquad (24)$$

where:

K_p	=	Dermal permeability coefficient of compounds in water (cm/hr)
K_{ow}	=	Octanol/water partition coefficient of the non-ionized species (dimensionless)
MW	=	Molecular weight (g/mole).

However, both measured K_p and estimated K_p are subject to substantial variability. Measured K_p variability can be due to species of skin (human, rat, swine), thickness of skin, method of skin preparation, or the receptor fluid used in the method. Estimated K_p is based on the relationship of the K_{ow} and the molecular weight of the compound of interest. However the relationship does not hold well for small polar molecular weight compounds or for large lipophilic compounds which make up most of the chemicals of interest to the Agency. The degree of variability can be illustrated in the selection of the K_p for benzene for a dermal exposure assessment in a Superfund investigation. In RAGS E, 0.015 cm/hr is the recommended K_p but the California EPA recommends a K_p of 0.19 cm/hr based on the average of two studies reported in the literature.

3.2.3. Selection of a Transfer Coefficient

Various assumptions are used to estimate chemical transfer from treated or contaminated surfaces to skin. This is largely due to the lack of data concerning residue concentrations on affected surfaces, how much can be removed by contact with skin, and the nature and extent of activities where skin contact with affected surfaces occurs. Transfer coefficients used in OPPT PIRAT are 14,500 cm^2/hr for adults and 5,200 cm^2/hr for small children. In the OPP SOPs, 20% of an outdoor pesticide application is assumed to be transferable and 50% of an application indoors to carpets or to hard floors. The transfer coefficient default values for adults for outside applications are typically 10,000 cm^2/hr with a high end default of 43,000 cm^2/hr 5,000 cm^2/hr for children age 10-12 and 8,700 cm^2/hr for young children. For indoor applications transfer coefficient default values are 16,700 cm^2/hr for adults and 6,000 cm^2/hr for children.

3.3. DERMAL EXPOSURE ASSESSMENT METHODOLOGY FOR VARIOUS MEDIA

The following tables, Tables 4-8, provide brief descriptions of the methods used by the various U.S. EPA offices to estimate dermal exposures to chemicals in environmental and occupational media.

Table 6. Dermal exposure assessment methodology for chemical contaminates in soil

EPA Office	
OPPTS: ChemSTEER	Not covered.
OPPTS: EFAST	Not covered.
OPP	Some chemical-specific studies have looked at hand-press transfer. Treated soil may be assessed using specific study data or surrogate, depending on the chemical and the method of exposure, e.g., potting, gardening, etc.
OSWER: Superfund	Methods for evaluating dermal-soil exposure included. Soil adherence factors and dermal absorption values for 10 specific chemicals; screening estimates for semivolatile organics. Assumed significant only if soil absorption >10% of direct ingestion dose.
OW	Not covered.
ORD	Current research methods, e.g., hand press, hand wipes, soil scrapings to obtain concentrations (ng/g) and loadings (ng/m^2). Development of transfer coefficients and activity-related residential exposure data.

Table 7. Dermal exposure assessment methodology for treated surfaces

EPA Office	Comments
OPPTS: ChemSTEER	Pre-set scenarios for worker contact during four industrial operations. A user-defined option is available.
OPPTS: EFAST	Pre-set scenarios for consumer contact with products applied to hard surfaces
OPP	Standard Operating Procedures for transfer from treated surfaces based on dislodgeable residues, transfer coefficients, and dissipation rate. Post-application from impregnated materials, such as painted surfaces, based on flux rate of ai from material.
OSWER: Superfund	Methods for evaluating dermal-surface exposure included.
OW	Not covered.
ORD	Research methods: Solid surface wipes to give concentrations (ng/g) and loadings (ng/m^2). Vacuum dust collections from carpeted surfaces. Transferable (dislodgeable) residue collections though PUF roller and other methods.[a]

[a] See, for example, Wilson et al. (2004), Morgan et al. (2004).

Table 8. Dermal exposure assessment methodology for occupational sources

EPA Office	Comments
OPPTS: ChemSTEER	Pre-set scenarios for worker exposure during industrial operations: adhesives formulation, new and refinishing spray-coating of automobiles, and recirculating water-cooling towers. One-hand liquid, two-hand liquid, and mass balance models require selection of a manufacturing operation and an activity. Default parameters and user input.
OPPTS: EFAST	Not covered.
OPP	Standard Operating Procedures for residential pesticide applications by commercial applicators and by consumers. Exposure estimates from direct contact during application and from contact with treated surfaces after application. OPP's Antimicrobial Division has SOPs for industrial operations, such as industrial mixing of paint.
OSWER: Superfund	Methods for evaluating dermal exposure to occupational sources included. Default exposure values for dermal-water and dermal-soil pathways.
OW	Not covered.
ORD	Not covered.

