

March 14, 1999
Final Draft

**NOTE: DRAFT VERSION CURRENTLY UNDER REVIEW
and REVISION BY DERMAL WORKGROUP**

**RISK ASSESSMENT GUIDANCE FOR SUPERFUND
VOLUME I: HUMAN HEALTH EVALUATION MANUAL
SUPPLEMENTAL GUIDANCE
DERMAL RISK ASSESSMENT
INTERIM GUIDANCE**

NOTICE

The policies in this document do not represent final Agency action, but are intended solely as interim guidance. They are not intended, nor can they be relied upon, to create any rights enforceable by any party in litigation with the United States. EPA officials may decide to follow the guidance provided in this document, or to act at variance with the guidance, according to site-specific circumstances. The Agency also reserves the right to modify this guidance at any time without public notice.

Office of Emergency and Remedial Response
U.S. Environmental Protection Agency
Washington, D.C. 20460
DISCLAIMER

8/11/99

DRAFT-DO NOT CITE OR QUOTE

TABLE OF CONTENTS

1. INTRODUCTION AND FLOWCHART	1-1
1.1 INTRODUCTION	1-1
1.2 ORGANIZATION OF DOCUMENT	1-2
1.3 FLOWCHARTS	1-3
2. HAZARD IDENTIFICATION	2-1
2.1 CHOOSING CONTAMINANTS OF CONCERN FOR THE DERMAL-WATER PATHWAY	2-1
2.2 CHOOSING CONTAMINANTS OF CONCERN FOR THE DERMAL-SOIL PATHWAY	2-3
3. EXPOSURE ASSESSMENT	3-1
3.1 ESTIMATION OF DERMAL EXPOSURES TO CHEMICALS IN WATER	3-2
3.1.1 Standard Equation for Dermal Contact with Chemicals in Water	3-2
3.1.2 Exposure Parameters	3-4
3.1.2.1 Permeability coefficient for compounds in water (K_p in cm/hr)	3-5
3.1.2.2 Chemical concentration in water	3-7
3.1.2.3 Skin surface area	3-8
3.1.2.4 Event time, frequency and duration of exposure	3-8
3.2 ESTIMATION OF DERMAL EXPOSURE TO CHEMICALS IN SOIL ...	3-11
3.2.1 Standard Equation for Dermal Contact with Chemicals in Soil	3-11
3.2.2 Exposure Parameters	3-12
3.2.2.1 Skin surface area	3-12
3.2.2.2 Soil-to-skin adherence factors	3-14
3.2.2.3 Recommended soil adherence factors	3-17
3.2.2.4 Dermal absorption fraction from soil	3-23
3.2.2.5 Age-adjusted dermal factor	3-27
3.2.2.6 Event time, exposure frequency and duration	3-27
4. TOXICITY ASSESSMENT	4-1
4.1 PRINCIPLES OF ROUTE-TO-ROUTE EXTRAPOLATION	4-1
4.2 ADJUSTMENT OF TOXICITY FACTORS	4-2
4.3 CALCULATION OF ABSORBED TOXICITY VALUES	4-4
4.4 DIRECT TOXICITY	4-5
5. RISK CHARACTERIZATION	5-1
5.1 QUANTITATIVE RISK EVALUATION	5-1
5.1.1 Risk Calculations	5-1
5.1.2 Risks for all routes of exposure	5-2
5.2 UNCERTAINTY ASSESSMENT	5-2
5.2.1 Hazard Identification	5-3

March 14, 1999
Final Draft

**NOTE: DRAFT VERSION CURRENTLY UNDER REVIEW
and REVISION BY DERMAL WORKGROUP**

**RISK ASSESSMENT GUIDANCE FOR SUPERFUND
VOLUME I: HUMAN HEALTH EVALUATION MANUAL
SUPPLEMENTAL GUIDANCE
DERMAL RISK ASSESSMENT
INTERIM GUIDANCE**

NOTICE

The policies in this document do not represent final Agency action, but are intended solely as interim guidance. They are not intended, nor can they be relied upon, to create any rights enforceable by any party in litigation with the United States. EPA officials may decide to follow the guidance provided in this document, or to act at variance with the guidance, according to site-specific circumstances. The Agency also reserves the right to modify this guidance at any time without public notice.

Office of Emergency and Remedial Response
U.S. Environmental Protection Agency
Washington, D.C. 20460
DISCLAIMER

8/11/99

DRAFT-DO NOT CITE OR QUOTE

This document is an internal draft for review purposes only and does not constitute U.S. Environmental Protection Agency policy. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

8/11/99

ii

DRAFT-DO NOT CITE OR QUOTE

11.1910

TABLE OF CONTENTS

1. INTRODUCTION AND FLOWCHART	1-1
1.1 INTRODUCTION	1-1
1.2 ORGANIZATION OF DOCUMENT	1-2
1.3 FLOWCHARTS	1-3
2. HAZARD IDENTIFICATION	2-1
2.1 CHOOSING CONTAMINANTS OF CONCERN FOR THE DERMAL-WATER PATHWAY	2-1
2.2 CHOOSING CONTAMINANTS OF CONCERN FOR THE DERMAL-SOIL PATHWAY	2-3
3. EXPOSURE ASSESSMENT	3-1
3.1 ESTIMATION OF DERMAL EXPOSURES TO CHEMICALS IN WATER	3-2
3.1.1 Standard Equation for Dermal Contact with Chemicals in Water	3-2
3.1.2 Exposure Parameters	3-4
3.1.2.1 Permeability coefficient for compounds in water (K_p in cm/hr)	3-5
3.1.2.2 Chemical concentration in water	3-7
3.1.2.3 Skin surface area	3-8
3.1.2.4 Event time, frequency and duration of exposure	3-8
3.2 ESTIMATION OF DERMAL EXPOSURE TO CHEMICALS IN SOIL ...	3-11
3.2.1 Standard Equation for Dermal Contact with Chemicals in Soil	3-11
3.2.2 Exposure Parameters	3-12
3.2.2.1 Skin surface area	3-12
3.2.2.2 Soil-to-skin adherence factors	3-14
3.2.2.3 Recommended soil adherence factors	3-17
3.2.2.4 Dermal absorption fraction from soil	3-23
3.2.2.5 Age-adjusted dermal factor	3-27
3.2.2.6 Event time , exposure frequency and duration	3-27
4. TOXICITY ASSESSMENT	4-1
4.1 PRINCIPLES OF ROUTE-TO-ROUTE EXTRAPOLATION	4-1
4.2 ADJUSTMENT OF TOXICITY FACTORS	4-2
4.3 CALCULATION OF ABSORBED TOXICITY VALUES	4-4
4.4 DIRECT TOXICITY	4-5
5. RISK CHARACTERIZATION	5-1
5.1 QUANTITATIVE RISK EVALUATION	5-1
5.1.1 Risk Calculations	5-1
5.1.2 Risks for all routes of exposure	5-2
5.2 UNCERTAINTY ASSESSMENT	5-2
5.2.1 Hazard Identification	5-3

5.2.2 Exposure Assessment	5-4
5.2.2.1 Dermal exposure to water - Uncertainties associated with the model for DA_{event}	5-4
5.2.2.2 Dermal Exposure to Soil	5-6
5.2.3 Toxicity Assessment	5-10
5.2.4 Risk Characterization	5-11
6. CONCLUSIONS/RECOMMENDATIONS	6-1
6.1 Summary Conclusions	6-1
6.2 General guidelines for evaluating Dose from dermal contact	6-3
7. REFERENCES	7-1

LIST OF TABLES

Table 3.1	Permeability Coefficients for Inorganics	3-7
Table 3.2	Recommended Dermal Exposure Values for Central Tendency and RME Residential Scenarios - Water Contact	3-10
Table 3.3	Activity Specific-Surface Area Weighted Soil Adherence Factors	3-22
Table 3.4	Recommended Dermal Absorption Factor from Soil	3-26
Table 3.5	Recommended Dermal Exposure Values for Central Tendency and RME Residential and Industrial Scenarios - Soil Contact	3-29
Table 4.1	Summary of Gastrointestinal Absorption Efficiencies and Recommendations for Adjustment of Toxicity Factors for Specific Compounds	4-6
Table 5.1	Summary of Dermal Risk Assessment Process	5-2
Table 5.2	Summary of Uncertainties Associated with Dermal Exposure Assessment ..	5-12

PREFACE

This guidance was developed by the Superfund Dermal Workgroup, which included Regional and Headquarters staff in EPA's Office of Emergency and Remedial Response, staff EPA's Office of Research and Development, and staff from the Texas Natural Resource Conservation Commission. Jim Konz of the State/Tribal/Site Identification Center in Headquarters OERR provided overall project management and technical coordination of its development.

OERR would like to acknowledge the efforts of the other Superfund Dermal Workgroup members who supported development of the interim guidance by providing technical input regarding the content and scope of the guidance.

Ann-Marie Burke, Region I

Mark Maddaloni, Region II

Mark Johnson, Region V

Kim Hoang¹, ORD/NCEA-W

Dan Stralka, Region IX

Loren Lund²/Steve Rembish², Texas Natural Resource Conservation Commission.

Several appendices (Appendices A and C) are included in this guidance to support the summary calculations presented in the main body of the document, to provide tables for screening chemicals for the water pathway and to provide physical constants for specific chemicals (Appendix B).

¹ Currently associated with U.S. EPA Region IX

² Currently associated with Parsons Engineering Science, Inc.

Abbreviations

τ	Lag time (hr)
ABS_d	Fraction of contaminant absorbed dermally
ABS_{GI}	Fraction of contaminant absorbed in gastrointestinal tract
B	Dimensionless ratio of the permeability of the stratum corneum relative to the permeability across the viable epidermis
AF	Adherence factor of soil to skin. Referred to as contact rate in RAGS, Part A.
AT	Averaging time (days)
BW	Body weight (kg)
C_{soil}	Contaminant concentration in soil (mg/kg)
DA_{event}	Absorbed dose per event (mg/cm ² -event)
DAD	Dermally absorbed dose (mg/kg-day)
DEA	Dermal Exposure Assessment: Principles and Applications (U.S. EPA, 1992a)
ED	Exposure duration (years)
EF	Exposure frequency (days/year)
EFH	Exposure Factors Handbook (U.S. EPA, 1997a)
EPA	U. S. Environmental Protection Agency
EPC	Exposure point concentration
EV	Event frequency (events/day)
GI	Gastrointestinal
IR	Water ingestion rate (liters/day)
$K_{b/w}$	Blood-to-water partition coefficient
K_{ow}	Octanol/water partition coefficient
K_p	Dermal permeability coefficient from water
$K_{p,max}$	Maximum permeability coefficient from water
$K_{p,ve}$	Steady-state permeability coefficient through the viable epidermis (ve)
MW	Molecular weight (g/mole)
NCEA	National Center for Environmental Assessment
OHEA	Office of Health and Environmental Assessment

ORD	Office of Research and Development
q_b	Cutaneous blood flow rate per unit area of skin
RAGS	Risk Assessment Guidance for Superfund.
RfD_o	Oral (administered) noncancer reference dose (mg/kg-day)
RfD_{abs}	Absorbed noncancer reference dose (mg/kg-day)
RME	Reasonable maximum exposure
SA	Skin surface area available for contact (cm ²)
SDG	1998 Superfund Interim Guidance for Dermal Risk Assessment
SF_o	Oral (administered) cancer slope factor (mg/kg-day) ⁻¹
SF_{abs}	Absorbed cancer slope factor (mg/kg-day) ⁻¹
SFS_{adj}	Age-adjusted dermal exposure factor (mg-yrs/kg-event)
TCDD	Tetrachlorodibenzodioxin
t_{event}	Exposure time (hr)
THQ	Target Hazard Quotient
TRL	Target Risk Level (cancer)

1. INTRODUCTION AND FLOWCHART

1.1 INTRODUCTION

In January 1992, the Office of Health and Environmental Assessment (OHEA), in the Office of Research and Development (ORD), U. S. Environmental Protection Agency (EPA) issued an interim report, *Dermal Exposure Assessment: Principles and Applications* (U.S. EPA, 1992a). The 1992 ORD document, from now on referred to as *DEA*, provided guidance for conducting dermal exposure assessments. The conclusions of the *DEA* were summarized at the National Superfund Risk Assessors Conference in January 1992 when Regional risk assessors requested that a workgroup be formed to prepare an interim dermal risk assessment guidance for the Superfund program based on the *DEA*. This Superfund program guidance serves to promote consistency in procedures used by the Regions to assess dermal exposure pathways at Superfund sites. In August 1992, a draft Superfund Interim Dermal Risk Assessment Guidance was circulated for comment but was never issued as an OSWER Directive. This current guidance supersedes the 1992 Superfund document.

This 1999 Superfund Interim Guidance for Dermal Risk Assessment (from now on referred to as Superfund Dermal Guidance, or *SDG*) is the result of Superfund Dermal Workgroup meetings from FY 95 through FY 99 on issues associated with the characterization of risk resulting from the dermal pathway of exposure. The *SDG* updates recommendations presented in the *DEA*, the updated Exposure Factors Handbook (U.S. EPA, 1997a), and additional information from literature as cited. Users of this guidance are strongly encouraged to review and understand the material presented in the *DEA*. This guidance is considered interim, pending release of any update to the *DEA* from ORD. As more data become available, the *SDG* may be updated.

It should be noted that this document limits its guidance on dermal exposure assessment to the discussion of systemic chronic health effects resulting from low dose long term exposure. However, acute chemical injury to the skin should also be examined to present accurate and comprehensive assessment of toxicity through the dermal route. The potential for dermal effects such as allergic contact responses, urticarial reactions, hyperpigmentation, and skin cancer should be discussed qualitatively in the exposure section of the risk assessment.

This document does not provide guidance on quantifying dermal absorption of chemicals resulting from exposure to vapors. The Superfund Dermal Workgroup agreed with the finding in the *DEA* report that many chemicals, with low vapor pressure and low environmental concentrations, cannot achieve adequate vapor concentration to pose a dermal exposure hazard. For chemicals with the potential to achieve adequate vapor concentrations, this guidance assumed that they are primarily absorbed through the respiratory tract. Additional information on dermal absorption of chemical vapors can be found in the *DEA*, Chapter 7.

1.2 ORGANIZATION OF DOCUMENT

This guidance is structured to be consistent with the four steps of the Superfund risk assessment process, namely, hazard identification, exposure assessment, toxicity assessment, and risk characterization:

Section 2: Hazard Identification-- identifies those chemicals which contribute to the majority of exposure and risk at a Superfund site.

Section 3: Exposure Assessment-- evaluates the pathways by which individuals could be exposed to chemicals present at a Superfund site.

Section 4: Toxicity Assessment-- identifies the potential adverse health effects associated with the contaminants of concern identified at the site.

Section 5: Risk Characterization-- incorporates information from the three previous sections to evaluate the potential risk to exposed individuals at the site. This section also contains a discussion of the uncertainties associated with estimating risk for the dermal pathway.

Section 6: Conclusions/Recommendations - provides a summary of the main points for each step in the dermal risk assessment process and recommendations for future data needs to improve the evaluation of dermal exposures.

1.3 FLOWCHARTS

The following flowcharts will facilitate the process for performing a dermal risk assessment, by identifying the key steps and the location of specific information. Separate flowcharts are provided for the water and the soil pathways:

Water Pathway-- A screening process will identify those chemicals that should be evaluated for the dermal pathway. The screen identifies those chemicals where the dermal pathway has been estimated to contribute more than 10% of the oral pathway, using conservative residential exposure criteria. Screening tables in Appendix B (Table B.3 for organics and Table B.4 for inorganics) provide a recommendation as to whether the dermal pathway should be evaluated for a given chemical. If so, the next step is to determine the rate of migration of the chemical through the skin, using the permeability coefficient (K_p), derived from either experimentally measured or predicted values. If default residential exposure assumptions are appropriate for the risk assessment, then the DA_{event} term can be extracted from either Table B.3 or B.4, and used with the chemical concentration to

calculate the Dermal Dose (DAD) term. If default residential exposure assumptions are not appropriate, the specific equations and information sources are provided in the flowchart. Finally, the procedures for the toxicity assessment and risk characterization steps are also outlined.

Soil Pathway-- There is no screening process for eliminating chemicals in a soil matrix from a dermal risk assessment, as there is for the water pathway. The first step in the hazard identification process is to determine if quantitative dermal absorption from soil (ABS) values are available for the chemical to be evaluated. If not, the decision needs to be made whether default values are to be used as a surrogate for those chemicals without specific recommended values. If data are available, a site-specific ABS value could be used. The exposure assessment section summarizes exposure parameter values for a RME exposure scenario and also activity-specific values. The steps in the toxicity assessment and risk characterization are the same as for the water pathway.

Figure 1.1 WATER PATHWAY

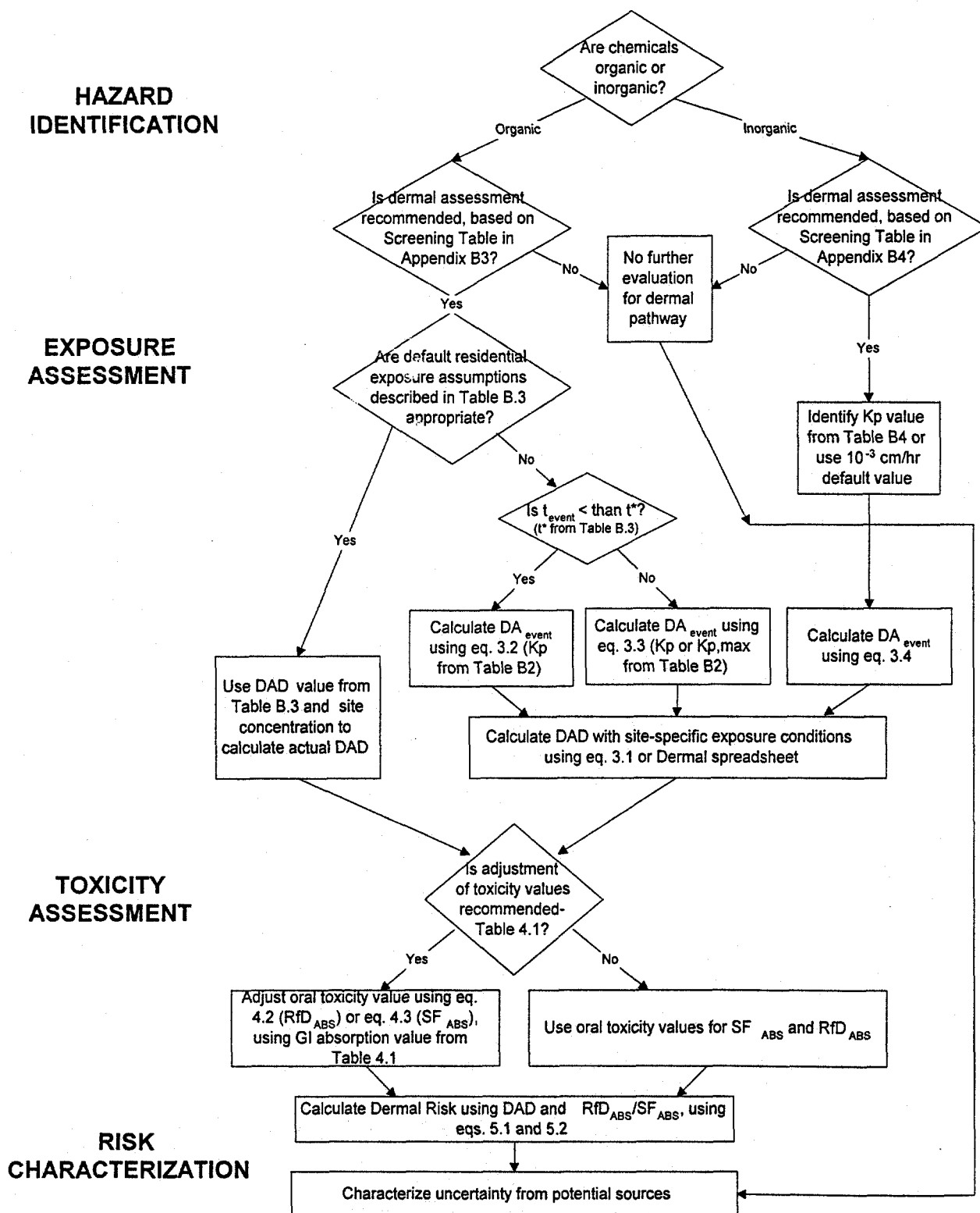


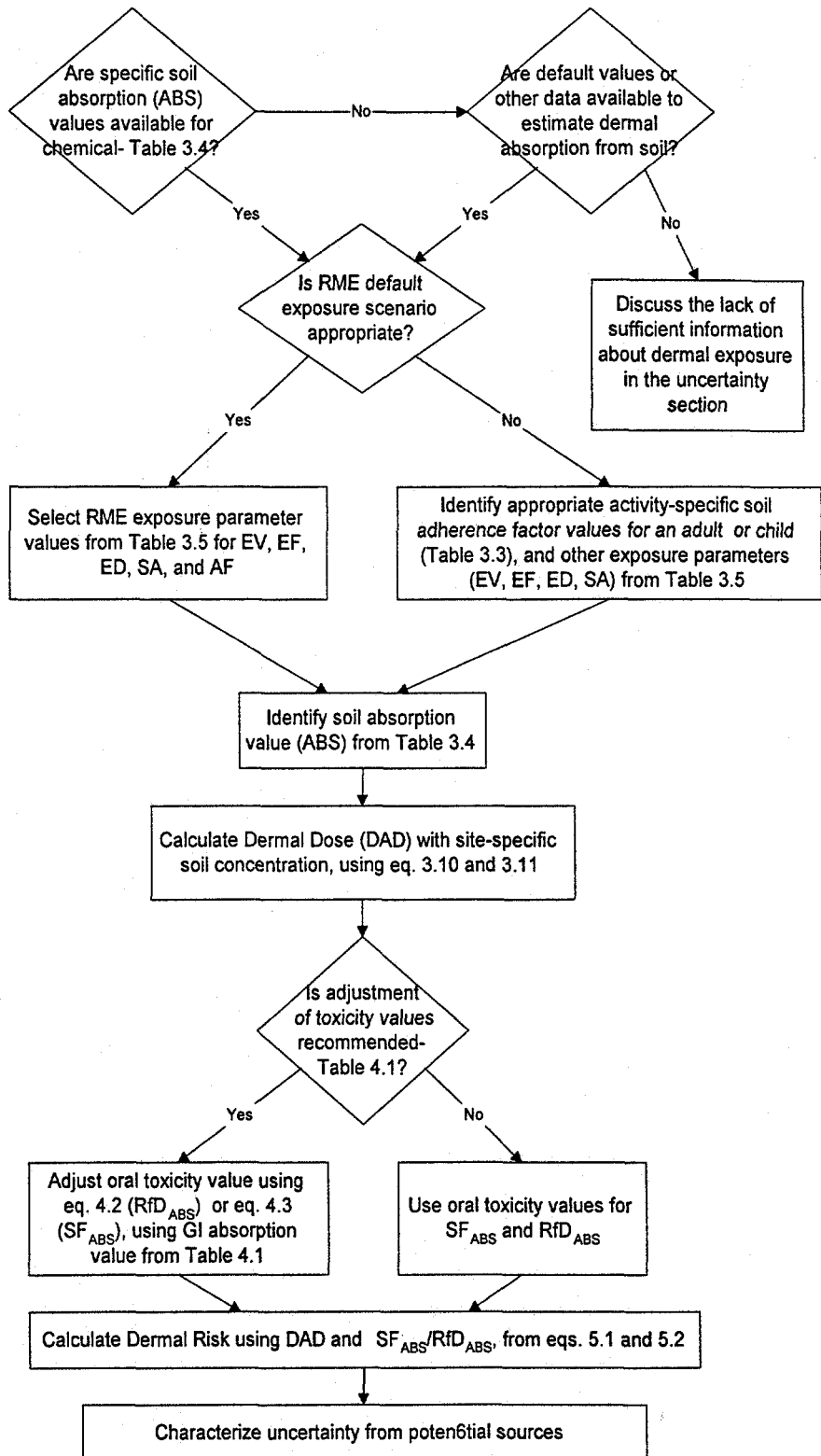
Figure 1.2 SOIL PATHWAY

**HAZARD
IDENTIFICATION**

**EXPOSURE
ASSESSMENT**

**TOXICITY
ASSESSMENT**

**RISK
CHARACTERIZATION**



2. HAZARD IDENTIFICATION

The hazard identification step identifies those chemicals which contribute to the majority of exposure and risk at a Superfund site. The "contaminants of concern" are chemicals chosen because of their occurrence, distribution, fate, mobility and persistence in the environment. Each chemical's concentration and toxicity are also considered. Algorithms, permeability constants and other parameter values presented in this guidance supersede the dermal methodology provided in *DEA* and the Risk Assessment Guidance for Superfund (*RAGS*, U.S. EPA, 1989).

2.1 CHOOSING CONTAMINANTS OF CONCERN FOR THE DERMAL-WATER PATHWAY

For scoping and planning an exposure and risk assessment, assessors will find it useful to know the importance of considering dermal exposure pathways. These assessors must decide the level (from cursory to detailed) of analysis needed to make this decision. The following screening procedure addresses this issue primarily by analyzing when the dermal exposure route is likely to be significant compared to the other routes of exposure. This discussion is based on the methodology in the *DEA*, Chapter 9, using parameters provided in this guidance. Readers are encouraged to consult the *DEA* document for more details.

Table B.3 in Appendix B provides the results of a screening procedure to identify organic chemicals that do not contribute significantly to the risk at a site for the dermal route. This screening procedure is based upon comparing two main household daily uses of water, as a source for drinking and for showering or bathing. This screening procedure is therefore limited to residential exposure scenarios where both ingestion and showering/bathing are considered in the site risk assessment. The screening procedure does not consider swimming exposures, and thus should not be used for screening chemicals in surface water where exposure may be through swimming activity. However, if swimming is an actual or potential exposure scenario in the site risk assessment, dermal exposure should be quantitatively evaluated, using input parameters described in the document.

Note that the results of this screening procedure are the actual results of a quantitative

exposure assessment for these two routes of exposure. All calculations needed for the evaluation of DAD for water, as described in Section 3 and in Appendices A and B, were performed for the list of chemicals presented in Table B.3 and Table B.4, using the exposure conditions specified in each table. These tables are provided as a screening tool for risk assessors to focus the dermal risk assessment on those chemicals that are more likely to make a contribution to the overall risk.

For this guidance the Superfund Dermal Workgroup decided that the dermal route would be significant if it contributed at least 10% of the exposure derived from the oral pathway. The screening results are provided in two columns in Table B.3 and Table B.4: the one labeled "Derm/Drink" gives the actual ratio of the dermal exposure route as compared to the ingestion route (two liters drinking water), and the next one labeled "Chem Assess" gives the result of the comparison as a Y (Yes) or N (No) using the 10% criterion discussed above. When these default exposure assumptions are not appropriate, stepwise instructions are provided in Section 3 and Appendix B to incorporate site-specific exposure parameters.

2.2 CHOOSING CONTAMINANTS OF CONCERN FOR THE DERMAL-SOIL PATHWAY

The number of contaminants evaluated in the risk assessment for the dermal-soil pathway will be limited by the availability of dermal absorption values for chemicals in soil. Very limited data exist in the literature for the dermal absorption of chemicals from soil. Section 3 provides recommended dermal absorption factors for ten chemicals in soil based on well designed studies. If a detected compound does not have a dermal absorption value presented in Section 3, other sources of information such as new exposure studies presented in the peer reviewed literature, or site-specific *in vitro* and *in vivo* studies, may be considered to estimate a dermal absorption value. The EPA risk assessor should be consulted before conducting site-specific dermal absorption studies, to ensure that a scientifically sound study is developed and approved by the Agency.

3. EXPOSURE ASSESSMENT

The exposure assessment evaluates the type and magnitude of exposures to chemicals of potential concern at a site. The exposure assessment considers the **source** from which a chemical is released to the environment, the **pathways** by which chemicals are transported through the environmental medium and the **routes** by which individuals are exposed. Parameters necessary to quantitatively evaluate dermal exposures such as permeability coefficients, soil absorption factors, body surface area exposed and soil adherence factors are developed in the exposure assessment. In this section the dermal assessment is evaluated for two exposure media, water (Section 3.1) and soil (Section 3.2).

EPA's *Guidance for Risk Characterization* (U.S. EPA, 1995) requires that each Agency risk assessment provide a description of risks to individuals in average and high end portions of exposure distribution. Generally, within the Superfund program, to estimate exposure to an average individual (i.e., a central tendency), the 95% upper confidence limit on the arithmetic mean is chosen for the exposure point concentration and central estimates (i.e., arithmetic average, 50th percentile, median) are chosen for all other exposure parameters. This guidance document provides recommended central tendency values for dermal exposure parameters, using updated information from the Exposure Factors Handbook (U.S. EPA, 1997a).

In comparison with the average exposure, the "high end" exposure estimate is defined as the highest exposure that is reasonably expected to occur at a site but that is still within the range of possible exposures, referred to as the reasonable maximum exposure (**RME**) (U.S. EPA, 1989). According to the *Guidance on Risk Characterization for Risk Managers and Risk Assessors* (U.S. EPA, 1992b), risk assessors should approach the estimation of the RME by identifying the most sensitive exposure parameters. The sensitivity of a parameter generally refers to its impact on the exposure estimates, which correlates with the degree of variability of the parameter values. Parameters with a high degree of variability in the distribution of parameter values are likely to have a greater impact on the range of risk estimates than those with low variability. For one or a few of the sensitive parameters, the maximum or near-maximum values should be

used, with central tendency or average values used for all other parameters. The high-end estimates are based, in some cases, on statistically based criteria (95th or 90th percentiles), and in others, on best professional judgment. In general, exposure duration, exposure frequency and contact rate are likely to be the most sensitive parameters in an exposure assessment (U.S. EPA, 1989). In addition, for the dermal exposure route, the soil adherence factor term is also a very sensitive parameter. This guidance provides recommended upper end estimates for individual exposure parameters and a recommended RME exposure scenario for residential and industrial settings, using updated information from the Exposure Factors Handbook (U.S. EPA, 1997a) and other literature sources.