4. DERMAL EXPOSURE ASSESSMENT TRENDS AND RESEARCH NEEDS

The variety of methods, models, tools, and techniques described in this report underscore the diversity of situations where the Agency considers dermal exposure in regulatory activities. The complexity of the dermal pathway and the limited understanding of key aspects such as dermal penetration and residue transfer efficiency necessitate continued efforts to better characterize and assess dermal exposure in the Agency. This section describes various research needs to develop a more complete understanding about the dermal penetration process and an improved characterization of exposure events where dermal contact occurs, especially for contact with soil, sediment, and surfaces. Though methods exist to estimate skin loading only a few studies with soil and sediment have been conducted. Likewise methods have been described that can estimate the amount of residue that can be transferred to skin from turf or surfaces but few studies have been conducted to estimate the amount of transfer associated with actual activities. More time location activity information would be useful to estimate the nature and extent of activities where skin contact occurs from these sources for use in dermal exposure assessment models and guidance documents.

4.1. WATER

The effective predicted domain used by Superfund for K_p estimates is based on the Flynn database contained in DEA (U.S. EPA, 1992a). The Flynn database has not been expanded with any new introduction of data from the literature though there are provisions to update the RAGS E Appendix when new data are found in the scientific literature. A key issue pertains to obtaining K_p for highly lipophilic compounds. Current in vitro dermal absorption methods are suitable only for chemicals in aqueous solutions. The solubility of highly lipophilic compounds in these systems is limited to the point that the chemical is tied up in the skin layer and does not penetrate through to a sufficient concentration to be measured. Yet many of the chemicals addressed in Superfund site investigations are highly lipophilic compounds such as PCBs and dioxins. In the absence of suitable K_p estimates for these compounds, Superfund managers must perform uncertainty analyses as part of their assessments to account for the lack of quantitative data for these compounds.

To get into and through the skin, the chemical must dissolve into the stratum corneum, which is a stabilized lipid barrier. Hence lipid solubility is required initially, followed by water solubility, to pass through the water-based gel portion of the skin and the human body, which is water-based. Unlike the water solubility data, no lipid solubility data have been collected, which leaves a gap in the knowledge. Because the Flynn database chemicals were not measured in the same vehicle nor across the same dose range and were studied with different procedures, the results are difficult to compare. Research is needed to evaluate the Flynn database in

conjunction with more recent reports of K_p in the literature to improve and expand the predicted domain.

4.2. SOIL

In Superfund risk assessments, soil exposure is evaluated for residential and occupational scenarios that incorporate exposure time and type of human contact with soil. Skin soil loading is determined using activity-specific surface area-weighted adherence factors as exposure factors for soil. Empirical values are used for the specific fraction of chemicals absorbed to compensate for the lack of data on soil matrix effects, such as contaminate aging on soils, soil carbon and moisture content of soils, and percent absorbed and fraction absorbed from the soil matrix.

Studies have shown that dermal loading depends on the type of activity, type of soil, fineness of soil, soil moisture level, and moisture on the skin (which typically increases transfer to skin). Particle loading, mass balance and particle replacement rates are issues that are not addressed well in existing Agency methods and models. Research is needed to better understand the effects of soil composition such as carbon, clay, and moisture content and particle size on skin loading and on dermal absorption of chemically contaminated soil.

4.3. TREATED SURFACES

Dermal exposure to treated surfaces is poorly characterized. Efforts are underway in OPP and OSWER to better describe the parameters responsible for dermal exposure from these sources. In OPP, a transfer coefficient (TC) combined with the fraction of the amount of material applied constitutes the basis for dermal exposure assessment from treated foliage and surfaces. When application specific data are unavailable assumptions are used to estimate the fraction of applied material available for transfer (usually 5-10% depending on the treatment site) and the amount transferred which is estimated from choreographed simulation studies designed to represent the activities of interest. Efforts are underway to revise the SOPs that guide these kinds of dermal exposure assessments. Additionally, studies are being conducted to determine the key features that influence TC such that more reasonable assumptions can be incorporated into the SOP guidance. OSWER is expanding dermal exposure assessments to include contact with chemically contaminated surfaces. Both the Agency report: World Trade Center (WTC) Indoor Environment Assessment: Selecting Contaminants of Potential Concern and Setting Health-Based Benchmarks (U.S. EPA, 2003b), and the OSWER guidance document for PCBs under development address this issue. The report incorporates transfer efficiencies derived from the scientific literature to assess dry particle transfer to skin from hard surfaces. The PCB draft guidance document contains information to calculate site-specific cancer and non-cancer risks for dermal and ingestion pathways for PCB exposures. Appendix E of the document addresses risks from PCB-contaminated solid surfaces using the protocol and method from the WTC site investigation and some industrial site investigations in Region 3. Default values have

been provided to develop screening levels for adults and children in a residential scenario and for an indoor worker in an industrial scenario. The guidance differs from the WTC approach by including exposure form porous (e.g., wood, brick, concrete) and non-porous (stainless steel and vinyl) surfaces. The approach used is a modification of the OPP approach. Parameters for application rates and residues are modified to reflect wipe samples, mass loading of dust, children exposures over a 30-year period from age 1 to 31, and the introduction of a dissipation factor to allow for removal of contaminants by cleaning. More research is needed to evaluate the generalizability of this guidance to other instances of exposure to contaminated surfaces.