3.1 ESTIMATION OF DERMAL EXPOSURES TO CHEMICALS IN WATER

3.1.1 Standard Equation for Dermal Contact with Chemicals in Water

The same mathematical model for dermal absorption recommended in *DEA* is used here. The skin is assumed to be composed of two main layers, the stratum corneum and the viable epidermis, with the stratum corneum as the main barrier. A two-compartment distributed model was developed to describe the absorption of chemicals from water through the skin as a function of both the thickness of the skin and the duration of exposure (the mass balance equation follows Fick's second law and is a partial differential equation with concentration as a function of both time and distance). The exact solution of this model is approximated by two algebraic equations: (1) to describe the absorption process when the chemical is only in the stratum corneum, i.e., non-steady state, where absorption is a function of $\sqrt{t_{\text{event}}}$; and (2) to describe the absorption process as a function of t_{event} , once steady state is reached.

The following procedures present recommendations from the *DEA*, modified by updates. For chemicals in water, the following equations are used to evaluate the dermal absorbed dose:

$$DAD = \frac{DA_{\text{event}} EV ED EF SA}{BW AT} \quad (3.1)$$

where:

- DAD = Dermal Absorbed Dose (mg/kg-day)
 DA_{event} = Absorbed dose per event per area of skin exposed (mg/cm²-event)
 SA = Skin surface area available for contact (cm²)
 EV = Event frequency (events/day)
 EF = Exposure frequency (days/year)
 ED = Exposure duration (years)
 BW = Body weight (kg)
 AT = Averaging time (days), for noncarcinogenic effects AT = ED * 365 days/yr,
 and for carcinogenic effects AT = 70 year * 365 days/yr or 25,550 days

DA_{event} (mg/cm²-event) is calculated as follows :

For organic compounds:

$$\text{If } t_{event} \leq t^*, \text{ then: } DA_{event} = 2 K_p C_w \sqrt{\frac{6 \tau_{event} t_{event}}{\pi}} \quad (3.2)$$

$$\text{If } t_{event} > t^*, \text{ then: } DA_{event} = K_p C_w \left[\frac{t_{event}}{1 + B} + 2 \tau_{event} \left(\frac{1 + 3B + 3B^2}{(1 + B)^2} \right) \right] \quad (3.3)$$

where:

K_p = Skin permeability constant for compounds in water (cm/hr)

C_w = Chemical concentration in water (mg/cm³)

(Note: if water concentration units are µg/L, then multiply by 10⁻⁶ to convert to mg/cm³)

τ_{event} = Lag time per event (hr/event)

t_{event} = Event duration (hr/event)

t^* = Time to reach steady-state (hr) = 2.4 τ_{event}

B = Dimensionless ratio of the permeability of the stratum corneum relative to the permeability across the viable epidermis (and any other limitations to chemical transfer through the skin, including clearance into the cutaneous blood).

For short exposure times (Equation 3.2), calculating B is not necessary, because neither the viable epidermis nor the cutaneous blood flow will limit dermal absorption during such short times. For long exposure times, Equation 3.3 should be used to estimate DA_{event} for all chemicals. Because the skin has limited capacity to hold either inorganic or highly ionized organic chemicals, the lag time is shortened. In addition, the viable epidermis will contribute insignificantly as a barrier to these chemicals. Consequently, it is appropriate to assume that τ_{event} and B are both nearly zero. This would reduce Equation 3.3 to the following, used for both inorganic or highly ionized organic chemicals:

$$DA_{event} = K_p C_w t_{event} \quad (3.4)$$

Detailed discussion of the dermal absorption model and equations for calculating all the parameters to evaluate the dermal absorbed dose (DA_{event} in Equations 3.3 and 3.4) are in Appendix A.1. Discussion on the permeability coefficient (K_p) and all other parameters for water media are summarized in Section 3.1.2, with detailed discussion and data in Appendix A.2. Appendix B (Tables B-3 and B-4), contains chemical-specific DA_{event} and DAD values per unit

concentration, using default assumptions. A spreadsheet with instructions for calculating DA_{event} and DAD values with site-specific exposure assumptions will be provided with the document and will also be available on the Internet.

3.1.2 Exposure Parameters

3.1.2.1 Permeability coefficient for compounds in water (K_p in cm/hr)

Some discussion of criteria for selecting an experimental K_p was presented in *DEA*, Chapter 5. Because of the difficulty of selecting standard experimental conditions, most representative K_p of human exposure conditions and lacking experimental K_p values for most contaminants of concern, the procedure recommended by this SDG to estimate the permeability coefficient (K_p) of a compound is obtained from review of this subject in *DEA*. Updated K_p values for over two hundred common organic compounds in water are provided in Appendix B, as estimated using procedures described below. It is recommended that these K_p values be used in Equations 3.2 and 3.3. K_p values for several inorganic compounds and a default permeability constant for all other inorganic compounds are given in Table 3.1, to be used in Equation 3.4.

3.1.2.1.1 Organics:

The permeability coefficient is a function of the path length of chemical diffusion (defined here as stratum corneum thickness, l_{sc}), the membrane/vehicle partition coefficient (here as octanol/water partition coefficient K_{ow}) of the chemical, and the diffusion coefficient (D_{sc}) of the chemical in the stratum corneum, and can be written for a simple isotropic membrane as:

$$K_p = \frac{K_{ow} D_{sc}}{l_{sc}} \quad (3.5)$$

or:

$$\log K_p = \log K_{ow} + \log \frac{D_{sc}}{l_{sc}} \quad (3.6)$$

In this approach, K_p is estimated via an empirical correlation as a function of K_{ow} and MW (Potts and Guy, 1992) obtained from an experimental data base (the Flynn data base composed of about 90 chemicals, see *DEA*, Chapter 4, and Appendix A of this document) of absorption of chemicals from water through human skin in vitro:

$$\log K_p = -2.80 + 0.67 \log K_{ow} - 0.0056 MW \quad (r^2 = 0.66) \quad (3.7)$$

where: K_p = permeability coefficient (cm/hr)
 K_{ow} = octanol/water partition coefficient
 MW = molecular weight of the compound.

For ionized organic compounds, Equation 3.7 can be used to estimate K_p with the appropriate K_{ow} value. Note that for ionizable organic chemicals, the K_{ow} value used in Equation 3.7 should be the K_{ow} of only species not ionized. Organic chemicals which are always ionized (including ionized but uncharged zwitterions) and ionized species of ionizable organic chemicals at the conditions of interest should be treated the same as inorganic chemicals.

Based on the Flynn data set, the above equation can be used to predict the permeability coefficient of chemicals with K_{ow} and MW within the following "Effective Predictive Domain"(EPD), determined via a statistical analysis (see Appendix A, Section A.2):

$$-0.069 \leq 0.508 \times 10^{-4} MW + 0.0565 \log K_{ow} \leq 0.559 \quad (3.8)$$

If the $\log K_{ow}$ and MW are outside the predictive domain, a maximum K_p ($K_{p,max}$) can be estimated as presented in Appendix A.2. The appropriate use of K_p and $K_{p,max}$ in Equations 3.2

$$-0.301 \leq -0.508 \times 10^{-4} MW + 0.0565 \log K_{ow} \leq 0.146 \quad (3.9)$$

and 3.3 is also discussed in detail there. Estimations of K_p and its application into the estimation of DA_{event} , and subsequently DAD are included in Table B.3 for about two hundred chemicals.

3.1.2.1.2 Inorganics

Table 3.1 summarizes permeability coefficients for inorganic compounds, obtained from specific chemical experimental data, as modified and updated from *DEA* Table 5-3 and from J.J. Hostynek, *et al.* (in press). Permeability coefficients from these references are condensed for each metal and for individual valence states of specific metals. To be most protective of human health, the value listed in this table represents the highest reported permeability coefficient. More detailed information is presented in Appendix A (Table A.2).

Table 3.1 Permeability Coefficients for Inorganics

Compound	Permeability Coefficient K_p (cm/hr)
Cadmium	1×10^{-3}
Chromium (+6)	2×10^{-3}
Chromium (+3)	1×10^{-3}
Cobalt	4×10^{-4}
Lead	1×10^{-4}
Mercury (+2)	1×10^{-3}
Methyl mercury	1×10^{-3}
Mercury vapor	0.24
Nickel	2×10^{-4}
Potassium	2×10^{-3}
Silver	6×10^{-4}
Zinc	6×10^{-4}
All other inorganics	1×10^{-3}

3.1.2.2 Chemical concentration in water

One of the issues regarding the bioavailability of chemicals in water is the state of ionization, with the nonionized form being much more readily absorbed than the ionized form.. The fraction of the chemical in the nonionized state is dependent of the pH of the water and the specific ionization constant for that chemical (pK_a). Further information on the formulas for calculating these fractions are provided in the *DEA* and in Appendix A. However, given the complexities of calculating the nonionized fraction across multiple samples and multiple chemicals, it is recommended that a standard risk assessment should make the conservative assumption that the chemical is entirely in the nonionized state. Therefore, C_w should be equal to the total concentration of the chemical in water.

3.1.2.3 Skin surface area

The surface area (SA) parameter describes the amount of skin exposed to the contaminated media. The amount of skin exposed depends upon the exposure scenario. For dermal contact with water, the total body surface area for adults and children is assumed to be exposed for both swimming and bathing. Since body weight and SA are dependent variables, all SA estimates used 50th percentile values in order to correlate with the average body weights. The recommended SA exposed to contaminated water for the adult resident is 18,000 cm². This SA value was calculated by incorporating data from *EFH* (U.S. EPA, 1997a), Tables 6.2 and 6.3, averaging the 50th percentile values for males and females.

The recommended SA value for exposure to contaminated water for the child resident is 6,600 cm². This SA was calculated by incorporating the data from of the *EFH* (U.S. EPA, 1997a), for the 50th percentile of the total body surface area for male and female children and calculating a time weighted average surface area for a 0<6 year old child. However, lack of data, led to a conservative assumption that a 0<1 year old and 1<2 year old had the same surface area as a 2<3 year old. This recommended child SA was calculated by averaging the male and female surface areas.

3.1.2.4 Event time, frequency and duration of exposure

Table 3.2 summarizes the default exposure values for both surface area and exposure duration, presented as central tendency and RME. All the central tendency values were obtained from the *EFH* (U.S. EPA, 1997a), while the RME values were derived as previously presented. Recommended event duration values are provided for a showering activity. Even though children may be bathing for a longer duration, the showering adult remains the most highly exposed receptor.

Table 3.2 Recommended Dermal Exposure Values for Central Tendency and RME Residential Scenarios - Water Contact

Exposure Parameters	Central Tendency Scenario				RME Scenario			
	Showering/ Bathing		Swimming		Showering/ Bathing		Swimming	
Concentration- C_w (mg/cm ³)	Site-specific		Site-specific		Site-specific		Site-specific	
Event frequency (events/day)	1		Site-specific		1		Site-specific	
Exposure frequency (days/yr)	350		Site-specific		350		Site-specific	
Event duration (hr/event)	Adult ¹	Child ²	Adult	Child	Adult ¹	Child ²	Adult	Child
	0.25	0.33	Site-specific		0.58	1.0	Site-specific	
Exposure Duration (yr)	9	6	9	6	30	6	30	6
Skin surface area (cm ²)	18,000	6,600	18,000	6,600	18,000	6,600	18,000	6,600
Permeability coefficient- K_p (cm/hr)	Chemical-specific values (Tables B.3 and B.4)							

¹ Adult showering scenario used as the basis for the chemical screening for the dermal pathway, as shown in Appendix Tables B.3 and B.4. Event duration for adult exposure is based on showering data from the *EFH* (U.S. EPA, 1997a).

² Event duration for child exposure is based on bathing data from the *EFH* (U.S. EPA, 1997a).

3.2 ESTIMATION OF DERMAL EXPOSURE TO CHEMICALS IN SOIL

3.2.1 Standard Equation for Dermal Contact with Chemicals in Soil

The general guidance for evaluating dermal absorption of compounds from soil is presented in Risk Assessment Guidance for Superfund (RAGS, U.S. EPA, 1989) and is expanded upon in the ORD, *DEA* (U.S. EPA, 1992a). This section briefly discusses the rationale and update specific parameters. The standard equation for dermal contact with chemicals in soil is the same as that in Section 3.

$$DAD = \frac{DA_{event} EF ED EV SA}{BW AT} \quad (3.10)$$

where:

DAD	=	Dermal absorbed dose (mg/kg-day)
DA_{event}	=	Absorbed dose per event (mg/cm ² -event)
SA	=	Skin surface area available for contact (cm ²)
EF	=	Exposure frequency (events/year)
ED	=	Exposure duration (years)
EV	=	Event/day (default assumption= 1 event/day)
BW	=	Body weight (kg)
AT	=	Averaging time (days), for noncarcinogenic effects AT = ED * 365 days/yr, and for carcinogenic effects AT = 70 years * 365 days/yr or 25,550 days

DA_{event} (mg/cm²-event) for soil can be calculated as follows.

$$DA_{event} = C_{soil} CF AF ABS_d \quad (3.11)$$

where:

- C_{soil} = Contaminant concentration in soil (mg/kg)
- CF = Conversion factor (10^{-6} kg/mg)
- AF = Adherence factor of soil to skin (mg/cm²-event) (also referred to as Contact rate in RAGS, Part A)
- ABSd = Dermal absorption fraction

A discussion of each parameter follows in the next section.

3.2.2 Exposure Parameters

3.2.2.1 Skin surface area

The skin surface area parameter (SA) describes the amount of skin exposed to the contaminated media. The amount of skin exposed depends upon the exposure scenario. Clothing is expected to limit the extent of the exposed surface area in cases of soil contact. All SA estimates used 50th percentile values to correlate with average body weights used for all scenarios and pathways. This was done to prevent inconsistent parameter combinations since body weight and SA are dependent variables. Body part-specific SAs were calculated for adult (>18 years old) and child (<1 to <6 years old) residents as described below and documented in Appendix C.

3.2.2.1.1 Adult resident

The adult resident was assumed to wear a short-sleeved shirt, shorts and shoes and therefore, the exposed skin surface is limited to the head, hands, forearms and lower legs. The recommended SA exposed to contaminated soil for the adult resident is 5700 cm² and is the average of the 50th percentile for males and females greater than 18 years of age. Surface area data were taken from *EFH* (U.S. EPA, 1997a), Tables 6-2 (adult male) and 6-3 (adult female). Exposed SA for the adult resident was calculated using Equation 3.12, documented in Appendix C with the assumption that the female adult forearm SA was 45% of the arm SA.

$$\text{Exposed SA (Adult Resident)} = SA_{\text{head}} + SA_{\text{forearms}} + SA_{\text{hands}} + SA_{\text{lower legs}} \quad (3.12)$$

3.2.2.1.2 Adult commercial/industrial.

The adult commercial/industrial receptor was assumed to wear a short-sleeved shirt, long pants, and shoes; therefore, the exposed skin surface is limited to the head, hands, and forearms. The recommended SA exposed to contaminated soil for the adult commercial/industrial receptor is 3300 cm² and is the average of the 50th percentile for males and females greater than 18 years of age. Surface area data were taken from *EFH*, Tables 6-2 (adult male) and 6-3 (adult female). Exposed SA for the adult commercial/industrial receptor was calculated using Equation 3.13 and is documented in Appendix C with the assumption that the female adult forearm SA was 45% of the arm SA (based on the adult male forearm-to-arm SA ratio).

$$\text{Exposed SA (Adult Commercial/Industrial)} = SA_{\text{head}} + SA_{\text{forearms}} + SA_{\text{hands}} \quad (3.13)$$

3.2.2.1.3 Child

The child resident (<1 to <6 year old) was assumed to wear a short-sleeved shirt and shorts (no shoes) and therefore, the exposed skin is limited to the head, hands, forearms, lower legs, and feet. The recommended SA exposed to contaminated soil for the child resident is 2800 cm² and is the average of the 50th percentile for males and females (<1 to <6 years old). Body part-specific data for male and female children were taken from *EFH*, Table 6-8, as a fraction of total body surface area. Total body SAs for male and female children were taken from *EFH*, Tables 6-6 (male) and 6-7 (female), and used to calculate average male/female total SA (see Appendix C). Exposed SA for the child resident was calculated, using Equations 3.14 and 3.15 and is documented in Appendix C with the following assumptions: (1) because of the lack of data for certain ages, the fraction of total SA was assumed to be equal to the next oldest age group that had data and (2) the forearm-to-arm ratio (0.45) and lower leg-to-leg ratio (0.4) are equivalent to those of an adult. These assumptions introduce some uncertainty into the calculation, but are

used in the absence of age-specific data.

$$\text{Fraction of Total } SA_{\text{body part } i} = \frac{SA \text{ fraction}_{\text{age } <1} + SA \text{ fraction}_{\text{age } 1<2} + \dots + SA \text{ fraction}_{\text{age } 5<6}}{6} \quad (3.14)$$

$$\text{Exposed } SA = (FTSA_{\text{head}})(SA_{\text{total}}) + (FTSA_{\text{forearms}})(SA_{\text{total}}) + (FTSA_{\text{hands}})(SA_{\text{total}}) + (FTSA_{\text{lowerlegs}})(SA_{\text{total}}) + (FTSA_{\text{feet}})(SA_{\text{total}}) \quad (3.15)$$

where:

FTSA = Fraction total surface area for the specified body part (unitless);

SA_{total} = Total body surface area (cm²); and

(FTSA_i)(SA_{total}) = Surface area for body part "i" (cm²).

While clothing scenarios described above for the adult and child residents may not be appropriate for all regions, the climate in some areas would allow a short-sleeved shirt and/or shorts to be worn throughout a majority of the year. In addition, in some regions of the country children may remain barefoot throughout a major portion of the year. These clothing scenarios were chosen to ensure adequate protection for those receptors that may be exposed in the warmer climates and with the realization that risks would likely be overestimated for some seasons. reduced. For colder climates, the surface area may be weighted for different seasons after coordination with the project risk assessors. As some studies have suggested that exposure can occur under clothing (Maddy *et al.*, 1983), these clothing scenarios are not considered to be overly conservative and the site specific factors should be evaluated when selecting the surface area.

3.2.2.2 Soil-to-skin adherence factors

The adherence factor (AF) describes the amount of soil that adheres to the skin per unit of surface area. Recent data (Kissel *et al.*, 1996a; Kissel *et al.*, 1996b; Kissel *et al.*, 1998; and Holmes *et al.*, 1999) provide evidence to demonstrate that, 1) soil properties influence adherence, 2) soil adherence varies considerably across different parts of the body; and 3) soil adherence varies with activity.

Given these results, the workgroup recommends that an activity which best represents all soils, body parts, and activities be selected (U.S. EPA, 1997a). Body part-weighted AFs can then be calculated and used in estimating exposure via dermal contact with soil based on assumed exposed body parts.

Given that soil adherence depends upon the body part, an overall body part-weighted AF must be calculated for each activity. The assumed clothing scenario determines which body part-specific AFs are used in calculating the 50th and 95th percentile weighted AFs. The weighted AFs are used with the relative absorption, exposure frequency and duration, exposed surface area, body weight, and averaging time to estimate the dermal absorbed dose.

The general equation used to calculate the weighted AF for a particular activity is shown in Equation 3.16.

$$\text{Weighted AF} = \frac{(AF_1)(SA_1) + (AF_2)(SA_2) + \dots + (AF_i)(SA_i)}{SA_1 + SA_2 + \dots + SA_i} \quad (3.16)$$

where:

AF_i = Overall soil adherence factor for body part "T"; and

SA_i = Surface area for body part "T"

3.2.2.2.1 Adult resident

The adult resident (>18 years old) was assumed to wear a short-sleeved shirt, shorts and shoes; therefore, the exposed skin surface was limited to the face, hands, forearms and lower legs. The weighted AFs for adult residential activities (e.g., grounds keepers, landscapers, and gardeners) were calculated, using Equation 3.17, documented in Appendix C. Note: This calculation differs from that presented in section 3.2.2.1 in the areas used for head and face. In the total surface area calculation presented earlier the total head area was used. For the soil-to-skin adherence factor, empirical measurements were from the face only and the face surface

area was estimated to be 1/3 the total head surface area.

$$\text{Weighted } AF_{\text{adult resident}} = \frac{(AF_{\text{face}})(SA_{\text{face}}) + (AF_{\text{forearms}})(SA_{\text{forearms}}) + (AF_{\text{hands}})(SA_{\text{hands}}) + (AF_{\text{lowerlegs}})(SA_{\text{lowerlegs}})}{SA_{\text{face}} + SA_{\text{forearms}} + SA_{\text{hands}} + SA_{\text{lowerlegs}}} \quad (3.17)$$

3.2.2.2.2 Adult commercial/industrial

The adult commercial/industrial receptor was assumed to wear a short-sleeved shirt, long pants, and shoes; therefore, the exposed skin surface was limited to the face, hands, and forearms. The weighted AFs for adult commercial/industrial activities (e.g., grounds keepers, landscapers, irrigation installers, gardeners, construction workers, equipment operators, and utility workers) were calculated, using Equation 3.18, and documented in Appendix C.

$$\text{Weighted } AF_{\text{adult commercial}} = \frac{(AF_{\text{face}})(SA_{\text{face}}) + (AF_{\text{forearms}})(SA_{\text{forearms}}) + (AF_{\text{hands}})(SA_{\text{hands}})}{SA_{\text{face}} + SA_{\text{forearms}} + SA_{\text{hands}}} \quad (3.18)$$

3.2.2.2.3 Child resident

The child resident (<1 to <6 year old) was assumed to wear a short-sleeved shirt and shorts (no shoes); therefore, the exposed skin was limited to face, hands, forearms, lower legs, and feet. Weighted AFs for day care kids and "staged" children playing in dry and wet soil activities were calculated, using Equation 3.19, and documented in Appendix C.

$$\text{Weighted } AF_{\text{child}} = \frac{(AF_{\text{face}})(SA_{\text{face}}) + (AF_{\text{forearms}})(SA_{\text{forearms}}) + (AF_{\text{hands}})(SA_{\text{hands}}) + (AF_{\text{lowerlegs}})(SA_{\text{lowerlegs}}) + (AF_{\text{feet}})(SA_{\text{feet}})}{SA_{\text{face}} + SA_{\text{forearms}} + SA_{\text{hands}} + SA_{\text{lowerlegs}} + SA_{\text{feet}}} \quad (3.19)$$

As noted in Appendix C, body part-specific AFs for both child and adult receptors were not always available for all body parts assumed to be exposed. Weighted adherence factors for receptors were calculated, using only those body parts for which AFs were available because of

the difficulty in trying to assign an AF for one body part to another body part. For example, the weighted AF for the day care kids was based on the forearms, hands, lower legs, and feet (AFs for the face were not available). However, the surface area for all exposed body parts was used in calculating the dermal absorbed dose. For the day care child example, the surface area used in estimating the DAD included the whole head, forearms, hands, lower legs and feet. Therefore, the body part that may not have had AF data available was assumed, by default, to have the same amount of soil adhered as the weighted AF.

3.2.2.3 Recommended soil adherence factors

This section recommends default soil AFs for the child resident, the adult resident, and the adult commercial/industrial worker and provide the bases for the recommendations. EPA suggests selecting an activity from AF data which best represents the exposure scenario of concern and using the corresponding weighted AF in the dermal exposure calculations (U.S. EPA, 1997a). To make this selection, activities with available AFs were categorized as those that a typical residential child, residential adult, and commercial/industrial adult worker would be likely to engage in (see Appendix C). Within each receptor category, activities were ranked in order from the activity with the lowest to highest weighted AF (50th percentile). The 50th percentile weighted AF was used in ranking the activities from those with the lowest to highest weighted AFs, because the 50th percentile is a more stable estimation of the true AF (i.e., it is not affected as significantly by outliers as the 95th percentile).

Typically with other contact rates (e.g., soil ingestion), the recommended default value is a conservative, health protective value. To maintain consistency with this approach (i.e. recommending a high-end of a mean), two options exist when recommending default weighted AFs: (1) select a central tendency (i.e., typical) soil contact activity and use the high-end weighted AF (i.e., 95th percentile) for that activity; or (2) select a high-end (i.e., reasonable but higher exposure) soil contact activity and use the central tendency weighted AF (i.e., 50th percentile) for that activity.

It is not recommended that a high-end soil contact activity be used with a high-end weighted

AF for that activity, as this use would not be consistent with the use of a reasonable maximum exposure (RME) scenario. The use of these values also needs to be evaluated when combining multiple exposure pathways to insure that an overall RME is being maintained.

3.2.2.3.1 Adult resident

Given that there were data available for a wide variety of activities that an adult resident may engage in, a high-end soil contact activity was selected and the central tendency weighted AF (50th percentile) derived for that activity. In so doing, the recommended weighted AF for an adult resident is 0.07 mg/cm² and is based on the 50th percentile weighted AF for gardeners (the activity determined to represent a reasonable, high-end activity). The basis for this recommendation is as follows: (1) although no single activity would represent the activities an adult resident engages in, a comparison of the gardener 50th percentile weighted AF with the other residential-type activities (Appendix C) shows that the gardener represents a high-end soil contact activity; (2) common sense suggests that gardening represents a high-end soil contact activity, whereas, determining which of the other activities (i.e., grounds keeping and landscaping/rockery) would represent a reasonable, central tendency (i.e., typical) soil contact activity would be difficult; and (3) selecting the central tendency weighted AF (i.e., 50th percentile) of a high-end soil contact activity is consistent with an RME for contact rates.

3.2.2.3.2 Child resident (<1 to <6 years old)

Available data on soil AFs for children were limited to children (1-6 ½ years old) playing indoors and outdoors (3.5-4 hours) at a day care center (reviewed in U.S. EPA, 1997a) and children (8-12 year old) playing for 20 minutes with an assortment of toys and implements in a preconstructed 8'x8' soil bed (i.e., "staged" activity) containing dry or wet soil (see Kissel *et al.*, 1998, and Appendix C). Therefore, it was not possible to identify a reasonable worst-case soil contact activity as was done for the adult resident. As such, both approaches: (1) selecting a central tendency (i.e., typical) soil contact activity and using the high-end weighted AF (i.e., 95th percentile) for that activity; and, (2) selecting a high-end soil contact activity and using the central tendency weighted AF (i.e., 50th percentile) for that activity were used in determining the

appropriate weighted AF for children. The recommended weighted AF for a child resident (<1 to <6 years old) is 0.2 mg/cm² and is based on the 95th percentile weighted AF for children playing at a day care center (central tendency soil contact activity) or the 50th percentile for children playing in wet soil (high-end soil contact activity).

Children playing at a day care center represents a central tendency (i.e. typical) activity given that: (1) the children played both indoors and outdoors; (2) the clothing worn was not controlled (i.e., some subjects wore long pants, long-sleeve shirts, and/or shoes); and (3) soil conditions were not controlled (e.g., other soil types, moisture content, etc., could result in higher AFs). The 95th percentile weighted AF for children playing at the day care center is a known, reasonable, “real-life” activity that represents the majority of the population, given that children 1 to 6 years old are either in day care or at home and are likely engaging in activities similar to those at the day care center and represents a high-end of a typical activity.

The “staged” activity of children playing in wet soil for 20 minutes under controlled conditions (i.e., all subjects were clothed similarly, the duration of soil contact was controlled, and the soil properties were characterized) is a high-end soil contact activity because: (1) the children were in direct contact with soil for the full duration of the activity; and (2) the children played in wet soil, which is known to have higher AFs than dry soil, for the duration of the activity. The 50th percentile weighted AF for children playing in wet soil is a central tendency estimate of a high-end soil contact activity.

Use of the 95th percentile weighted AF for children playing at a day care center (0.2 mg/cm²) or the 50th percentile for children playing in wet soil (0.2 mg/cm²) as a recommended weighted AF for a child resident (<1 to <6 years old) is consistent with recommending a high-end of a mean for contact rates.

While this value (0.2 mg/cm²) is at the lower end of the range of soil adherence factors reported in U.S. EPA (1995) and based on Lepow *et al.* (1975) and Roels *et al.* (1980) studies, note that those studies were not designed to study soil adherence and only allowed calculation of soil adherence to hands. In addition, the central-tendency adherence factor of 0.2 mg/cm²

estimated here is based on soil adherence studies for all of the relevant body parts (i.e., head, hands, forearms, lower-legs, and feet). Kissel *et al.* (1998) reports soil adherence factors for children's hands of 0.5-3 mg/cm² (median of 1 mg/cm²) for relatively moist soil, which is comparable to the range of values previously reported for soil adherence to children's hands (0.5-1.5 mg/cm²; U.S. EPA, 1997a). Table C-4 contains data used to calculate the central tendency and high end AFs for children.

3.2.2.3.3 Commercial/industrial adult worker

Given that there were data available for a wide variety of activities that a commercial/industrial adult worker may engage in, a high-end soil contact activity was selected and the central tendency weighted AF (50th percentile) derived for that activity. In so doing, the recommended weighted AF for a commercial/industrial adult worker is 0.2 mg/cm² and is based on the 50th percentile weighted AF for utility workers (the activity determined to represent a high-end contact activity). The bases for this recommendation are as follows: (1) although no single activity would be representative of activities a commercial/industrial adult worker engages in, a comparison of the utility worker 50th percentile weighted AF with other commercial/industrial-type activities (Table 3.3) shows that the utility worker represents a high-end soil contact activity (i.e., grounds keepers, landscaper/rockery, irrigation installers, gardeners, construction workers); (2) a combination of common sense and data on the weighted AFs supports the assumption that utility worker activities represent a high-end soil contact activity, whereas, determining which of other measured activities might represent a reasonable, central tendency (i.e., typical) soil contact activity would be difficult; and (3) selecting the central tendency weighted AF (i.e., 50th percentile) of a high-end soil contact activity is consistent with a RME for contact rates.

3.2.2.3.4 Recreational

No specific default values are being recommended for a recreational scenario since many site-specific concerns will impact the choice of exposure variables, such as, climate, geography, location, and land-use. The risk assessors, in consultation with the project team, should reach

consensus on the need to evaluate this scenario and the inputs before incorporating this into the risk assessment. The *Exposure Factors Handbook* (U.S. EPA, 1997a) should be consulted to obtain appropriate exposure estimates.