There is a general assumption in dermal exposure assessment methods and models that clothing protects against exposure despite several studies that show this may not always be the case depending on the chemical, its matrix, nature of the activity where exposure occurs, and the type of clothing used for protection. Research is needed to evaluate the studies that have been conducted to characterize this issue and to conduct additional studies to determine the factors where clothing may not be protective.

5. CONCLUSIONS

The Agency's interest in harmonization of dermal exposure assessment approaches is based on the desire to generate transparent, reliable and reproducible risk assessments based on sound science. Appropriate harmonization is a tool for making the best use of technical resources, fostering consistency and a common basis for selection of test methods and exposure factors, and estimating dermal transport processes for dermal exposure assessment. This report shows that the kind of information that can be harmonized includes: databases of transport parameters from different program offices, K_p estimates from the Agency's Superfund program, transfer coefficients used by OPP for different pesticide application scenarios, and in vivo and in vitro dermal absorption test methods used by the Agency. Research is underway in many of these areas to generate data that could support harmonization efforts in the future.

The OSWER Dermal Workgroup is evaluating the approach described in the World Trade Center investigation and the OPP standard operating procedures (SOPs) for residential exposure assessments with other information to develop a protocol for dermal exposure to contaminated surfaces as a new appendix in RAGS E (U.S. EPA 2004a, U.S. EPA, 2003b; U.S. EPA, 1997a). The approach used is based on the procedures for contaminated soil to the extent possible in an effort to estimate dermal absorption from contact with other types of surfaces, such as floors, walls, furniture, and vehicle seats which can then be used with the other parts of RAGS E to address dermal risk from these surfaces. Additional research is needed to evaluate the similarities and differences of these approaches, to estimate contact with solids and to determine the critical parameters for dermal exposure assessments

In NERL, development and application of quantitative structure-activity relationship (predictive QSAR) models is underway to produce the necessary parameters for data-intensive PBPK models. Partition coefficients are used in PBPK/PD models to demonstrate the transfer of materials through the skin, as well as between skin and blood. QSAR data (on absorption, metabolic, tissue partitioning, enzyme inhibition and recovery parameters) can be tested in the body of a PBPK model to obtain information on where the chemical is in the body. The vehicle nature of the relationship of the skin to the stratum corneum and consequent absorption is a critical factor in assessing permeability especially when trying to compare *in vivo* and *in vitro* results. Skin permeability models relying on the K_{ow} (or Log P) and molecular size (molecular weight, V) are used as the main predictors. Steady state flux is measured in an *in vitro* system using water and is used to derive the permeability coefficient K_p for chemical compounds. The vehicle partition coefficient (Km/v) is a key part of the calculation and may be approximated by the octanol-water partition coefficient (K_{ow}).

Challenges associated with these approaches include: the difficulty to assess lag time and path length; that in vitro, aqueous systems do not work for lipophilic compounds due to solubility issues; molecular weight is not an adequate parameter (molecular volume, Bondi's

constants, and molar refractivity are better); 33% of the variation in the regression remains unaccounted for; and a dichotomy exists between steady state in vitro and non-steady state in vivo approaches. PBPK modeling uses provisional estimates to circumvent some of these issues and to model dermal chemical absorption based on a permeation coefficient. Studies of chlorpyrophos, malathion and carbaryl are being conducted to improve the precision and accuracy of this approach.

NCEA is performing a critical review of the literature for soil models and evaluating their ability to estimate dermal absorption. This review is needed because of a lack of standard protocols for dermal exposure to chemically contaminated soil and a lack of data to validate them. Based on the results of the review, a protocol will be developed and a study of dermal absorption to chemically contaminated soil will be conducted to demonstrate the proper approach to generate data for chemically contaminated soil. Additionally a parallel effort is underway to investigate a dermal absorption model for chemicals in soil and sediment and to develop a mechanistic model. This effort will address the fact that the current percent absorbed approach falsely assumes that the same percentage applies under all exposure conditions. The approach will use in vitro experiments to explore absorption parameters and use the results to develop a mechanistic model. Preliminary experimental results show that the monolayer (soil particle layer immediately next to the skin) controls the flux and the layers above the monolayer contribute very little to dermal absorption such that flux does not increase as concentration exceeds the soil saturation level.

The results of the many activities and investigations summarized in this report serve as a reference document for Agency risk assessors who deal with assessing the consequences of dermal exposure to chemical contaminants in the environment. It is intended to foster discussion about information sharing and harmonization and to support additional research to improve dermal risk assessment methodology in the Agency.

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