Table 3.3 Activity Specific-Surface Area Weighted Soil Adherence Factors

EXPOSURE SCENARIO	Age (yr)	Weighted AF (mg/cm ²)	
		50th %	95th %
CHILDREN¹			
Children Playing (dry soil)	8-12	0.04	0.2
Day care Kids	1-6.5	0.06	0.2
Children Playing (wet soil)	8-12	0.2	2.7
Kids-in-mud ⁵	9-14	(22)	(123)
RESIDENTIAL ADULTS²			
Grounds keepers	>18	0.01	0.5
Landscape/Rockery	>18	0.04	0.1
Gardeners	>16	0.07	0.3
COMMERCIAL/INDUSTRIAL ADULTS³			
Grounds keepers	>18	0.02	0.7
Landscape/Rockery	>18	0.04	0.1
Irrigation Installers	>18	0.08	0.2
Gardeners	>16	0.1	0.4
Construction Workers	>18	0.1	0.3
Equip. Operators	>18	0.2	0.6
Utility Workers	>18	0.2	0.8
OTHER RECEPTORS⁴			
Soccer No. 1 (teens:moist conditions)	13-15	0.04	0.2
Soccer Nos. 2&3 (adults)	>18	0.01	0.07
Archeologists	>16	0.09	0.3
Farmers	>18	0.1	0.4
Rugby	>18	0.1	0.6
Reed Gatherers	>18	0.3	6.3

¹ Weighted AF based on exposure to face, forearms, hands, lower legs, & feet.

² Weighted AF based on exposure to face, forearms, hands, & lower legs.

³ Weighted AF based on exposure to face, forearms, & hands.

Note: this results in different weighted AFs for similar activities between residential and commercial/industrial exposure scenarios.

⁴Weighted AF based on all body parts for which data were available.

⁵Information on soil adherence values for the Kids-in-mud scenario is provided to illustrate the range of values for this type of activity. However, the application of these data to the dermal dose equations in this guidance will result in a significant overestimation of dermal risk. Therefore, it is recommended that these AF values not be used in a quantitative dermal risk assessment.

3.2.2.4 Dermal absorption fraction from soil

Methodologies for evaluating the applicability of experimental results to the exposure scenario of concern are presented in *DEA*, Chapter 6. In this document, ORD reviewed the available experimental data for dermal absorption from contaminated soil and presented recommendations for three compounds/classes. Recommendations were presented as ranges to account for uncertainty which may arise from different soil types, loading rates, chemical concentrations, and other conditions. In this interim dermal guidance for Superfund, selection of a single value is based on recommended ORD ranges to simplify the screening risk calculation. In addition, recommended values for other compounds according to review of literature and default values for classes of compounds are provided. For tetrachlorodibenzodioxin (TCDD), sufficient data allows specific recommendations based on organic carbon content of the soil.

Values in Table 3.4 have been determined to be applicable, using the Superfund default human exposure assumptions, and are average absorption values. Other values will be added to this list as results of further research become available. However, as an interim method, dermal exposure to other compounds should be treated qualitatively in the uncertainty section or quantitatively using default values after presenting the relevant studies to the regional risk assessors so that absorption factors can be agreed upon on a site-specific basis before the start of the risk assessment. Particular attention should be given to dermal active compounds, such as benzo(a)pyrene, and they should be addressed fully as to their elevated risk by this route of exposure.

This guidance provides default dermal absorption factors for semivolatile organic compounds (SVOCs) of 10% as a screening method for the majority of SVOCs without dermal absorption factors. This factor is suggested because the experimental values in Table 3.4 are considered representative of the chemical class for screening evaluations. If these are used quantitatively, they represent another uncertainty that should be presented and discussed in the risk assessment. There are no default dermal absorption values presented for volatile organic compounds nor inorganic classes of compounds. The rationale for this is that in the considered soil exposure scenarios, volatile organic compounds would tend to be volatilized from the soil on skin and should be accounted for via inhalation routes in the combined exposure pathway analysis. For inorganics, the speciation of the compound is critical to the dermal penetration, bioavailability and there is too little data to extrapolate a reasonable default value.

Although Equation 3.11 implies that the ABS_d is independent of AF , this independence may

not be the case. Experimental evidence suggests that ABS_d may be a function of AF (Duff and Kissel, 1996 and Yang, 1989). Specifically, ABS_d has been observed to increase as the AF decreases below the quantity of soil necessary to completely cover the skin in a thin layer of soil particles, which is discussed in the *DEA* as the mono-layer concept. This mono-layer will vary according to physical characteristics of the applied soil, e.g., particle size. Most significantly, nearly all experimental determinations of ABS_d have been conducted at loading rates larger than required to completely cover the skin, while the recommended default values for AF for both adult and children are at or less than that required to establish a mono-layer. The absolute effect of soil loading on these parameters is not sufficiently understood to warrant adjustment of the experimentally determined values. Consequently, actual ABS_d could be larger than experimentally determined and the effect of this uncertainty should be appropriately presented in the risk assessment.

Equation 3.11 includes no explicit effect of exposure time which also adds to the uncertainty and consequently assumes exposure time is the same as in the experimental study that measured ABS_d . For values presented, the exposure time per event is 24 hours. Site-specific exposure scenarios should not adjust ABS_d per event but rather adjust the exposure frequency (EF) and exposure duration (ED) to account for site conditions.

A discussion of theoretical models that estimate DA_{event} on the basis of a soil permeability coefficient rather than ABS_d is presented in *DEA* (U.S. EPA, 1992a). The permeability coefficient approach offers some advantages in that the partitioning coefficient from soil should remain constant over a wider range of conditions, such as the amount of soil on the skin and the concentration of the contaminant in the soil. However, as soil partitioning procedures are not well developed, the workgroup recommends that the absorbed fraction per event procedures presented in this guidance be used to assess dermal uptake for soil.

Table 3.4 Recommended Dermal Absorption Fraction from Soil

Compound	Dermal Absorption Fraction (ABS_d)¹	Reference
Arsenic	0.03	Wester, <i>et al.</i> (1993a)
Cadmium	0.001	Wester, <i>et al.</i> (1992a) U.S. EPA (1992a)
Chlordane	0.04	Wester, <i>et al.</i> (1992b)
2,4-Dichlorophenoxyacetic acid	0.05	Wester, <i>et al.</i> (1996)
DDT	0.03	Wester, <i>et al.</i> (1990)
TCDD and other dioxins -if soil organic content is >10%	0.03 0.001	U.S. EPA (1992a)
Lindane	0.04	Duff & Kissel (1996)
Benzo(a)pyrene and other PAHs	0.13	Wester, <i>et al.</i> (1990)
Aroclors 1254/1242 and other PCBs	0.14	Wester, <i>et al.</i> (1993b)
Pentachlorophenol	0.25	Wester, <i>et al.</i> (1993c)
Generic default for screening		
Semivolatile organic compounds	0.1	

¹ The values presented are experimental mean values.

3.2.2.5 Age-adjusted dermal factor

An age-adjusted dermal factor (SFS_{adj}) is used when dermal exposure is expected throughout childhood and into adult years. This accounts for changes in surface area, body weight and adherence factors over an extended period of time. The use of SFS_{adj} incorporates body weight, surface area, exposure duration and adherence factor parameters from the risk equation. To calculate SFS_{adj} , assumptions recommended above for the child (age 0-6 years) and adult (age 7-30 years) were calculated using data from the *EFH* (U.S. EPA, 1997a) and the methodology described for the residential child. The recommended age-adjusted dermal factor is calculated as follows:

$$SFS_{adj} = \frac{(SA_{1-6})(AF_{1-6})(ED_{1-6})}{(BW_{1-6})} + \frac{(SA_{7-31})(AF_{7-31})(ED_{7-31})}{(BW_{7-31})} \quad (3.20)$$

$$SFS_{adj} = \frac{(2800cm^2)(0.2mg/cm^2-event)(6yr)}{(15kg)} + \frac{(5700cm^2)(0.07mg/cm^2-event)(24yr)}{(70kg)}$$

$$SFS_{adj} = 360 \text{ mg-yrs/kg-event}$$

3.2.2.6 Event time, exposure frequency, and duration

This guidance assumes one event per day; that during this event, a percentage of a chemical is absorbed systemically; and that exposure time is the same as in the experimental study that measured ABS_d (i.e. 24 hours), as recommended in Table 3.3. Limited data suggest that absorption of a chemical from soil depends on time. However, information is insufficient to determine whether that absorption is linear, sublinear or supralinear with time. Whether these assumptions would result in an over- or underestimate of exposure and risk is unclear. Site-specific exposure scenarios should not scale the dermal absorption factor of the event time.

The exposure frequency for the RME is referenced from RAGS, Part A (USEPA, 1989) but may be adjusted to reflect site-specific conditions.

The recommended central tendency and RME values for exposure duration are referenced from RAGS PartA (USEPA, 1989), but may be adjusted to reflect site-specific conditions.

Table 3.5 Recommended Dermal Exposure Values for Central Tendency and RME Residential and Industrial Scenarios - Soil Contact

Exposure parameters		Central Tendency		RME Scenario	
		Residential	Industrial	Residential	Industrial
Concentration- C_{soil} (mg/kg)		site-specific values			
Event frequency (events/day)		1	1	1	1
Exposure frequency (days/yr)		site-specific	219	350	250
Exposure duration (yr)		9	9	30	25
Skin surface area (cm ²)	Adult	5,700	3,300	5,700	3,300
	Child	2,800	-	2,800	-
Soil adherence factor (mg/cm ²)	Adult	0.01	0.02	0.07	0.2
	Child	0.06	-	0.2	-
Dermal absorption fraction		chemical-specific values (Table 3.4)			

4. TOXICITY ASSESSMENT

4.1 PRINCIPLES OF ROUTE-TO-ROUTE EXTRAPOLATION

Dermal contact with contaminants can result in direct toxicity at the site of application and/or contribute to systemic toxicity via percutaneous absorption. The issue of direct toxicity is addressed in Section 4.4. Ideally, a route-specific (i.e., dermal) toxicity factor would not only consider portal-of-entry effects (i.e. direct toxicity) but would also provide dosimetry information on the dose-response relationship for systemic effects via percutaneous absorption.

In the absence of dermal toxicity factors, EPA has devised a simplified paradigm for making route-to-route (oral-to-dermal) extrapolations for systemic effects. This process is outlined in Appendix A of the Risk Assessment Guidance for Superfund (U.S. EPA, 1989). Primarily, it accounts for the fact that most oral RfDs and slope factors are expressed as the amount of substance administered per unit time and body weight, whereas exposures estimates for the dermal pathway are expressed as absorbed dose. The process utilizes the dose-response relationship obtained from oral administration studies and makes an adjustment for absorption efficiency to represent the toxicity factor in terms of absorbed dose.

This approach is subject to a number of factors that might compromise the applicability of an oral toxicity factor for dermal exposure assessment. The estimation of oral absorption efficiency, to adjust the toxicity factor from administered to absorbed dose, introduces uncertainty. Part of this uncertainty relates to distinctions between the terms "absorption" and "bioavailability." Typically, the term absorption refers to the "disappearance of chemical from the gastrointestinal lumen," while oral bioavailability is defined as the "rate and amount of chemical that reaches the systemic circulation unchanged." That is, bioavailability accounts for both absorption and pre-systemic metabolism. Although pre-systemic metabolism includes both gut wall and liver metabolism, for the most part it is liver metabolism or liver "first pass effect" that plays the major role.

Technically, toxicity adjustment should be based on bioavailability rather than absorption

because the dermal pathway purports to estimate amount of parent compound entering the systemic circulation. Metabolism in the gut wall and skin can serve to complicate this otherwise simplified adjustment process. Simple adjustment of the oral toxicity factor, based on absorption efficiency, does not account for metabolic by products that might occur in the gut wall but not the skin, or conversely in the skin by not the gut wall.

More importantly the oral administered dose experiences the liver first pass effect. The efficiency of "first pass" metabolism and whether this is an activating or detoxifying process determines the nature of the impact this effect has on route-to-route extrapolations. For example, if a compound was believed to be well-absorbed orally (based on its disappearance from the gastrointestinal tract) and experienced a prominent "first pass" effect that created a highly toxic reactive metabolite, the adjusted dermal toxicity factor would likely overestimate the true dose-response relationship via the dermal pathway because it incorporated a rate and extent of reactive metabolite genesis not likely to be evidenced by direct dermal contact with the chemical in question.

Toxicity is a function of contaminant concentration at critical sites-of-action. Absorption rate, as well as extent, determines contaminant concentration at a site-of-action. Differences in the anatomic barriers of the gastrointestinal tract and the skin can effect rate as well as the extent of absorption; therefore, the route of exposure may have significant dose-rate effects at the site-of-action.

4.2 ADJUSTMENT OF TOXICITY FACTORS

Methodologies for evaluating percutaneous absorption, as described in *DEA*, give rise to an estimation of absorbed dose. However, IRIS verified indices of toxicity (e.g. RfDs, Slope Factors) are typically based on administered dose. Therefore, to characterize risk from the dermal exposure pathway, adjustment of the oral toxicity factor to represent an absorbed rather than administered dose is necessary. This adjustment accounts for the absorption efficiency in the "critical study," which forms the basis of the RfD. For example, in the case where oral absorption in the critical study is essentially complete (i.e., 100%) the absorbed dose is

equivalent to the administered dose, and therefore no toxicity adjustment is necessary. When gastrointestinal absorption of a chemical in the critical study is poor (e.g., 1%) the absorbed dose is much smaller than the administered dose; thus, toxicity factors based on absorbed dose must be adjusted to account for the difference in the absorbed dose relative to the administered dose.

In effect, the magnitude of toxicity factor adjustment is inversely proportional to the absorption fraction in the critical study. That is, when absorption efficiency in the critical study is high, the absorbed dose approaches the administered dose resulting in little difference in a toxicity factor derived from either the absorbed or administered dose. As absorption efficiency in the critical study decreases, the difference between the absorbed dose and administered dose increases. At some point, a toxicity factor based on absorbed rather than administered dose needs to account for this difference in dose. In practice, an adjustment in oral toxicity factor (to account for "absorbed dose" in the dermal exposure pathway) should be made when the following conditions are met: (1) the toxicity value derived from the critical study is based on an administered dose (e.g., delivery in diet or by gavage) in its study design; (2) a scientifically defensible data base demonstrates that the gastrointestinal (GI) absorption of the chemical in question, from a media (e.g., water, feed) similar to the one employed in the critical study, is significantly less than 100% (i.e. <50%). A cutoff of 50% GI absorption is recommended to reflect the intrinsic variability in the analysis of absorption studies. Thus, this cutoff level obviates the need to make comparatively small adjustments in the toxicity value that would otherwise impart on the process a level of accuracy that is not supported by the scientific literature.

If these conditions are not met, a default value of complete (i.e., 100%) oral absorption should be assumed, thereby eliminating the need for oral toxicity-value adjustment. The uncertainty analysis should note that employing the oral absorption default value may result in underestimating risk, the magnitude of which being inversely proportional to the true oral absorption of the chemical in question..

The recommended GI absorption values (ABS_{GI}) for those compounds with chemical-specific dermal absorption factors from soil are presented in Table 4.1. For those organic

chemicals that do not appear on the table, the recommendation is to assume a 100% ABS_{GI} value, based on review of literature, indicating that organic chemicals are generally well absorbed (>50%) across the GI tract. Absorption data for inorganics are also provided in Table 4.1, indicating a wide range of absorption values for inorganics. Therefore, the recommendation is to assume a 100% ABS_{GI} value for inorganics that do not appear in this table. This assumption may contribute to an underestimate of risk for those inorganics that are actually poorly absorbed. The extent of this underestimation is inversely proportional to the actual GI absorption. These criteria are recommended for the adjustment of toxicity values for the assessment of both soil and water contact.

Equations 4.1 indicates that as the ABS_{GI} value decreases, the greater the contribution of the dermal pathway to overall risk relative to the ingestion pathway. Therefore, the ABS_{GI} can greatly influence the comparative importance of the dermal pathway in a risk assessment.

$$\frac{\text{Dermal Risk}}{\text{Ingested Risk}} \propto \frac{1}{ABS_{GI}} \quad (4.1)$$

4.3 CALCULATION OF ABSORBED TOXICITY VALUES

Once the criteria for adjustment has been met and a specific ABS_{GI} value has been identified, a toxicity factor that reflects the absorbed dose can be calculated from the oral toxicity values as follows:

$$SF_{ABS} = \frac{SF_O}{ABS_{GI}} \quad (4.2)$$

$$RfD_{ABS} = RfD_O \times ABS_{GI} \quad (4.3)$$

Where:

RfD_o = oral reference dose (administered)

RfD_{ABS} = absorbed reference dose

SF_o = oral slope factor (administered)

SF_{ABS} = absorbed slope factor

The RfD_{ABS} and SF_{ABS} are then used in the calculation of dermal risk, as described in Section 5.

4.4 DIRECT TOXICITY

The discussion in Section 4.2 on toxicity factor adjustment is based on the evaluation of chronic systemic effects resulting from GI absorption. Section 3 of this document provides a methodology for estimating a systemically absorbed dose secondary to dermal contact with chemicals in water and soil. However, dermal contact with a chemical may also result in direct dermal toxicity, such as allergic contact dermatitis, urticarial reactions, chemical irritation, and skin cancer. EPA recognizes that the dose-response relationship for the port of entry effects in the skin are likely to be independent of any associated systemic toxicity exhibited by a particular chemical. Accordingly, the agency is in the process of developing dermal-specific toxicity factors for the host of chemical contaminants commonly found at hazardous waste sites. However, at this time, chemical specific dermal toxicity factors are not available. Therefore, this dermal risk assessment guidance does not address potential dermal toxicity associated with direct contact. The dermal risk assessment methodology in this guidance may be revised to incorporate additional information on port of entry effects as it becomes available.

Table 4.1 Summary of Gastrointestinal Absorption Efficiencies and Recommendations for Adjustment of Toxicity Factors for Specific Compounds

Compound	GI Absorption				IRIS Critical Toxicity Study			Adjust?
	Ref ¹	Species ²	Dosing Regimen	% Absorbed	Species ²	Dosing Regimen	Toxicity Factor	
Organics								
Chlordane	12,26	R	assume aqueous gavage	80%	M	diet	SF	No
					M	inhalation	RfD	
2,4-Dichlorophenoxyacetic acid (2,4-D)	27	R	assume aqueous gavage	>90%	R	diet	RfD	No
	20							
DDT	19	R	vegetable oil	70-90%	R	dissolved in oil, mixed with diet	RfD	No
Pentachlorophenol	21	R	diet	76%	R	diet	RfD	No
	24	R	water	100%				

8/11/99

DRAFT-DO NOT CITE OR QUOTE

Compound	GI Absorption				IRIS Critical Toxicity Study			Adjust?
	Ref ¹	Species ²	Dosing Regimen	% Absorbed	Species ²	Dosing Regimen	Toxicity Factor	
Polychlorinated biphenyls (PCBs)	2	R	squalene	96%	R	diet	SF	No
	25h	R	emulsion	80%				
	33	R	corn oil	81%				
Polycyclic aromatic hydrocarbons(PAH)	6	R	starch solt'n	58%	M	diet	SF	No
	16	R	diet	89%				
TCDD	14	R	diet	50-60%	under review			No
	28	R	diet	70%				
	30	R	corn oil	70-83%				
Other Dioxins/ Dibenzofurans	3			>50%	under review			No
All other organic compounds	multiple references			generally >50%			RfD or SF	No
Inorganics								
Antimony	35	R	water	15%	R	water	RfD	Yes
Arsenic (arsenite)	5	H	assume aqueous	95%	H	water	SF	No
Barium	8, 34	D	water	7%	H	water	RfD	Yes

8/11/99

DRAFT-DO NOT CITE OR QUOTE

Compound	GI Absorption				IRIS Critical Toxicity Study			Adjust?
	Ref ¹	Species ²	Dosing Regimen	% Absorbed	Species ²	Dosing Regimen	Toxicity Factor	
Beryllium	29	R	water	0.7%	R	water	RfD	Yes
Cadmium	17	H	diet	2.5%	H	diet and water	RfD	Yes
		H	water	5%				Yes
Chromium (III)	10,18	R	diet/water	1.3%	R	diet	RfD	Yes
Chromium (VI)	10,23, 32	R	water	2.5%	R	water	RfD	Yes
Cyanate	13	R	assume aqueous	>47%	R	diet	RfD	No
Manganese	9, 17	H	diet/water	4% ?	H	diet/water	RfD	Yes
	17, 31	H	diet	0.7-10% (6%) ?				
Mercuric chloride (other soluble salts)	17			7%	R	oral gavage in water; 2X/week	RfD	Yes
Insoluble or metallic mercury		H	acute inhalation of Hg vapor	2%	H	Inhalation	RfC	Yes
				<7%				

8/11/99

DRAFT-DO NOT CITE OR QUOTE

Compound	GI Absorption				IRIS Critical Toxicity Study			Adjust?
	Ref ¹	Species ²	Dosing Regimen	% Absorbed	Species ²	Dosing Regimen	Toxicity Factor	
Methyl mercury	1	H	aqueous	95%	H	diet	RfD	No
Nickel	11	H	diet/water	4%	R	diet	RfD	Yes
Selenium	36	H	diet	30-80%	H	diet	RfD	No
Silver	15, 17	D	?	4%	H	i.v. dose	RfD	Yes
Thallium	22	R	?	100%	R	water gavage	RfD	No
Vanadium	7	R	gavage	2.6%	R	diet as V ₂ O ₅	RfD	Yes
Zinc	4			highly variable	H	diet supplement	RfD	No

8/11/99

DRAFT-DO NOT CITE OR QUOTE

¹ Literature references are listed here by first author. Complete citations are provided in Reference Section.

(1) Aberg; (2) Albro, 1972; (3) ATSDR, 1994a; (4) ATSDR, 1994b; (5) Bettley, 1975; (6) Chang, 1943; (7) Conklin, 1982; (8) Cuddihy and Griffith, 1972; (9) Davisson, (Mn); (10) Donaldson and Barreras, 1966; (11) Elakhovskay, 1972; (12) Ewing, 1985; (13) Farooqui and Ahmed, 1982; (14) Fries, 1975; (15) Furchner, 1968; (16) Hecht, 1979; (17) IRIS, 1999; (18) Keim, 1987; (19) Keller, 1980; (20) Knopp, 1992; (21) Korte, 1978; (22) Lie, 1960; (23) MacKenzie, 1959; (24) Meerman, 1983; (25) Muhlebach, 1981; (26) Ohno, 1986; (27) Pelletier, 1989; (28) Piper, 1973; (29) Reeves, 1965; (30) Rose, 1976; (31) Ruoff, 1995; (32) Sayto, 1980; (33) Tanabe, 1981; (34) Taylor, 1962; (35) Waitz, 1965; (36) Young, 1982

² Species abbreviations are as follows: H- human, D- dog, R- rat, M- mice

5. RISK CHARACTERIZATION

5.1 QUANTITATIVE RISK EVALUATION

5.1.1 Risk Calculations

In contrast to calculation of average lifetime dose for the oral and inhalation routes of exposure, which is based on an administered dose, the evaluation of exposure for the dermal route is based on an estimated absorbed dose, or dermal absorbed dose (DAD), as described in Section 3. The DAD term is calculated separately for the cancer and non-cancer endpoints, with age-adjusted child/adult the most sensitive receptor for the cancer risk, and the child as the most sensitive receptor for evaluating the hazard index. As described in Section 4, the oral toxicity values are adjusted according to the estimated extent of gastrointestinal absorption in critical toxicity study. Once the DAD and the adjusted toxicity values have been derived, the cancer risk and hazard index for the dermal route are calculated using the following equations.

$$\text{Dermal cancer risk} = \text{DAD} \times SF_{ABS} \quad (5.1)$$

$$\text{Dermal hazard quotient} = \text{DAD}/RfD_{ABS} \quad (5.2)$$

The steps involved in the dermal risk assessment are summarized in Table 5.1.

Table 5.1 Summary of Dermal Risk Assessment Process

Risk Assessment Process		Cancer Risk		Hazard Index	
Hazard ID		Sec. 2		Sec. 2	
Exposure Assessment	Child or Adult	Water Dose	Soil Dose	Water Dose	Soil Dose
		Sec. 3.1, eq 3.1-3.4	Sec. 3.2, eq. 3.10/3.11	Sec. 3.1, eq. 3.1-3.4	Sec. 3.2, eq. 3.10/3.11
	Age-adjusted Child/Adult		Sec. 3.2.2.5, eq. 3.20		Sec. 3.2.2.5, eq. 3.20
Toxicity Assessment		Sec. 4, SF _{ABS} , eq. 4.2		Sec. 4, RfD _{ABS} , eq. 4.3	
Risk Characterization		Sec. 5.1, eq. 5.1 DAD x SF _{ABS}		Sec. 5.1, eq. 5.2 DAD/RfD _{ABS}	
		Uncertainty Analysis Sec. 5.2			

5.1.2 Risks for all routes of exposure

Endpoints for assessment of risk for the dermal pathway are based on induction of systemic toxicity and carcinogenesis, as they are for the oral and the inhalation routes of exposure. Therefore, the estimate of total risk for exposure to either soil or water contaminants is based on the summation of individual risks for the oral, the inhalation, and the dermal routes.

5.2 UNCERTAINTY ASSESSMENT

The importance of adequately characterizing uncertainty in the risk assessment is emphasized in several U.S. EPA documents (EPA, 1992b; EPA, 1995; EPA, 1997a; EPA, 1997b). EPA's 1995 Policy for Risk Characterization calls for greater clarity, transparency, reasonableness and consistency in Agency risk assessments. To ensure transparency and clarity, the workgroup recommends that an assessment of the confidence, uncertainties, and influence of these uncertainties on the outcome of the risk assessment be presented.

Several sources of uncertainty exist in the recommended approach for estimating exposure and risks from dermal contact with water and soil. Many of these uncertainties are identified in the *DEA*, Chapter 10. Exposure parameters with highly variable distributions are likely to have a greater impact on the outcome of the risk assessment than those with lower variability. Which exposure parameters will vary the most will depend on the receptor, (i.e. residential adult, commercial adult, adolescent trespasser) and chemical evaluated. For the dermal-soil pathway, the adherence factor and the value used to represent the concentration in soil are likely to be sensitive variables regardless of the receptor. For the dermal-water pathway, the K_p and the value used to represent the concentration in water are likely to be sensitive variables.

A detailed analysis of the uncertainty associated with every exposure model and exposure variable presented in this guidance is not possible due to insufficient data. The SDG recommends that a qualitative evaluation of key exposure variables and models, and their impact on the outcome of the assessment, be conducted when the database does not support a quantitative uncertainty analysis. Below is a discussion of key uncertainty issues associated with the recommended approach for dermal risk assessments in this guidance.

5.2.1 Hazard Identification

Uncertainty is associated with the assumption that the only chemicals of concern in the risk assessment for the dermal-water pathway are those which contribute 10% or more of the dose that is achieved through the drinking water pathway. Although this is a reasonable assumption for exposure assessments in which the drinking water pathway is evaluated, this may result in a slight underestimate of the overall exposure and risk. In addition, the selection of chemicals of concern for the dermal-soil pathway is limited by the availability of dermal absorption values for soil. If soil dermal absorption values are not available, a chemical may be dropped out of the quantitative evaluation of risk, which could potentially result in an underestimate of risk. The recommended default screening value of 10% for semivolatile organic chemicals should limit the degree of underestimation associated with this step of the dermal risk assessment approach.

5.2.2 Exposure Assessment

5.2.2.1 Dermal exposure to water -Uncertainties associated with the model for DA_{event}

When evaluating uncertainties, it is important to keep in mind that the model used to estimate exposure can contribute significantly to uncertainty. Uncertainty in model predictions arise from a number of sources, including specification of the problem, formulation of the conceptual model, interpretation, and documentation of the results. Although some attempts have been made to validate the model for DA_{event} utilized in this document, a greater effort and more formal process will be necessary before a more accurate assessment of the sources of uncertainty associated with the model can occur. A detailed discussion of the model for DA_{event}, its validation and remaining uncertainties is presented in Appendices A.1.2 and A.4.

◆ **Concentration in water (C_w)**

The value used for C_w in the equation for DA_{event} is dependent on two factors: (1) how the overall exposure point concentration (EPC) is estimated (i.e., as a 95% upper confidence limit of the mean [95%UCL], a maximum concentration, etc.); and (2) the ionization state of the chemical present in water. The Superfund program advocates the use of the 95%UCL in estimating exposure to contaminants in environmental media. This policy is based on the assumption that individuals are randomly exposed to chemicals in soil, water, sediment, etc., in a given exposure area and that the arithmetic mean best represents this exposure. To develop a conservative estimate of the mean, a 95% UCL is adopted. However, when data are insufficient to estimate the 95%UCL, any value used for C_w (whether it be a 95%UCL, maximum value or arithmetic mean) is likely to contribute significantly to the uncertainty in estimates of the DA_{event} . The degree to which the value chosen for the EPC contributes to an over- or under-estimate of exposure depends on the representativeness of existing data and the estimator used to represent the EPC.

The bioavailability of a chemical in water is dependent on the ionization state of that chemical, with the nonionized forms more readily available than the ionized forms. To be most accurate in estimating the dermally absorbed dose, the DA_{event} should be equal to the sum of the DA_{event} values for the nonionized and ionized species (see Section 3.1.2.2). For most Superfund risk assessments, however, the DA_{event} is most likely to be based on a C_w which is derived directly from a laboratory report. The value presented in a laboratory report represents the total concentration of ionized and nonionized species and thus does not provide the information necessary to calculate separate DA_{event} values for ionized and nonionized groups. A slight overestimate of exposure for organic chemicals of low molecular weight is likely to occur if the equations presented in Section 3.1.2.2 are not utilized.

In addition, since the concentration of some compounds in water decreases greatly during showering, the impact of volatilization should be considered when estimating C_w for the dermal-

water pathway. The exposure analysis for the inhalation pathway should account for compounds which volatilize.

◆ Exposure Time

The recommended default assumptions for exposure time are 15 minutes for the central tendency scenario and 35 minutes for the RME scenario. This is consistent with the recommended 50th and 95th percentiles for showering presented in EPA's Exposure Factor Handbook (U.S. EPA, 1997a). If a showering/bathing scenario exceeded 35 minutes (the recommended central tendency and RME exposure parameters for bathing time are 20 and 60 minutes, respectively), the default assumption for exposure time might result in a slight underestimate of risk. The degree of underestimation is dependent on the actual showering time.

◆ Permeability coefficients (K_p)

Permeability coefficients have been identified as major parameters contributing uncertainty to the assessment of dermal exposure to contaminants in aqueous media (DEA, page 10.5). Measuring or predicting K_p is fairly uncertain for most compounds, especially those with high and low K_{ow} and MW, and for those chemicals which are partially or completely ionized. Predicted K_p s are highly dependent on their associated K_{ow} value. The accuracy and design of experiments conducted to measure K_{ow} vary considerably from experiment to experiment, so that all K_{ow} s are not of equal value. The same is true for experiments designed to measure K_p . Several design elements, such as the data analysis method, species utilized, *in vivo* or *in vitro* method applied, temperature, duration, occlusion or not, etc., influence the resulting K_p . Since the variability between the predicted and measured K_p values is no greater than the variability in interlaboratory replicated measurements, this guidance recommends the use of predicted K_p s. This approach will ensure consistency between Agency risk assessments in estimating the dermally absorbed dose from water exposures. It is important to keep in mind, however, that the Flynn database upon which predicted K_p s are derived contains mostly smaller hydrocarbons and pharmaceutical drugs which bear little resemblance to the typical compounds detected at

Superfund sites. This could introduce further uncertainty in the use of estimated K_p s in the assessment of exposure and risk from the dermal-water pathway.

5.2.2.2 Dermal Exposure to Soil

◆ Concentration in Soil (C_{soil})

The Superfund program advocates the use of the 95%UCL in estimating exposure to contaminants in environmental media. This policy is based on the assumption that individuals are randomly exposed to chemicals in soil, water, sediment, etc., in a given exposure area and that the arithmetic mean best represents this exposure. To develop a conservative estimate of the mean, a 95% UCL is adopted. However, when there is insufficient data to estimate the 95%UCL, any value used for C_{soil} (whether it be a 95%UCL, maximum value or arithmetic mean) is likely to contribute significantly to the uncertainty in estimates of the DA_{event} . The degree to which the value chosen for the EPC contributes to an over- or under-estimate of the exposure is dependent on the representativeness of the existing data and the estimator used to represent the EPC.

◆ Event time (EV)

In order to be consistent with assumptions about absorption, the equation for DAD presented in this guidance assumes (by default) that the event time is 24 hours, (i.e. that no washing occurs and the soil remains on the skin for 24 hours). This assumption probably overestimates the actual exposure time for most site-specific exposure scenarios and is likely to result in an overestimate of exposure. The degree to which exposure could be overestimated is difficult to determine without information on absorption rates for each chemical.

◆ Surface area and frequency of exposure

Default adherence values recommended in this guidance are weighted by the surface area exposed and are based on the assumption that adults will be wearing short sleeved shirts, shorts and shoes and that a child will be wearing a short-sleeved shirt, shorts and no shoes. This may not match the year-round exposure scenario assumed to exist at every site. For instance, there is a four-fold difference between the surface area exposed for a residential adult based on the default assumption of clothing worn versus an assumption that an adult is wearing a long-sleeved shirt, and long pants. There is also a four-fold difference between the surface area exposed of a residential child based on the default assumption of clothing worn versus an assumption that a child is wearing a long-sleeved shirt, long pants, shoes and socks. The value chosen for surface area can introduce a moderate degree of uncertainty into exposure and risk estimates. Risk assessors may need to adjust defaults depending upon site conditions such as climate and activity patterns.

The value chosen for frequency can also introduce moderate amounts of uncertainty into exposure and risk assessment estimates. For instance, it is assumed that a resident comes into contact with residential soils 350days/yr. If the actual frequency is significantly less (for instance one day per week, equivalent to 52 days/yr), a seven-fold difference occurs, which directly impacts exposure and risk estimates.

◆ Adherence factors

Although the SDG provides dermal adherence factors for several different types of receptors, the conditions at a particular site may not match the conditions in the study upon which the default dermal adherence factor is based, (i.e. specific activity, clothing worn, soil type, soil moisture content, exposure duration, etc). For example, Kissel, *et al.* (1996), has found that finer particles adhere preferentially to the hands unless soils are greater than 10% moisture. Some studies have found that soil particles greater than 250 microns do not adhere readily to skin. Thus the soil type, including moisture content, can affect the adherence of soil. In addition, the specific

activity which occurs in the site-specific exposure scenario may not directly match the activities for which adherence factors are available in this guidance. All of these factors can introduce significant uncertainties into the exposure assessment. Each of these factors should be carefully evaluated in each risk assessment conducted for the dermal pathway.

◆ **Dermal-soil absorption factors**

The amount of chemical absorbed from soil is dependent on a number of chemical, physical and biological factors of both the soil and the receptor. Examples of factors in soil which can influence the amount of chemical that is available to be absorbed include; soil type, organic carbon content, cation exchange capacity, particle size, temperature, pH, etc. For example, increasing particle size has been found to correspond with decreased absorption across the skin for some chemicals. Chemical factors which can affect absorption include lipid solubility, chemical speciation, aging of the chemical, etc. Physical factors which can impact absorption include soil loading rate, surface area exposed to soil, soil contact time and soil adherence. For example, absorption from soil is dependent on the soil loading. In general as the soil loading decreases the total absorption increases, until one gets below some critical level at which the skin surface is not uniformly covered by soil (i.e. the monolayer). Since nearly all existing experimental determinations of absorption have been conducted above the monolayer, the actual absorption could be larger than experimentally determined. At uniform loadings less than or equal to the monolayer, absorption should be constant. Biological factors which can affect absorption include diffusivity of skin, skin blood flow, age of the receptor, etc. The exact relationship of all of these factors to dermal absorption is not known thus there is uncertainty in the default dermal absorption factors. This discussion should be presented in the risk assessment but until more is understood quantitatively about this effect, adjustment of the dermal-soil absorptions factors is not warranted.

◆ **Default Dermal Absorption Values for Semivolatile Organic Chemicals**

This guidance identifies a default dermal absorption value of 10% for semivolatile organic compounds as a class. This suggested value is based on the assumption that the observed experimental values presented in Table 3.4 are representative of all semivolatile organic compounds for which measured dermal-soil absorption values do not exist. Chemicals within classes vary widely in structure and chemical properties. The use of default dermal absorption values based on chemical class can introduce uncertainties into the risk assessment which can either over- or under-estimate the risk.

◆ **Lack of dermal-soil absorption values**

The ability to quantify the absorption of contaminants from exposure to soil is limited. Chemical-specific information is available for only a few chemicals. For most chemicals, no data are available, so dermal exposures have not been quantified. This lack of data results in the potential underestimation of total exposure and risk. The degree of the underestimation is dependent on the chemical being evaluated.

5.2.3 Toxicity Assessment

◆ **Oral reference doses and slope factors for dermal exposures**

Quantitative toxicity estimates for dermal exposures have not been developed by EPA. Therefore, oral reference doses and oral cancer potency factors are used to assess systemic toxicity from dermal exposures. The dermal route of exposure can result in different patterns of distribution, metabolism, and excretion than occur from the oral route. When oral toxicity values for systemic effects are applied to dermal exposures, uncertainty in the risk assessment is introduced because these differences are not taken into account. Since any differences between oral and dermal pathways would depend on the specific chemical, use of oral toxicity factors can

result in the over- or underestimation of risk, depending on the chemical. It is not possible to make a general statement about the direction or magnitude of this uncertainty.

♦ **Lack of a dermal slope factor for PAHs and other chemicals**

This guidance focuses on the expected systemic effects of dermal exposure from chemicals in soil and water. EPA does not have recommended toxicity values for the adverse effects that can occur at the skin surface. This lack of dermal toxicity values is considered to be a significant gap in the evaluation of the dermal pathway, particularly for carcinogenic PAHs. The statement in RAGS claiming that "it is inappropriate to use the oral slope factor to evaluate the risks associated with exposure to carcinogens such as benzo(a)pyrene, which causes skin cancer through direct action at the point of application" should not be interpreted to mean that the systemic effects from exposure to dermally active chemicals should not be evaluated. In fact, there is a significant body of evidence in the literature to generate a dose-response relationship for the carcinogenic effects of PAHs on the skin. In addition, PAHs have also been shown to induce systemic toxicity and tumors at distant organs. For these reasons, the lack of dermal toxicity values may significantly underestimate the risk to exposure to PAHs and potentially other compounds in soil. Until dermal dose-response factors are developed, EPA recommends that a quantitative evaluation be conducted for systemic effect of PAHs and other compounds and that a qualitative evaluation be conducted for the carcinogenic effects of PAHs and other compounds on the skin.

5.2.4 Risk Characterization

♦ **Lack of information for GI absorption**

One issue which arises in regards to the dermal-soil risk assessment approach presented in this guidance is how would the route comparison (i.e. oral to dermal) change if the GI tract absorption fraction were much less than the assumed 100%. As discussed in Chapter 10 of the *DEA*, cancer slope factors are intended to be used with administered dose. Since dermal doses

are absorbed, it is necessary to convert the SF to an absorbed basis which can be done in an approximate way by dividing it by the GI tract absorption fraction. When ABS_{GI} is high, adjustment of the SF to an absorbed dose is not as important and the earlier conclusions for when the dermal dose exceeds the ingested dose do not change. However, when ABS_{GI} is low the adjustment of the SF to an absorbed dose can substantially increase the importance of the dermal route relative to the ingestion route and it is important to consider. In the absence of information on gastrointestinal absorption, the risk characterization for the dermal pathway has used unadjusted reference doses and slope factors. This may result in underestimation of risk for dermal exposures to both soil and water.

Table 5.2 Summary of Uncertainties Associated with Dermal Exposure Assessment

Exposure Factor	High	Medium	Low
COPC selection for dermal-water pathway			X
C_w - exposure point concentration	site-specific, data-dependent		
C_w - ionization state			X
Exposure Time for showering (t_{event})			X
K_p	X		
C_s - exposure point concentration	site-specific, data-dependent		
Event time for dermal-soil pathway		X	
Surface area (SA) - dermal-soil pathway		X	
Exposure frequency (EF)		X	
Adherence Factor (AF)	X		
Default dermal-soil absorption values and lack of absorption values for other compounds (ABS_d)		X	
Lack of dermal slope factor for cPAHs and other compounds	X		

Lack of info on GI absorption (ABS_{GI})		X	
--	--	---	--

Above are general statements about the uncertainty associated with each parameter. The actual degree of uncertainty is dependent on the specific chemical, exposure pathway or statistic utilized.

6. CONCLUSIONS/RECOMMENDATIONS

6.1 Summary Conclusions

The following summary presents the major points made in each section of this guidance;

Hazard Identification

- For the dermal-water pathway, only those chemicals which contribute to more than 10% of the oral (drinking water) pathway are considered important to carry through the risk assessment.
- For the dermal-soil pathway, the limited availability of dermal absorption values is expected to result in a limited number of contaminants to carry through the risk assessment.

Exposure Assessment

- Since K_p has been identified as one of the major parameters contributing to uncertainty in the assessment of dermal exposures to contaminants in aqueous media, it is important that regions be consistent when estimating this parameter. Since the variability between the predicted and measured K_p s are no greater than the variability in interlaboratory replicated measurements, this guidance recommends the use of estimated K_p s based on the equations in Section 3. This approach facilitates the ease of evaluating the dermal-water pathway for regional risk assessors and maintains consistency in parameters used for K_p from region to region. The risk assessor should be able to choose the K_p directly from Appendices A and B.
- This guidance presents recommended default exposure values for all variables for the dermal-water and dermal-soil pathways in Tables 3.2 and 3.5, respectively.

- For dermal-water exposures, the entire skin surface area is assumed to be available for exposure when bathing and swimming occurs. The assessor should note that a wading scenario may result in lesser surface area exposed. For dermal-soil exposures, clothing is expected to limit the extent of exposed surface area. For the adult resident, the total default surface area includes the head, hands, forearms and lower legs. For a residential child the default surface includes the head, hands, forearms, lower legs and feet. For an adult commercial/industrial worker the total default surface area includes the head, hands and forearms.
- The default AF for adult residential activities ($0.07\text{mg}/\text{cm}^2$) is based on the central tendency AF values for a high-end soil contact activity (e.g. a gardener). The default adherence factor for a child resident ($0.02\text{mg}/\text{cm}^2$) is based on both the high end AF of a central tendency soil contact scenario (i.e. children playing in dry soil); and the central tendency AF of a high-end soil contact scenario (i.e. children playing in wet soil). The default AF for a commercial/industrial adult worker ($0.2\text{mg}/\text{cm}^2$) is based on the central tendency AF for a high-end soil contact activity (i.e. utility worker).
- Dermal-soil absorption values for ten compounds are provided in this guidance. Screening absorption values are provided for semi-volatile organic compounds as a class. As new information on dermal absorption from soil becomes available, this guidance will be updated.

Toxicity Assessment

- Before estimating risk from dermal exposures, the toxicity factor must be adjusted so that it is based on an absorbed dose. Adjustments of the toxicity factor are only necessary when the GI absorption of a chemical from a media similar to the one employee in the critical study is significantly less than 100%, (i.e. 50%). Recommended GI absorption values are presented in Table 4.1.

6.2 General guidelines for evaluating Dose from dermal contact

- For most contaminants, dermal contact with water during bathing or swimming will generally pose less of a threat than direct consumption of the water. The fastest penetrating contaminants (i.e., high K_p values) may pose hazards similar to or greater than direct consumption. Although these chemicals may not increase the total risk substantially, they may significantly impact the cost of remedial action. This would occur in a situation where the water was considered unsafe to drink and the remedial action plan called for replacement of drinking water only, which could be accomplished via use of bottled water. If some of these chemicals pose an equal risk via contact during bathing, it would be equally important to replace the water used for bathing and showering. For practical purposes, this suggests that replacing the entire household water supply would be necessary. It has not been well established how many of the environmental contaminants may have K_p values in this upper range, but it appears to be a minority.
- It appears that more soil is dermally contacted than is ingested during normal exposure scenarios. Dermal absorption from soils appears to be more significant than direct ingestion for those chemicals which have a percent absorbed exceeding about 10%.
- Current studies suggest that dermal exposure may be expected to contribute no more than 10% to the total body burden of those compounds present in the vapor phase. An exception may be workers wearing respiratory protection but not chemical protective clothing.
- Any compounds that are acutely toxic to the skin are important to consider even if less exposure occurs by skin contact than other routes.

7. REFERENCES

- Aberg, B., Ekman, L., Falk, R., Greitx, U., Persson, G., and Snihs, J. (1969) Metabolism of methyl mercury (^{203}Hg) compounds in man. *Arch Environ. Health* 19:453-484.
- Albro, P.W. and Fishbein L. (1972) Intestinal absorption of polychlorinated biphenyls in rats. *Bull. Environ. Contam. Toxicology* 8:26-31.
- Agency for Toxic Substances and Disease Registry (1994a) Toxicological Profile for Chlorodibenzofurans. US Dept. Health Human Services, Public Health Service.
- Agency for Toxic Substances and Disease Registry (1994b) Toxicological Profile for Zinc. US Dept. Health Human Services, Public Health Service.
- Bettley, F.R. and O'Shea, J.A. (1975) The absorption of arsenic and its relation to carcinoma. *Brit. J. Dermatol.* 92:563-568.
- Bunge, A.L. and Cleek, R.L. (1995) A new method for estimating dermal absorption from chemical exposure: 2. Effect of molecular weight and octanol-water partitioning. *Pharm. Res.* 12:88-95.
- Bunge, A. L. and McDougal, J. N. (1998, in press) Dermal Uptake. Ch. 6. Exposure to Contaminants in Drinking Water: Estimating Uptake through the Skin and by Inhalation. S. Olin. Boca Raton, FL, CRC Press.
- Chang LH. (1943) The fecal excretion of polycyclic hydrocarbons following their administration to the rat. *J. Biochemistry* 151:93-99.
- Cleek, R.L. and Bunge, A.L. (1993) A new method for estimating dermal absorption from

chemical exposure. 1. General approach. *Pharm. Res.* 10: 497-506.

Conklin, A.W., Skinner, S.C., Felten, T.L., and Sanders, C.L. 1982. Clearance and distribution of intratracheally instilled vanadium compounds in the rat. *Toxicol. Lett.* 11:199-203.

Cuddihy, R.G. and Griffith, W.C. (1972) A biological model describing tissue distribution and whole-body retention of barium and lanthanum in beagle dogs after inhalation and gavage. *Health Phys.* 23:621-633.

Davidsson, L., A. Cederblad, Lonnerdal, B. and Sandstrom, B. (1989) Manganese retention in man: A method for estimating manganese absorption in man. *Am. J. Clin. Nutr.* 49: 170-179.

Donaldson, R.M. and Barreras, R.F. (1996) Intestinal absorption of trace quantities of chromium. *J. Lab. Clin. Med.* 68:484-493.

Dowdy, D.; McKone, T.E.; and Hsieh, D.P.H. (1996) The Use of the Molecular Connectivity Index for Estimating Biotransfer Factors. *Environmental Science and Technology* 30, 984-989.

Duff, R.M. and Kissel, J.C. (1996) Effect of soil loading on dermal absorption efficiency from contaminated soils. *J. Tox. and Environ. Health* 48:93-106.

Elakhovskaya, N.P. (1972) The metabolism of nickel entering the organism with water. (Russian translation) *Gig Sanit* 6:20-22.

Ewing, A.D.; Kadry, A.M.; and Dorrough, H.W. (1985) Comparative disposition and elimination of chlordane in rats and mice. *Toxicol. Lett.* 26:233-239.

Farooqui, M.Y.H and Ahmed, A.E. (1982) Molecular interaction of acrylonitrile and potassium cyanide with rat blood. *Chem. Biol. Interact.* 38:145-159.

Flynn, G. L. (1990) Physicochemical determinates of skin absorption. In T. R. Gerrity and C. J. Henry (eds.), *Principles of Route-to-Route Extrapolation for Risk Assessment*, Elsevier, New York p. 93-127.

Fries, G.S. and Marrow, G.F. (1975) Retention and excretion of 2,3,4,8 tetrachlorodibenzo-p-dioxin by rats. *J. Agric. Food Chem.* 23:265-269.

Furchner JE, Richmond CR, Drake GA. (1968) Comparative metabolism of radionuclides in mammals-IV. Retention of silver-110m in the mouse, rat, monkey, and dog.. *Health Phys.* 6:505-14.

Hecht, S.S.; Grabowski, W.; Groth, K. (1979) Analysis of faeces for benzo[a]pyrene after consumption of charcoal-broiled beef by rats and humans. *Cosmet. Toxicology* 17:223-227.

Holmes, K.K. Jr.; Shirai, J.H.; Richter, K.Y.; Kissel, J. C. (1999) Field measurement of dermal soil loadings in occupational and recreational activities. *Environmental Research* (in press).

Hostynek, J.J.; Hinz, R.S.; Lorence, C.R; and Guy, R.H. (1999) Human Skin Penetration by Metal Compounds", in: *Dermal Absorption and Toxicity Assessment*, M.S. Roberts and K.A. Walters, Editors, Marcel Dekker, Inc., New York (in press).

IRIS-Integrated Risk Information System. (1999) U.S.EPA.

Jo, W.K.; Weisel, C.P.; and Liroy, P.J. (1990) Chloroform Exposure and Body Burden from Showering with Chlorinated Tap Water. *Risk Analysis* 10, 575-580.

Kasting, G. B. and Robinson, P. J. (1993) Can We Assign an Upper Limit to Skin Permeability? *Pharm. Res* 10: 930-93.

Keller, W. and Yeary, R. (1980) A comparison of the effects of mineral oil, vegetable oil, and

sodium sulfate on the intestinal absorption of DDT in rodents. *Clin. Toxicol.* 16:223-231.

Keim, K.S.; Holloway, C.L.; Hebsted, M. (1987) Absorption of Chromium as Affected by Wheat Bran. *Cereal Chem.* 64: 352-355.

Kissel, J.; Richter, K.Y.; and Fenske, R.A. (1996) Field Measurement of Dermal Soil Loading Attributed to Various Activities: Implications for Exposure Assessment. *Risk Analysis* 16:115-125.

Kissel, J.; Shirai, J.H.; Richter, K.Y.; and Fenske, R.A. (1998) Investigation of Dermal Contact with Soil Using a Fluorescent Marker. *J. Soil Contamination* 7:737-753.

Korte, F. (1978) Ecotoxicologic profile analysis. *Chemosphere* 1:79-102.

Knopp, D. and Schiller, F. (1992) Oral and dermal application of 2,4-dichlorophenoxyacetic acid sodium and dimethylamine salts to male rats: investigations on absorption and excretion as well as induction of hepatic mixed-function oxidase activities. *Arch Toxicol.* 66:170-174.

Leahy, D. E. (1990) Use of QSAR's to predict percutaneous absorption. In R. C. Scott, R.H. Guy and J. Hadgraft (eds.), *Prediction of Percutaneous Penetration*, IBC Technical Services Ltd, London, p.242-251.

Lepow, M.L.; Bruckman, L.; Gillette, M.; Markowitz, S.; Robino, R.; Kapish, J. (1975) Investigations into sources of lead in the environment of urban children. *Environ. Res.* 10:415-426.

Lie, R.; Thomas, R.G.; and Scot, J.K. (1960) The distribution and excretion of thallium²⁰⁴ in the rat suggested MPCs and a bioassay procedure. *Health Phys.* 2: 334-340.

Mackenzie, R.D.; Anwar, R.A.; Byerrum, R.U.; and Hoppert, C.A. (1959) Absorption and

Distribution of Cr⁵¹ in the Albino Rat. *Arch. Biochem. Biophys.* 79:200-205.

Maddy, K.T.; Wang, R.G.; Winter, C.K. (1983) Dermal Exposure Monitoring of Mixers, Loaders and Applicators of Pesticides in California. Workers Health and Safety Unit, Report HS-1069. California Department of Food and Agriculture, Sacramento, California.

Mandel, J. (1982) Use of the Singular Value Decomposition in Regression Analysis. *The American Statistician*, 36:15-24.

Mandel, J. (1985) The Regression Analysis of Collinear Data. *Journal of Research of the National Bureau of Standards*, 90(6):465-478.

McKone, T.E. and Howd, R.A. (1992) Estimating Dermal Uptake of Nonionic Organic Chemicals from Water and Soil: Part 1, Unified Fugacity-Based Models for Risk Assessments. *Risk Analysis*, 12, 543- 557.

McKone, T.E. (1993) Linking a PBPK Model for Chloroform with Measured Breath Concentrations in Showers: Implications for Dermal Exposure Models. *Journal of Exposure Analysis and Environmental Epidemiology* 3, 339-365.

Meerman JH., *et al.* (199) Use of pentachlorophenol as long-term inhibitor of sulfation of phenols and hydrooximic acids in the rat in vivo. *Biochem. Pharmacol.* 32:1587-1593.

Muhlebach, S. (1981) Pharmacokinetics in rats of 2,4,5,2,4,5 hexachlorobiphenyl and unmetabolizable lipophilic model compounds. *Xenobiotica* 11:249-257.

Ohno, Y.; Kawanishi, T.; Takahashi, A. (1986) Comparisons of the toxicokinetic parameters in rats determined for low and high dose gamma-chlordane. *J. Toxicol. Sci.* 11:111-124.

Pelletier, O.; Ritter, L.; and Somers, C.J. (1989) Disposition of 2,4-dichlorophenoxyacetic acid

dimethylamine by Fischer 344 rats dosed orally and dermally. *J Toxicol Environ Health*. 28: 221-234.

Piper, W.N. (1973) Excretion and tissue distribution of 2,3,7,8 tetrachlorodibenzo -p-dioxin in the rat. *Environ. Health Perspect.* 5:241-244.

Pirot, F.; Kalia, Y.N.; Stinchcomb, A.L.; Keating, G.; and others (1997) Characterization of the permeability barrier of human skin in vivo. *Proc. Natl. Acad. Sci., USA* 94:1562-1567.

Potts, R. O. and Guy, R. H. (1992) Predicting skin permeability. *Pharm. Res.* 9:663-669.

Reeves, A.L. (1965) The absorption of beryllium from the gastrointestinal tract. *Arch Environ. Health* 11:209-214.

Roels, HA; Buchet, J-P; Lauwerys, R.R.; Bruaux, P.; Claeys-Thoreau, F.; Lafontaine, A.; Verduyn, G. (1980) Exposure to lead by the oral and the pulmonary routes of children living in the vicinity of a primary lead smelter. *Environ. Res.* 22:81-94.

Rose RQ., *et al.* (1976) The fate of 2,3,7,8 tetrachlorodibenzo-p-dioxin following single and repeated oral doses to the rat. *Toxicol. Appl. Pharmacol.* 36:209-226.

Ruoff, W. (1995) Relative bioavailability of manganese ingested in food or water, In Proceedings Workshop on the Bioavailability and Oral Toxicity of Manganese. USEPA-ECAO, Cincinnati, OH.

Sayato, Y.; Nakamuro, K.; Matsui, S.; Ando, M. (1980) Metabolic Fate of Chromium Compounds. I. Comparative Behavior of Chromium in Rat Administered with Na₂ ⁵¹CrO₄ and ⁵¹CrCl₃. *J. Pharm. Dyn.* 3: 17-23.

Tanabe, S. (1981) Absorption efficiencies and biological half-life of individuals chlorobiphenyls

in rats treated with Kanechlor products. *Agric. Biol. Chem.* 45:717-726.

Taylor, D.M.; Bligh, P.H.; and Duggan, M.H. (1962) The absorption of calcium, strontium, barium, and radium from the gastrointestinal tract of the rat. *Biochem. J.* 83:25-29.

U.S. EPA. (1989) *Risk Assessment Guidance for Superfund, Volume I, Human Health Evaluation Manual (Part A)*. Interim Final EPA/540/1-89/002. Washington, DC.

U.S. EPA (1992a) *Dermal Exposure Assessment: Principles and Applications*. Office of Health and Environmental Assessment. EPA/600/6-88/005Cc.

U.S. EPA. (1992b) *Memorandum: Guidance on Risk Characterization for Risk Managers and Risk Assessors*. From F. Henry Habicht II, Deputy Administrator, USEPA, Washington, DC.

U.S. EPA. (1995) Policy for Risk Characterization. From Carol Browner, Administrator, USEPA, Washington, DC.

U.S. EPA. (1997a) Exposure Factors Handbook, EPA/600/P-95/002F.

U.S. EPA. (1997b) Policy for Use of Probabilistic Analysis in Risk Assessment. From Fred Hansen, Deputy Administrator, Washington, DC.

Vecchia, B.E. (1997) Estimating the dermally absorbed dose from chemical exposure: Data analysis, parameter estimation, and sensitivity to parameter uncertainties. M.S. Thesis, Colorado School of Mines, Golden, Colorado.

Waitz, J.A.; Ober, R.E.; Meisenhelder, J.E.; and Thompson, P.E. (1965) *WHO Bull.* 33:357-546.

Wester, R.C.; Melendres, J.; Logan, F.; Hui, X. ; Maibach, H.I. (1996) Percutaneous absorption of 2,4-dichlorophenoxyacetic acid from soil with respect to the soil load and skin contact time: in vivo absorption in Rhesus monkey and in vitro absorption in human skin. *J. Toxicol. Environ. Health* 47:335-44.

Wester, R.C.; Maibach, H.I.; Sedik, L.; Melendres, J. ;Wade, M. (1993a) In vivo and in vitro percutaneous absorption and skin decontamination of arsenic from water and soil. *Fund. Appl. Toxicol.* 20:336-40.

Wester, R.C.; Maibach, H.I.; Sedik, L.; Melendres, J.; Wade, M. (1993b) Percutaneous absorption of PCBs from soil: in vivo Rhesus monkey, in vitro human skin, and binding to powered human stratum corneum. *J. Toxicol. Environ. Health* 39:375-82.

Wester, R.C.; Maibach, H.I.; Sedik, L.; Melendres, J.; Wade, M. ; DeZio, S. (1993c) Percutaneous absorption of pentachlorophenol from soil. *Fund. Appl. Toxicology* 20: 68-71.

Wester, R.C.; Maibach, H.I.; Sedik, L.; Melendres, J. ; DeZio, S. ; Wade, M. (1992a) In vitro percutaneous absorption of cadmium from water and soil into human skin. *Fund. Appl. Toxicol.* 19:1-5.

Wester, R.C.; Maibach, H.I.; Sedik, L.; Melendres, J.; Laio, C.L.; DeZio, S. (1992b) Percutaneous absorption of [¹⁴C]chlordane from soil. *J. Toxicol. Environ. Health* 35:269-77.

Wester, R.C.; Maibach, H.I.; Bucks, D.A.W.; Sedik, L.; Melendres, J.; Laio, C.L.; DeZio, S.

(1990) Percutaneous absorption of [14C]DDT and [14C]benzo(a)pyrene from soil. *Fund. Appl. Toxicol.* 15:510-516.

Wilschut, A.; ten Berge, W.F.; Robinson, P.J.; and McKone, T.E. (1995) Estimating Skin Permeation—The Validation of Five Mathematical Skin Permeation Models. *Chemosphere* 30, 1275-1296.

Yang, J.J.; Roy, T.A.; Krueger, A.J.; Neil, W.; Mackerer, C.R. (1989) In vitro and in vivo percutaneous absorption of benzo[a]pyrene from petroleum crude-fortified soil in the rat. *Bull. Environ. Toxicol.* 43:207-214.

Young, V.R.; Naharetian, A.; Janghorbani, M. (1982) Selenium bioavailability with reference to human nutrition. *Am. J. Clin. Nutr.* 35: 1076-1088.

8/11/99

7-10

DRAFT-DO NOT CITE OR QUOTE

11.1989